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### Physicochemical Characterization of Hydrated 4-Sulphonato-Calix[n]arenes: Thermal, Structural, and Sorption Properties

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# Physicochemical Characterization of Hydrated 4-Sulphonato-Calix[*n*]arenes: Thermal, Structural, and Sorption Properties

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In this study, the thermal behavior of three hydrated water-soluble 4-sulphonato calix[*n*]arenes was investigated. The melting points, heats of fusion, and heats of solution of the calix[4]arene, calix[6]arene and calix[8]arene were 277, 262, and 270°C; 192, 242 and 351 kJ/mol; and 30, 58 and 63 kJ/mol, respectively. Lower heat of fusion, smaller increase in entropy and smaller heat of solution of the calix[4]arene compared to the calix[6]arene and calix[8]arene showed that less heat was required to break up the crystal lattice of the smaller macromolecule. This apparent anomaly is rationalized in terms of smaller cooperativity of interaction between the molecules of calix[4]arene in the crystal lattice, although the strength of the individual interactions is stronger as evidenced by the higher melting point. TGA analysis indicated that about 17–20% of water was associated with the calix[*n*]arenes. Both TGA and hot stage microscopy results indicated that upon heating these molecules underwent stepwise water loss. TGA kinetics showed that the 4-sulphonato-calix[8]arene lost water easier than the other two calixarenes. The moisture adsorption behavior of all calixarenes followed type II isotherms. For the same amount of material, the calix[6]arene adsorbed more moisture than the calix[4]arene and the calix[8]arene. Moreover, dehydrated less crystalline 4-sulphonic-calix[*n*]arenes powders are hygroscopic.

**Keywords:** 4-sulphonato-calix[*n*]arene; Melting; Hydration; Dehydration; Moisture sorption

## INTRODUCTION

The calixarenes are a class of cyclooligomers formed via phenol-formaldehyde reactions. Each calixarene contains a repeating phenolic unit formed into a

macrocycle via methylene bridges. The bridges function as points around which the phenolic groups rotate, leading to various rotamer conformations [1]. These compounds are cylinder-shaped with various cavity sizes and can form a variety of host–guest type inclusion complexes, similar to cyclodextrins.

Most calixarenes are insoluble in water and to overcome the zero solubility in aqueous solutions, carboxylates, phosphates, ammonium or sulphonated functional groups have been introduced either at the upper rim or at the lower rim of the parent calixarenes. Since water-soluble calixarenes possess hydrophobic and hydrophilic properties, they are capable of encapsulating neutral organic as well as ionic species [2]. Among the water-soluble calixarenes, the *p*-sulphonato-calixarenes are now widely used, and studied, because they possess the highest known aqueous solubility [3]. These macromolecules have generated particular interest in the pharmaceutical sciences because they form complexes with solvents, amino acids, steroids, and other drugs [2,4–9].

However, the physicochemical properties of the sulphonated calixarenes are not well documented. For this reason this study reports the results obtained after characterization of the 4-sulphonato-calix[*n*]arenes (*n* = 4, 6, 8) by differential scanning calorimetry (DSC), thermogravimetry (TGA), microcalorimetry, hot stage microscopy (HSM), variable temperature X-ray powder diffractometry (VTXRPD), and dynamic water vapor sorption analysis (DVS).

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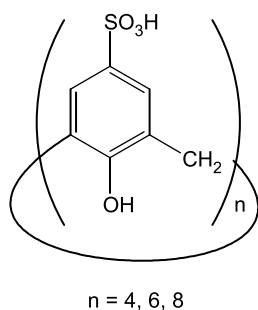


FIGURE 1 Chemical structure of 4-sulphonato-calix[*n*]arenes.

## RESULTS AND DISCUSSION

The chemical structure of the sulphonato-calixarenes used in this study is shown in Fig. 1. These molecules were first synthesized to overcome the lack of solubility of the parent calixarenes in biologically relevant aqueous systems. 4-sulphonato-calix[4]arene, 4-sulphonato-calix[6]arene and 4-sulphonato-calix[8]arene are water soluble with aqueous solubilities greater than 0.1 M [3,5]. In this study the calixarenes were recrystallized repeatedly from 1:1 v/v methanol water mixtures before being characterized.

### Melting Points and Heat of Melting

DSC thermograms of the 4-sulphonato-calix[*n*]arenes before and after dehydration are shown in Fig. 2. The melting points of three 4-sulphonato-calix[*n*]arenes were  $276.6 \pm 0.2$  ( $n = 4$ )  $> 269.9 \pm 0.7$  ( $n = 8$ )  $> 261.6 \pm 0.2$  ( $n = 6$ ) (Table I, in pans with pinhole in the lid), all above 250°C but 80–150°C lower than their parent calix[*n*]arenes, i.e. *p*-tert-butylcalix[*n*]arenes. For example, *p*-tert-butylcalix[4]arene melts at 342–344°C, *p*-tert-butylcalix[6]arene melts at 380–381°C, and *p*-tert-butylcalix[8]arene melts at 411–412°C [3,4].

The melting point increased with an increase in the ring size in the case of *p*-tert-butylcalix[*n*]arenes. However, the 4-sulphonato-calix[*n*]arenes did not follow this pattern. The 4-sulphonato-calix[4]arene melted at the highest temperature followed by 4-sulphonato-calix[8]arene, whereas 4-sulphonato-calix[6]arene had the lowest melting point. The DSC traces (Fig. 2) of these calix[*n*]arenes showed broad peaks instead of sharp peaks, indicative of less crystalline materials. The order of the heat absorbed upon melting was in the following order:

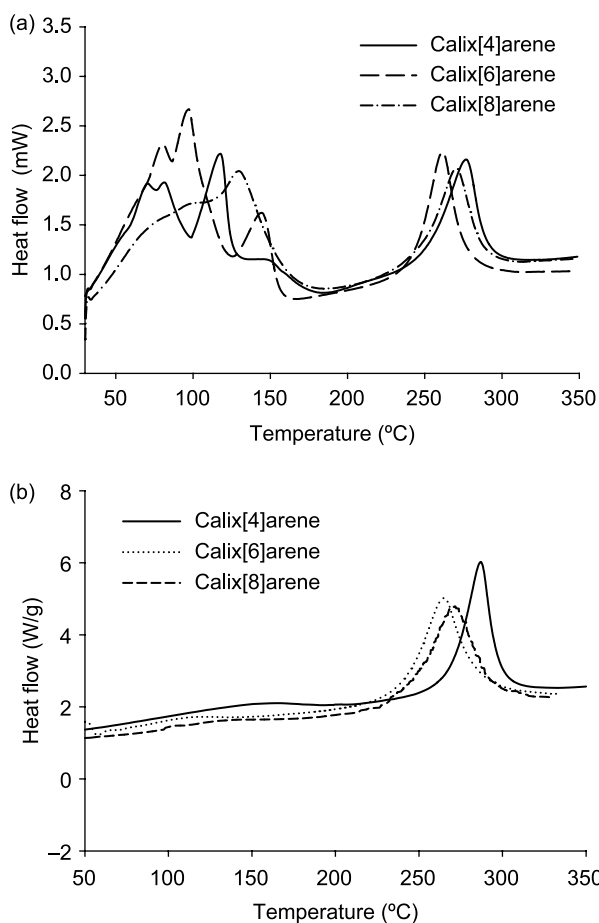


FIGURE 2 DSC thermograms of the 4-sulphonato-calix[*n*]arenes (a) before and (b) after dehydration.

