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The complex relationship between guest-free polymorphic products and desolvation of *p-tert*-butylcalix[4]arene inclusion compounds

Eric B. Brouwer, Gary D. Enright, Konstantin A. Udachin, Stephen Lang, Kristopher J. Ooms, Peter A. Halchuk and John A. Ripmeester*

Steacie Institute for Molecular Sciences, National Research Council of Canada, 100 Sussex Drive, Ottawa, Ontario, Canada K1A 0R6. E-mail: John.Ripmeester@NRC.CA; Fax: +1 613 998 7833; Tel: +1 613 993-2011

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Depending on the details of the technique employed, desolvation of tBC inclusion compounds leads to either a dense, guest-free polymorph, or a guest-free low density polymorph, the latter also having distinct high and low temperature forms.

The calixarenes are versatile materials that have been studied extensively, both as host materials and as platforms for the synthesis of designed, specific receptors.[1] As pointed out by Atwood *et. al*.,[2] the simple, symmetric calixarenes display interesting behaviour that may well serve as models for a variety of phenomena.[3] *p-tert*-Butylcalix[4]arene (tBC) is one of the smaller, simpler members of this subgroup, and is a versatile host that forms inclusion compounds with a variety of guest molecules.[4,5] The most common structural themes are based on bilayer structures of 1:1 and 1:2 host–guest stoichiometry where the guest either lies in a single cavity roofed by *tert*-butyl groups in the next layer, or in a capsule consisting of two opposed calixarene molecules.[4,5] So, guest–host systems based on a single host molecule may form one or more families of inclusion compounds, and these are commonly referred to as the β forms (1:1 form = β_1, 1:2 form = β_2), the α form being the dense, guest-free form. For tBC, the latter has been obtained by recrystallizing the host from tetradecane,[6] and it consists of an efficiently packed structure of mutually self-included tBC molecules, and it has been suggested that this form results on the desolvation of the β forms.[6,7] Atwood *et al*. have made a strong claim[2] that the low-density guest-free host (we label it β_o as it can considered to be the *apo*-host for the β form) obtained upon sublimation,[8] also is the product obtained upon the desolvation of the toluene guest–host compound. However, this leaves the thermodynamic relationship between the various β forms and the α form somewhat of a mystery. Clearly it is important to know the relationship among the various phases *e.g.* for model sensor applications where tBC is treated with solvents or desolvated thermally.[7]

Close examination of some of our results obtained for the desolvation of several tBC inclusion compounds suggests that the desolvation behaviour is quite complex. First of all, if we examine our DSC and TGA traces for the desolvation of tBC-toluene, the two-step behaviour reported by Atwood *et al*. is clearly observed. However, for our samples the second weight loss step observed at a scan rate of 5 °C min^{-1} was not abrupt, and weight loss continued above 200 °C. Examination of the DSC traces† of a fresh sample (Fig. 1a) showed that besides the endotherms associated with guest loss below 200 °C, additional endotherms that started at ~220 °C, and at ~286 °C were observed. DSC traces for samples that were heated for various lengths of time in air at ~220 K show the low temperature endotherm shifting to higher temperature, and the high temperature endotherm becoming weaker (Fig. 1b,c), so that these events apparently are connected. A scan for pure α phase obtained by recrystallization from tetradecane, is shown in Fig. 1d. Based on the DSC traces, one might guess that samples used for scans 1d and 1c are very similar. The products obtained after thermal treatment carried out to mimic the DSC samples were identified by solid state ^{13}C NMR spectroscopy†. Fig. 2 shows that the β_1 form converts to the β_2 form by heating at ~140 °C, with the β_1 and β_2 phases coexisting. After heating at ~200 °C the sample is pure β_2 phase, whereas prolonged heating at 220 °C gives the dense α form. The latter phase is easily distinguished from the other phases because of ^{13}C spectral complexity attributable to the large asymmetric unit.[6] The DSC

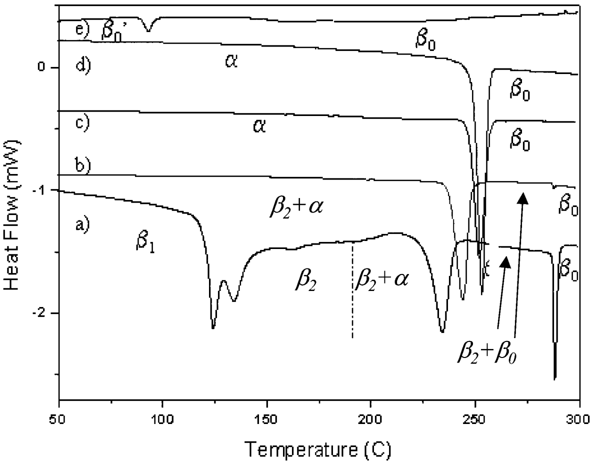

Fig. 1 Differential scanning calorimetry traces for the tBC-toluene compound as a function of thermal history, and traces for the two guest free polymorphs. The phases present in the temperature regions are indicated below each trace. a) fresh toluene-tBC; b) tBC-toluene sample after heating at 200 °C for several hours; c) tBC-toluene sample after heating for 12 h at 220 °C; d) tBC sample from tetradecane; e) tBC sample from tetradecane after heating at T > 260 °C.