$192.4 \pm 4.2$  kJ/mol ( $n = 4$ )  $< 242.4 \pm 5.8$  kJ/mol ( $n = 6$ )  $< 350.6 \pm 3.9$  kJ/mol ( $n = 8$ ); while the order of the entropy change upon melting ranked as:  $695.5 \pm 15.3$  J/mol°C ( $n = 4$ )  $< 926.7 \pm 22.3$  J/mol°C ( $n = 6$ )  $< 1299.0 \pm 14.6$  J/mol°C ( $n = 8$ ). The enthalpy and entropy changes involved in the melting process increased with increasing size of molecule.

For DSC analysis in pans without pinholes in the sample pan lids, the trend remained the same but with higher values and greater variations. The order of the enthalpy ranked as  $229.2 \pm 10.3$  kJ/mol ( $n = 4$ )  $< 296.0 \pm 14.2$  kJ/mol ( $n = 6$ )  $< 389.2 \pm 18.0$  kJ/mol ( $n = 8$ ); while the order of the entropy change upon melting ranked as  $828.5 \pm 37.6$  J/mol°C ( $n = 4$ )  $< 1131.6 \pm 54.3$  J/mol°C ( $n = 6$ )  $< 1442.1 \pm 66.5$  J/mol°C ( $n = 8$ ). These results indicated that water vapor sealed in the pans without pinholes

TABLE I Thermal parameters of 4-sulphonato-calix[*n*]arenes

<i>n</i>	$T_m$ (°C)	$\Delta H_m$ (kJ/mol)	$\Delta S_m$ (J/mol°C)	$C_p$ (kJ/mol°C)	$\Delta H_s$ (kJ/mol)	$E_a$ (kJ/mol)
4	$276.6 \pm 0.2$	$192.4 \pm 4.2$	$695.5 \pm 15.3$	$10.9 \pm 1.5$	$30.3 \pm 6.3$	$128.3 \pm 13.8$
6	$261.6 \pm 0.2$	$242.4 \pm 5.8$	$926.7 \pm 22.3$	$11.3 \pm 1.9$	$58.0 \pm 9.3$	$117.6 \pm 5.6$
8	$269.9 \pm 0.7$	$350.6 \pm 3.9$	$1299.0 \pm 14.6$	$12.6 \pm 1.5$	$62.8 \pm 8.3$	$79.8 \pm 4.2$

resulted in higher enthalpy and entropy values, and the varying amounts in the water vapor left in the pans led to greater variations. In addition, the DSC thermograms of dehydrated samples, Fig. 2(b), confirmed the position and magnitude of the melting endotherms.

The higher melting points recorded for 4-sulphonato-calix[4]arene indicated the strength of individual interactions was stronger in this macromolecule. However, since less heat was required to break up the crystal lattice and a smaller increase in the entropy was observed it suggested smaller cooperativity of interaction between molecules in the crystal lattice of this calixarene [10]. This might be due to stronger intramolecular hydrogen bonding in each molecule of the calix[4]arene. Similarly, lower melting points for 4-sulphonato-calix[6]arene and 4-sulphonato-calix[8]arene indicated weaker individual interactions; but more heat required to break up the crystal lattice and greater increase in entropy meant greater cooperative interaction existed between neighboring molecules involving many weak bonds in the crystal lattices of these macromolecules.

### Heat Capacity

The heat capacity, the heat required to raise the temperature of 1 mole of a substance by 1 degree, of each 4-sulphonato-calix[*n*]arene was calculated from its melting point using Eq. (1):

$$C_p = \frac{60E}{H_r} \times \frac{\Delta H \times MW}{m} \quad (1)$$

where *E* is a cell calibration coefficient at the temperature of interest (dimensionless), *H<sub>r</sub>* is the heating rate, in °C/minute,  $\Delta H$  is the difference in y-axis deflection between the sample and blank curves at the temperature of interest, in mW, MW is the molecular weight of the substance, *m* is the sample mass in mg, and *C<sub>p</sub>* is the heat capacity, in J/mol°C.

Since the quantity  $60E/H_r$  is constant under a given set of experimental conditions, it converts the measurement directly into units of heat capacity in J/g°C. In this experiment, sapphire was used as the calibration material to derive the value of  $60E/H_r$ . The values for  $\Delta H$  and *m* were substituted into Eq. (1) at the melting point of each calix[*n*]arene to calculate *C<sub>p</sub>*. The heat capacities for the 4-sulphonato-calix[*n*]arenes were: 10.9 kJ/mol°C (*n* = 4) = 11.3 kJ/mol°C (*n* = 6) = 12.6 kJ/mol°C (*n* = 8). Based on these results there was no significant difference between the heat capacity of the three calixarene indicating that the molecular interactions in the melt are independent of the ring size.

### Dehydration Under Hot Stage Microscope

The three calixarenes are fine powders (<50 μm) ranging in color from dark brown for 4-sulphonato-calix[4]arene, brown for 4-sulphonato-calix[6]arene and light reddish brown for 4-sulphonato-calix[8]arene. Results of the HSM analysis of the 4-sulphonato-calix[*n*]arene samples are shown in Fig. 3. Under the microscope, bubbles that formed in the silicon oil upon heating confirmed the liberation of water from the powders. However, the melting of the calixarenes at 230–300°C also produced bubbles in the oil. This could be the release of gaseous degradation products produced when the calixarenes decompose upon melting. At room temperature the powdered calixarenes had different morphologies; the calix[4]arene and calix[6]arene look more crystalline compared to the very fine amorphous calix[8]arene particles. All three calixarenes start to lose water at around 50°C. The release was slow with large bubbles slowly growing in the silicon oil. For 4-sulphonato-calix[4]arene this process continued but the smaller bubbles start to form more rapidly at around 80–90°C. This process continued up to 220°C, at which point the remaining particles have turned completely black confirming that dehydration was complete.

For the 4-sulphonato-calix[6]arene fewer bubbles that grew in size continued to form from 50–90°C. However, at around 100°C the speed of the formation of the bubbles increased with many smaller bubbles rapidly appearing. This looked like the bubbles formed when water boils. This process continued up to 180°C. The number and size of the bubbles then decreased rapidly and at around 230°C, no more bubbles were released in the silicon oil from the now black, opaque dehydrated particles.

The 4-sulphonato-calix[8]arene powder was much finer than the other two calixarenes. Very small bubbles were released from the powder aggregates and these bubbles merged to form larger bubbles. This slow release of water with increased growth of bubbles continued from 50 to 200°C. At 220°C no more bubbles were formed and the fine particles turned a dark red brown, opaque color indicating that desolvation was completed.

### Water of Crystallization and Dehydration

All three 4-sulphonato-calix[*n*]arenes are hydrates that contain between 17–20% of water (Table II). Upon heating, each lost its water at different temperatures as shown by the DSC and HSM (Figs. 2 and 3). Using the TG and DTG curves in Fig. 4 it was difficult to resolve each particular step of the water liberation suggesting a complex pattern of dehydration. The 4-sulphonato-calix[4]arene lost about 8% (four water molecules) starting at 43°C, then about 10% (five water molecules) at above 83°C

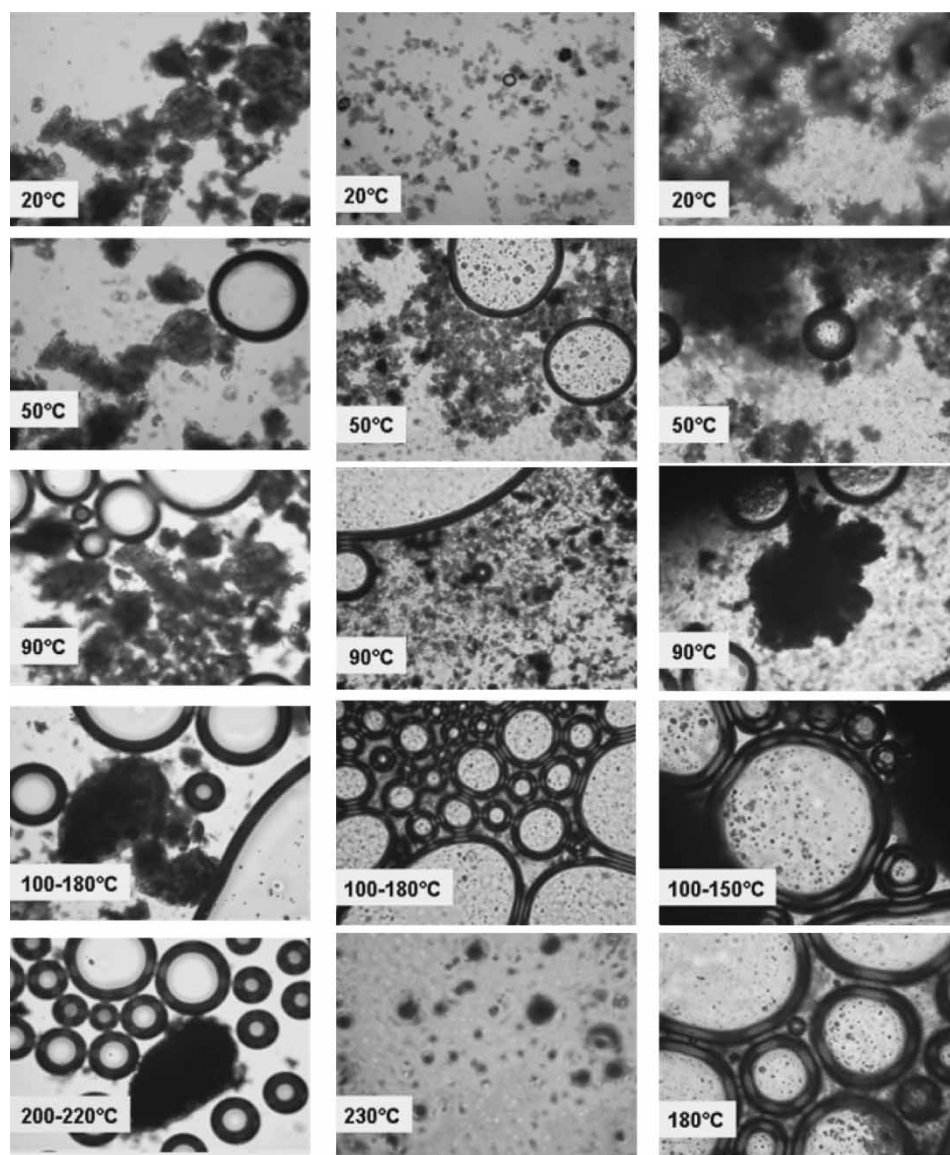


FIGURE 3 HSM photomicrographs of 4-sulphonato-calix[4]arene (left, top to bottom), 4-sulphonato-calix[6]arene (middle, top to bottom) and 4-sulphonato-calix[8]arene (right, top to bottom).

for a total weight loss of about 18% (9 water molecules). 4-Sulphonato-calix[6]arene lost about 12% (9 water molecules) starting at 50°C, another 4.5% (4 water molecules) at about 101°C for a total weight loss of about 17% (13 water molecules). 4-Sulphonato-calix[8]arene lost about 6% (7 water molecules) starting at 42°C, then another 13% (13 water molecules) at about 80°C for a total weight loss of about 19% (20 water molecules). The water content

of the calixarenes were confirmed by Karl Fisher titration, Table II.

The stepwise loss of water from the calixarenes indicated that some portion of the water is loosely bound while the rest is involved in strong interactions with the calix[*n*]arene molecules in the crystal lattice (Fig. 4). Measured water content was in line with that reported for 4-sulphonato-calix[4]arene (20%) and 4-sulphonato-calix[6]arene (14%)

TABLE II Structural properties and kinetics of the hydrated 4-sulphonato-calix[*n*]arenes

Calix[ <i>n</i> ]arene	MW	Crystal H <sub>2</sub> O (%) <sup>a</sup>	Karl Fisher (%) <sup>b</sup>	<i>E<sub>a</sub></i> (dehydration) (kJ/mol)
4	745	18.1 ± 2.0	17.56 ± 0.98	128.3 ± 13.8
6	1117	17.4 ± 1.8	16.91 ± 0.88	117.6 ± 5.6
8	1489	20.2 ± 3.5	20.27 ± 1.08	79.8 ± 4.2

<sup>a</sup> Measured by TG analysis (*n* = 5). <sup>b</sup> Measured by Karl Fischer titration (*n* = 5)

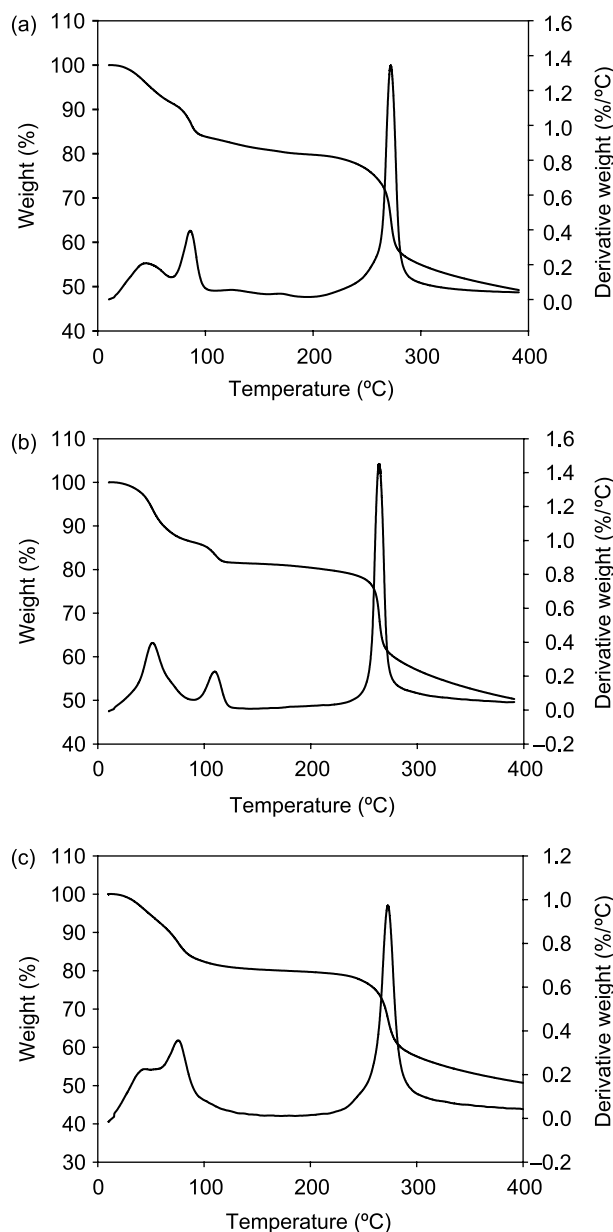


FIGURE 4 TGA and DTGA curves of (a) 4-sulphonato-calix[4]arene, (b) 4-sulphonato-calix[6]arene and (c) 4-sulphonato-calix[8]arene.

[3]. Assuming that the dehydration of the calixarenes followed first order kinetics upon heating, the kinetic parameters describing dehydration were determined by TGA using the kinetics program supplied with the TGA (Universal Analysis software, TA instruments, New Castle, DE).

This method is based upon a standard test (ASTM E1641-04). TGA thermograms were recorded at heating rates of 3, 5, 7, and 10 K/min ( $n = 3$ ). For each thermal curve, the absolute temperature at constant conversion,  $\alpha$ , for each of the conversion values as shown in Figs. 5–7 was determined. Plots of the log[heating rate] against the reciprocal of the absolute temperature at which the conversion occurs were linear as shown in these curves. There was also

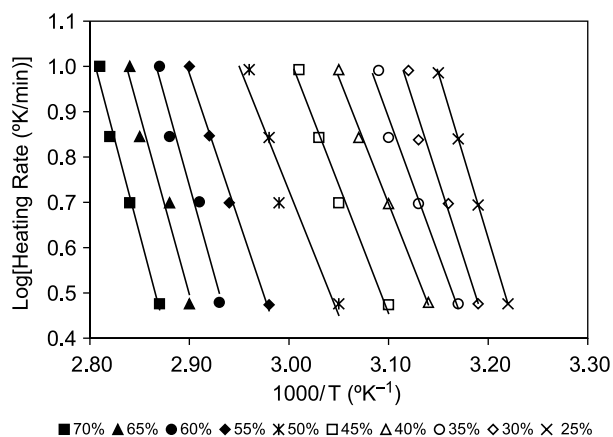


FIGURE 5 Arrhenius plot of heating rate versus temperature of constant conversion data obtained from TGA curves of 4-sulphonato-calix[4]arene at different heating rates ranging from 3, 5, 7 and 10 K/min.

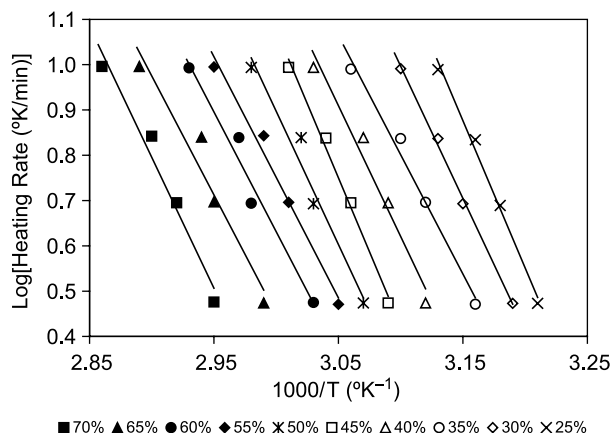


FIGURE 6 Arrhenius plot of heating rate versus temperature of constant conversion data obtained from TGA curves of 4-sulphonato-calix[6]arene at different heating rates ranging from 3, 5, 7 and 10 K/min.

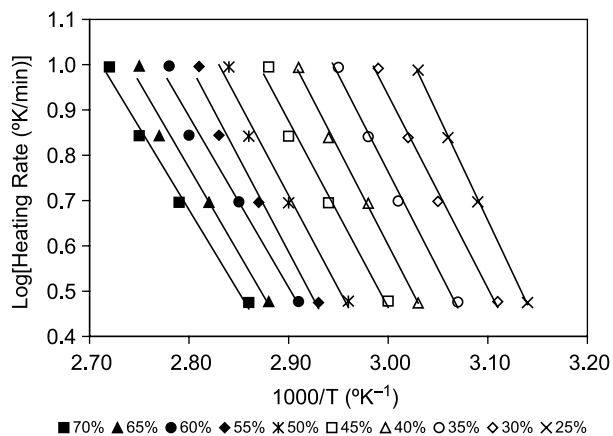


FIGURE 7 Arrhenius plot of heating rate versus temperature of constant conversion data obtained from TGA curves of 4-sulphonato-calix[8]arene at different heating rates ranging from 3, 5, 7 and 10 K/min.

a parallel shift in the relationship between the  $\log[\text{heating rate}]$  and  $T^{-1}$  across the selected conversion values. This showed that the procedure was applicable to the dehydration of the 4-sulphonato-calix[ $n$ ]arenes. However, although this relationship was also linear for the calix[4]arene, Fig. 5, parallel shifts was not as good as for the other two calixarenes. This might be because the bonds between the calix[4]arene molecule and some of water molecules were stronger causing dehydration stages to overlap.

The plots shown in Figs. 5–7 were used to calculate an estimation of the activation energy ( $E$ ) for dehydration of the 4-sulphonato-calix[ $n$ ]arene using Eq. (2)

$$E_r = -\left(\frac{R}{b}\right) \times \frac{\Delta(\log \beta)}{\Delta(1/T)} \quad (2)$$

where  $\Delta(\log \beta)/\Delta(1/T)$  is the slope of the lines as shown in Figs. 5–7,  $R$  is the gas constant and  $b$  is an approximation derivative taken from published tables and refined by calculation [11–13]. The activation energy for dehydration for 4-sulphonato-calix[4]arene was higher than that for calix[6]arene which in turn was higher than that for calix[8]arene (Table II). This showed that the interaction between the water molecules and the smaller calixarene molecules was stronger than with the larger calixarene molecules.

### Heat of Solution in Water

When a solid dissolves in a solvent such as water, the process always has an endothermic or exothermic energy change associated with it depending on whether more energy was used to break the bonds (endothermic), or more energy was released when new bonds were formed (exothermic). The heat of solution,  $\Delta H$ , is calculated using Eq. 3.

$$\Delta H = \frac{q}{\text{mol}} \quad (3)$$

Since the heat ( $q$ ) comes from the chemical reaction of the solute,  $\Delta H$  is per moles solute, not per mol solution. The value of  $\Delta H$  is positive for endothermic dissolution (temperature decreases) and negative for exothermic dissolution (temperature increase).

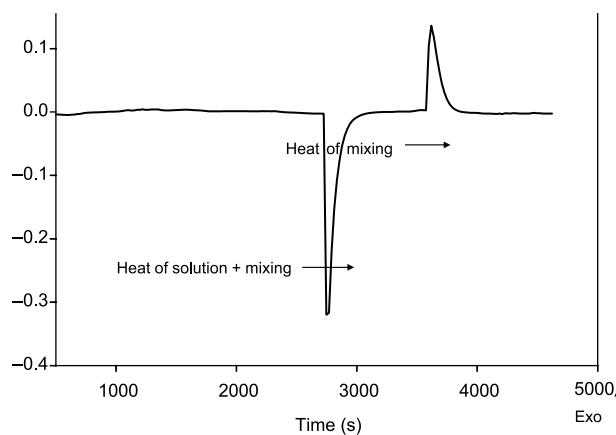


FIGURE 8 MDSC thermogram used for determining the heat of solution of 4-sulphonato-calix[4]arene.

The heat of solution for all three 4-sulphonato-calix[ $n$ ]arenes gave similar plots. Fig. 8 is an example of a thermogram used to calculate the heat of solution of 4-sulphonato-calix[4]arene. The first peak was due to the heat of solution and mixing, whereas the second peak was due to the mixing. As shown in Table III, the heats of solution of the three 4-sulphonato-calix[ $n$ ]arenes were  $30.3 \pm 6.3$  ( $n = 4$ ),  $58.0 \pm 9.3$  ( $n = 6$ ),  $62.8 \pm 8.3$  ( $n = 8$ ) kJ/mol respectively. These results indicated that the calix[4]arene dissolved more easily than the calix[6]arene and the calix[8]arene, i.e. less heat is needed to break up the crystal lattice although the individual interaction between the molecules is stronger as evidenced by its higher melting point. This corresponded with the prediction of smaller cooperativity of the interactions in the crystal lattice that we surmised from the melting behavior of these calix[ $n$ ]arenes.

### Isothermal and Variable Temperature X-ray Powder Diffractometry

X-ray powder diffractometry is widely used for the identification of solid phases. It is also used to identify the solvated and the unsolvated (anhydrous) forms of a compound, provided the crystal lattices of the two are different [14]. As shown in Fig. 9–11, the three 4-sulphonato-calix[ $n$ ]arenes exhibited different X-ray patterns at ambient temperature. The peak intensities for both the commercial and samples recrystallized from water were low in all three samples, suggesting a low degree of crystallinity.

TABLE III Weight loss (loss) steps and starting temperature ( $T_s$ ) for the hydrated 4-sulphonato-calix[ $n$ ]arenes measured by TGA

$n$	Dehydration steps									
	Loss (%)	$T_s$ (°C)	Loss (%)	$T_s$ (°C)	Loss (%)	$T_s$ (°C)	Loss (%)	$T_s$ (°C)	Loss (%)	$T_s$ (°C)
4	7.7	42.6	7.6	83.2	2.2	123.2	0.95	170.4	27.6	271.8
6	12.2	51.3	–	–	4.5	110.2	–	–	27.1	264.1
8	5.6	41.8	13.2	81.1	–	–	–	–	30.7	271.9

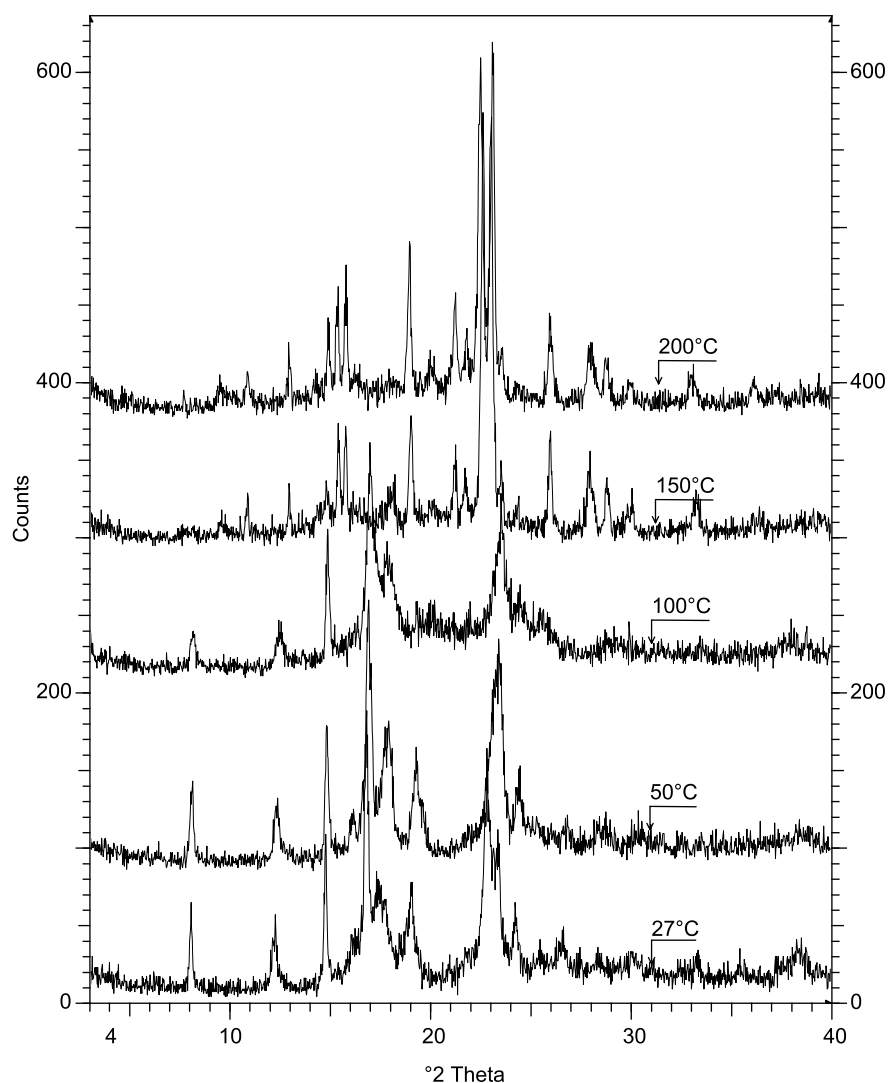


FIGURE 9 VTFRPD patterns of the hydrated 4-sulphonato-calix[4]arene.

More peaks are observed in the 4-sulphonato-calix[4]arene and 4-sulphonato-calix[6]arene than in 4-sulphonato-calix[8]arene, so the former two samples were more crystalline than the latter one. Since the single crystal structure of the hydrated 4-sulphonato-calix[6]arene is known [16] it was used to calculate its x-ray powder pattern (Fig. 12). Although the major peaks (7, 9, 15, 18 and 21°2 $\theta$ ) in the less crystalline commercial or recrystallized material corresponds to those in the calculated pattern the differences in intensity clearly show the low degree of crystallinity of the commercial 4-sulphonato-calix[6]arene sample (Fig. 10).

To follow crystal structure changes during dehydration samples of the 4-sulphonato-calix[4]arene were heated and the XRPD patterns measured as shown in Fig. 9. Upon heating three different X-ray patterns were observed: one between 25 and 50°C, one around 100°C, and one between 150 and 200°C. This indicated that when heated, 4-sulphonato-calix[4]arene underwent

a crystal form transformation during heating. This corresponded with HSM (Fig. 3) and TGA (Fig. 4) results that showed that the calix[4]arene started to lose water at 50°C, then at about 80°C, then at about 120°C. VTFRPD suggest that each dehydration step corresponds to a change in the crystal structure of the calix[4]arene and there was an increase in the crystallinity of the sample as shown by the increase in intensity and number of sharp peaks.

When the 4-sulphonato-calix[6]arene was heated, Fig. 10, less peaks were observed at higher temperatures. This indicated that upon dehydration there was a decrease in the crystallinity of the 4-sulphonato-calix[6]arene suggesting the collapse of its crystal structure. The reported single crystal structure of the 4-sulphonato-calix[*n*]arenes and their sodium salts show that disordered water molecules occupy channels in the structure [15,16] and it is known that upon dehydration channel compounds tend to low



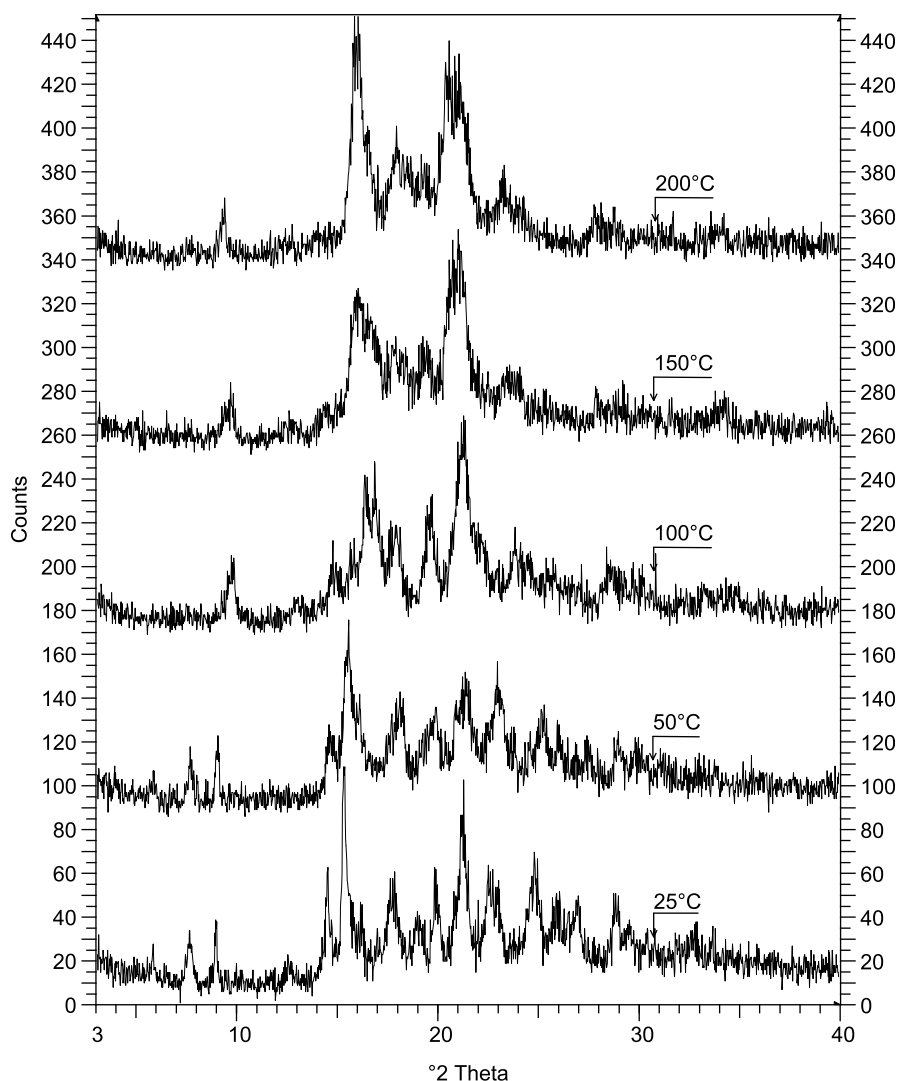


FIGURE 10 VT-XRPD patterns of the hydrated 4-sulphonato-calix[6]arene.

crystallinity due to structure collapse [16,17]. This phenomenon is more obvious in the case of 4-sulphonato-calix[8]arene, Fig. 11, because upon dehydration this compound became completely amorphous.

### Moisture Sorption

Since calix[*n*]arenes have a fair amount of water associated with them, analysis of moisture sorption data gives valuable information about the nature of interactions between water molecules and calix[*n*]arenes. As seen in Fig. 13, dried, dehydrated, samples of the three calixarenes exhibit a typical type II isotherm, indicating that the heat of sorption is greater than the heat of condensation. In addition, type H3 type hysteresis loops were observed [18]. The existence of a hysteresis loop in the isotherms is indicative of the presence of mesopores, whereas the shape of the hysteresis loop is related to the shape of the mesopores [19]. Type H3 hysteresis loops indicate that the adsorbent calixarenes might have

slit-shaped pores or plate like particles. The high affinity of calix[*n*]arenes for water molecules is clearly indicated by the amount of moisture uptake (~80–85% at 90% RH). Although an adsorption isotherm provides simple information about the amount of moisture uptake at specified relative humidity, further analysis of the data is required to understand the degree of interaction between the sample and water molecules.

Several mathematical expressions have been proposed which attempt to derive physically relevant parameters, one such being the GAB equation (4) [20]:

$$W = \frac{W_m C K a_w}{(1 - K a_w)(1 - K a_w + C K a_w)} \quad (4)$$

Where  $a_w$  is the water activity,  $W_m$  is the monolayer coverage,  $C$  is the sample/water affinity,  $K$  is the correction factor. The GAB parameters, estimated using non-linear regression, are given in Table IV. From a phenomenological point of view,

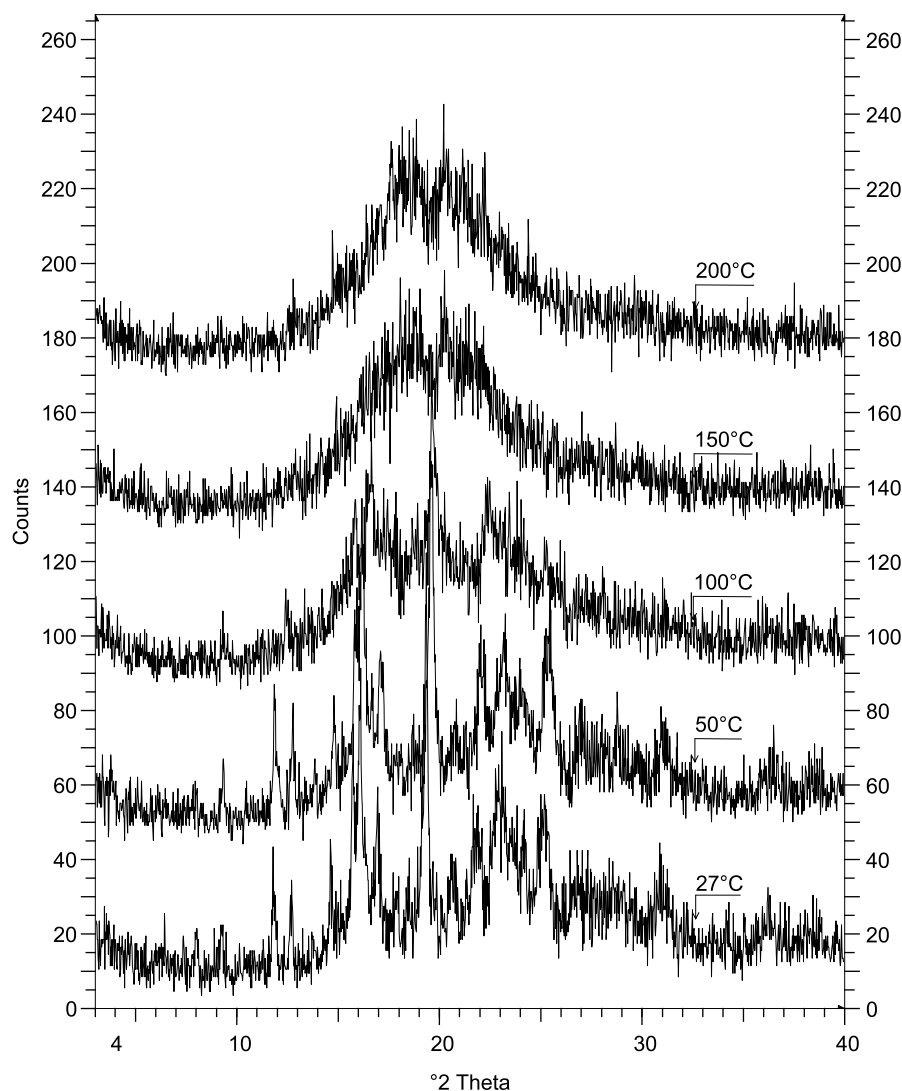


FIGURE 11 VT-XRPD patterns of the hydrated 4-sulphonato-calix[8]arene.

the region of interest for any sorption isotherm is at low humidity, primarily because this region provides information about the interaction of water molecules with the dry sample. As the humidity is increased, the process is merely reduced to the condensation of water molecules over the already existing ones.

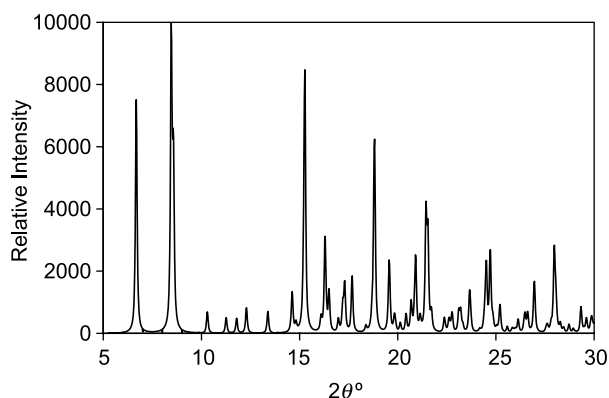


FIGURE 12 XRPD pattern of 4-sulphonato-calix[6]arene calculated from single crystal structure data.

Hence, the parameters of interest include “ $C$ ”, an indication of the affinity of the sample for the water molecules and “ $W_m$ ”, the so-called monolayer coverage, or more appropriately, the amount of water sorbed at low relative humidity.

As indicated by Table IV, the interaction parameter for the three calix[ $n$ ]arenes follows the order calix[8]arene > calix[4]arene > calix[6]arene. One would expect  $C$  to be the highest for 4-sulphonato-calix[8]arene followed by calix[6]arene and calix[4]arene, as the water molecules would have more available sites in the form of hydroxyl groups as “ $n$ ” increases. Interestingly, calix[6]arene seems to be an aberration and has the lowest  $C$  among the three samples. This is probably due to the secondary bonding between the functional groups in calix[6]arene as compared to the other two samples. This secondary bonding reduces the number of primary sites and hence lowers the interaction between the sample and water molecules. The value for  $W_m$  follows the order calix[6]arene > calix[4]arene > calix[8]arene. Although the interaction parameter for

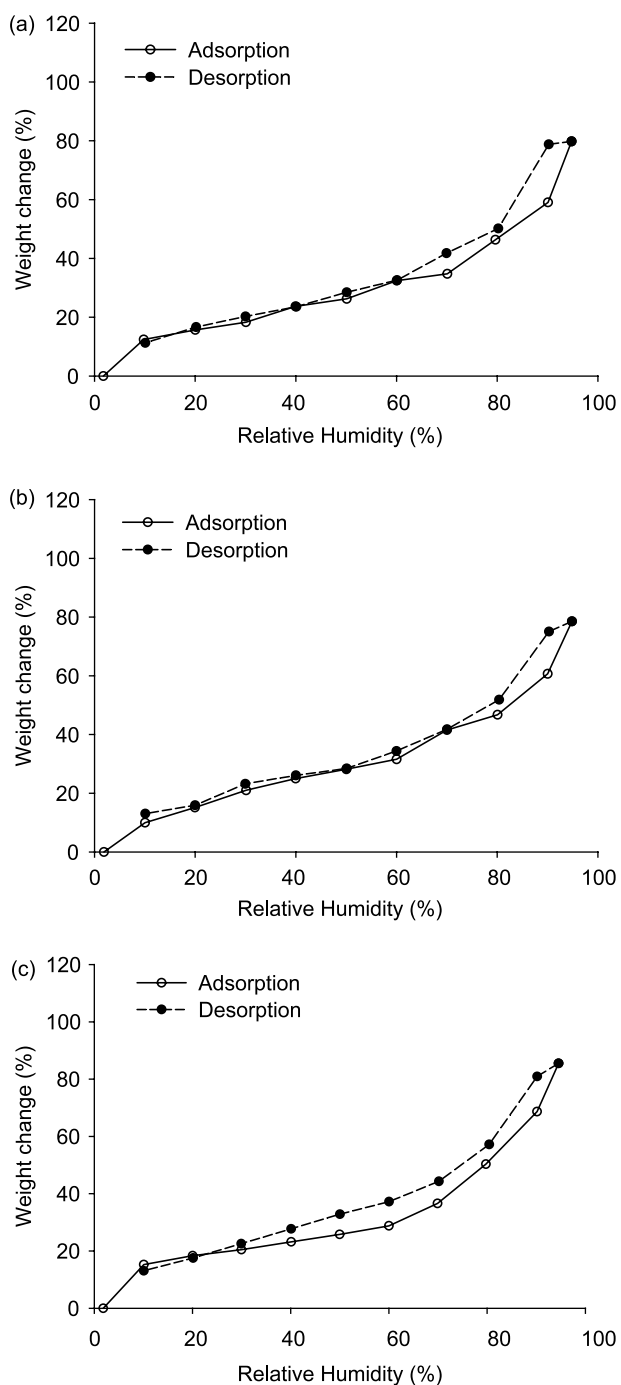


FIGURE 13 Moisture sorption-desorption isotherms of the 4-sulphonato-calix[*n*]arenes: (a) *n* = 4; (b) *n* = 6; (c) *n* = 8.

calix[6]arene is the lowest, the amount of moisture adsorbed at low humidity is the highest. This indicates that for calix[6]arene there should be very

TABLE IV GAB parameters for the moisture sorption isotherms of the 4-sulphonato-calix[*n*]arenes

Calix[ <i>n</i> ]arene	C	K	$W_m$ (g/g)
4	14.904	0.785	0.1776
6	9.359	0.740	0.2113
8	25.961	0.855	0.1585

small difference between the heat of sorption and heat of condensation.

## CONCLUSION

This study for the first time reports some fundamental physicochemical properties of the water soluble 4-sulphonato-calix[*n*]arenes where *n* = 4, 6 or 8. Thermal analysis showed that the three 4-sulphonato-calix[*n*]arenes melted at temperatures above 250°C. The higher melting temperature of the 4-sulphonato-calix[4]arene, compared to 4-sulphonato-calix[6]arene and 4-sulphonato-calix[8]arene, indicated greater strength and higher number of intermolecular interactions in the smaller calixarene. However, lower heat of fusion, smaller increase in entropy and smaller heat of solution of the calix[4]arene compared to the calix[6]arene and calix[8]arene showed that less heat was required to break up the crystal lattice of the smaller macromolecule. This apparent anomaly is rationalized in terms of smaller cooperativity of interaction between the molecules of calix[4]arene in the crystal lattice. Although the crystallized 4-sulphonato-calix[*n*]arenes showed a certain lack of crystallinity the calix[4]arene was more crystalline than the larger macromolecules. This was confirmed by XRPD analysis. However, when heated VT-XRPD showed the calix[4]arene apparently transformed to another more crystalline crystal form whereas the calix[6]arene and calix[8]arene became amorphous.

The water content of the 4-sulphonato-calix[*n*]arenes ranged between 17–20%. Some water was bound to the calix[*n*]arene molecules very tightly because heating to above 100°C was required to remove it completely. Overall, the calix[8]arene dehydrated easier than the calix[4]arene and calix[6]arene. The three 4-sulphonato-calix[*n*]arenes showed a high affinity for water vapor. The moisture adsorption behavior of all calixarenes followed type II isotherms. For the same amount of material, the calix[6]arene adsorbed more moisture than the calix[4]arene and the calix[8]arene. Moisture sorption behavior correlated well with the apparent crystallinity and dehydration behavior of the calixarenes and showed that the dehydrated 4-sulphonato-calix[*n*]arenes were hygroscopic.

## MATERIALS AND METHODS

### Materials

4-Sulphonato-calix[4]arene hydrate ( $C_{28}H_{24}O_{16}S_4 \cdot 9 H_2O$ , purity 95%, anhydrous MW = 744.75), 4-sulphonato-calix[6]arene hydrate ( $C_{42}H_{36}O_{24}S_6 \cdot 13 H_2O$ , purity 95%, anhydrous MW = 1117.13),

4-sulphonato-calix[8]arene hydrate ( $C_{56}H_{48}O_{32}S_8 \cdot 21 H_2O$ , purity 97%, anhydrous MW = 1489) were purchased from Acros Organics (Geel, Belgium). The calixarenes were used as received or after repeated recrystallization (up to 4 times) from a water methanol mixture (1:1 v/v).

### Thermal Analysis

Many calixarenes, especially those with free hydroxyl groups, have melting points which are usually above 250°C [1]. However, the melting points for sulphonato-calixarenes have not been reported. In this study, the melting points of three 4-sulphonato-calix[*n*]arenes were measured with a Differential Scanning Calorimetry (DSC) 2920 (TA Instruments, New Castle, DE). Samples weighing approximately 3 mg were heated at 10 K/min under nitrogen gas flow of 35 ml/min. The experiments were done in pans both without and with a pinhole in the lid.

The heat capacities of the calixarenes were measured with the DSC 2920 (TA Instruments, New Castle, DE). Samples weighing approximately 3 mg were heated at 10 K/min under nitrogen gas flow of 35 ml/min. The heat capacity at melting point for each calix[*n*]arene was calculated using sapphire (22.299 mg) as the calibration material.

HSM analysis was carried out under a Nikon Eclipse E400 microscope (Nikon Instruments Inc., Melville, NY, USA), equipped with a Metrathem 1200 heating unit (Leitz Wetzlar, Germany). The effects of temperature increase on the crystal behavior of the samples were studied by placing approximately 3 mg of each on an object glass, covering it with a cover slip, and gradually increasing the temperature to about 200°C at a heating rate of 10 K/min. Dehydration was observed with samples immersed in silicone oil (Fluka, Switzerland). Photographs were taken using a Nikon Coolpix 5400 digital camera.

Thermogravimetric analysis (TGA) and derivative thermogravimetric analysis (DTGA) were performed on the calix[*n*]arenes to determine the water content in the materials. TGA and DTGA traces were measured with a Hi-Res Modulated TGA 2950 (TA Instruments, New Castle, DE). Samples weighing approximately 5 mg were heated at 20 K/min under nitrogen gas flow of 90 ml/min. TGA dehydration kinetics were measured at heating rate of 3, 5, 7, and 10 K/min, respectively.

The water content of the calix[*n*]arenes was also determined with a Mettler DL18 Karl Fischer titrator (Mettler-Toledo, Inc., 1900 Polaris Parkway, Columbus, OH, 43240). The Karl Fischer solution was calibrated against a known mass of water. Twenty-milligram samples were accurately weighed and added to the methanol, previously neutralized with the Karl Fischer solution, in the titration beaker.

The mixture was stirred magnetically and titrated with the Karl Fischer solution. The experiment was done in five replicates and the percentage water (w/w) calculated.

For the microcalorimetric analysis a Micro-DSC III (Setaram, Caluire, France) was used. Samples weighing approximately 1 mg were analyzed in a mixing "batch" vessel under nitrogen purging with about 0.15 g deionized water used as the solvent (Nanopure, Barnstead International, Dubuque, Iowa). The vessel is composed of a cylinder and a set of parts mounted on a rod provided for dividing the experimental volume into two distinct chambers with a volume of 0.2 cm<sup>3</sup> for the upper chamber and 0.55 cm<sup>3</sup> for the lower chamber. The powder was placed in the bottom of the mixing vessel while the solvent was added to the top reservoir. Once the instrument was equilibrated at 25°C, the rod was pushed down allowing the solvent to come in contact with the calixarene powder. The heat measured, once corrected for the heat involved in stirring (second peak in Fig. 8), represent the heat involved in the dissolution of the calixarene powders in water. All measurements were repeated 6 times.

### Isothermal and Variable Temperature X-ray Powder Diffractometry

Ambient XRPD determinations were measured using a Bruker D8 Advance diffractometer (Bruker, Germany). The measurement conditions were: target, Cu; voltage, 40 kV; current, 30 mA; divergence slit, 2 mm; anti-scatter slit, 0.6 mm; receiving slit, 0.2 mm; monochromator; detector slit, 0.1 mm; scanning speed, 2°/min (step size 0.025°, step time, 1.0 sec). Approximately 300 mg samples were weighed into aluminum sample holders, taking care not to introduce a preferential orientation of crystals.

Variable temperature X-ray powder diffraction (VTXRPD) patterns were recorded with an Anton Paar TTK 450 heating stage (Anton Paar, Austria) attached to the Bruker D8 Advance diffractometer (Bruker, Germany). A heating rate of 10 K/minute was used during all of these determinations. The isothermal measurement conditions were: target, Cu; voltage, 40 kV; current, 30 mA; divergence slit, 2 mm; anti-scatter slit, 0.6 mm; receiving slit, 0.2 mm; monochromator; detector slit, 0.1 mm; scanning speed, 2°/min (step size 0.025°, step time, 1.0 sec). Approximately 150 mg samples were weighed into the sample holder, taking care not to introduce a preferential orientation of crystals.

### Moisture Sorption

All samples were vacuum dried at 50°C for over three days prior to inducing the sample in the sorption analyzer. Moisture sorption isotherms were generated

at 25°C using a Symmetric Vapor Sorption Analyzer (model SGA-100, VTI, Hialeah, FL). The SGA-100 is equipped with an electronic microbalance (CI Electronics, Wiltshire, UK) and dew point analyzer (Edgetech, Milford, MA) for the accurate measurement of weight and relative humidity (RH), respectively. The instrument was calibrated using sodium chloride and polyvinylpyrrolidone (PVP) K30. The procedure involved drying the samples in the VTI instrument at 60 °C and ~0% RH until the instrument recorded a weight loss of less than 1 µg over a period of 5 minutes. This was followed by exposing the samples to 10% steps in RH from 0 to 95% RH. Equilibrium was assumed when there was no weight change of more than 1 µg over a period of 5 minutes. Sorption data was analyzed according to the Eq. proposed by Guggenheim, Anderson and de Boer (GAB). The GAB parameters were estimated by non-linear regression using SPSS 11.5 for Windows (SPSS Inc., Chicago, IL.).

### Statistical Analysis

The melting point of three calix[*n*]arenes (*n* = 4, 6, or 8) with 3 replicates, the water content of three calix[*n*]arenes (*n* = 4, 6, or 8) with 5 replicates, and the heat of solution of three calix[*n*]arenes (*n* = 4, 6, or 8) with 6 replicates were evaluated using a one-way ANOVA (SAS Institute, Inc., Cary, NC, USA). In all cases, post-hoc comparisons of the means of individual groups were performed using DUN-CAN's test. A significance level of  $p < 0.05$  denoted significance in all cases.

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