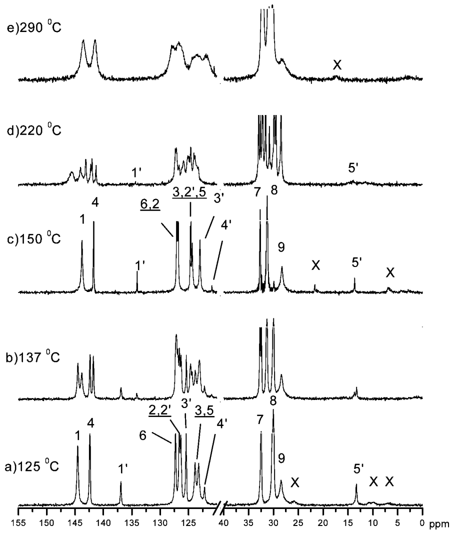

Fig. 2 ^{13}C NMR spectra for tBC-toluene obtained at room temperature after being heated to the temperatures indicated. a) 1:1 (β_1) phase b) mixed 1:1 β_1 and 2:1 phases c) pure β′ phase d) guest-free α phase e) guest-free β_0′ phase. Primed labels are guest resonances; x marks spinning sidebands.

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traces show that as more guest is driven off by heating at 220 °C, the transition observed at ~220 °C moves to higher temperatures, meanwhile the transition at 286 °C becoming weaker. We conclude that desolvation by prolonged heating at 220 °C produces the α form, and that the transition that occurs between ~230 and 253 °C is in fact an $\alpha \longrightarrow \beta_o$ transition. Since for the pure α form the $\alpha \longrightarrow \beta_o$ transition takes place above 250 °C we suggest that residual toluene acts as a trapped impurity that remains in equilibrium with residual β_2 phase, thus lowering the phase transition temperature. According to the DSC results the residual β_2 phase finally transforms to the β_o form at 286 °C (Fig. 1a,b). Desolvation by sublimation of the β_2 phase clearly is able to remove residual toluene quite efficiently, and the product in this case is the β_o form without the α form having been observed. For the tBC compounds, one should not necessarily expect that desolvated samples prepared by slow heating in a gas stream and samples prepared by vacuum degassing at a different temperature will be identical.

The α form apparently has a relatively small temperature range where it can be prepared by desolvation, the exact temperature range depending on how easily the guest is lost. This can be quite difficult for guests trapped in the calixarene capsules of the β_2 form. If desolvation can occur at lower temperatures, as for the pentane compound (Fig. 3 (bottom)), the sample transforms quite readily to the α form. Fig. 3(top) shows a ^{13}C NMR spectrum for a mixture of the β_2 and α forms which resulted on heating the pure β_1 pentane compound (Fig. 3 (bottom) at ~150 °C. Further heating at 150 °C transforms the sample completely to the α form.

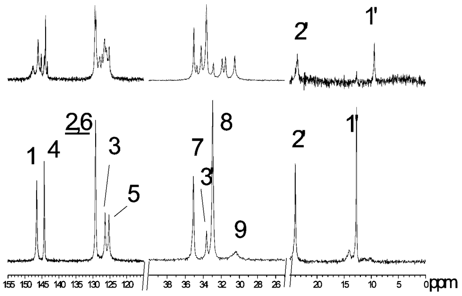
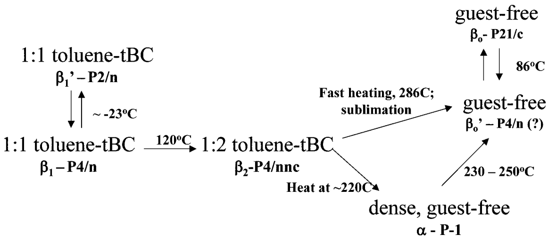


Fig. 3 ^{13}C NMR spectra (bottom) pentane-tBC as obtained; (top) after heating at 150 °C ($\beta' + \alpha$).

In terms of thermodynamic stability, the α form must be the stable form for guest-free tBC at room temperature. It is interesting to note that the low-density β_o form does indeed become the stable form above ~ 250 °C. This suggests that the ^{t}Bu group is not able to stabilize the lattice any longer by being included in the cavity of neighbouring molecules. The ^{t}Bu group is known to be highly dynamic, so that its effective size is likely to increase with temperature, whereas the free cavity size is fixed or decreases because of thermal motion. The $\alpha \longrightarrow \beta_o$ transition can be attributed to the expulsion of the ^{t}Bu groups from the tBC cavities. Once the β_o phase is formed it does not transform back to the α form on cooling, so it must be metastable below ~250 °C.

When the β_o form is cooled below ~60 °C, it does transform yet again, this time to the structure reported by Atwood *et. al.*,[8] which we label β_o', the $\beta_o' \longrightarrow \beta_o$ transition occurring at 92 °C (Fig. 1e). So, actually, the phase that Atwood *et al.*[8] found upon sublimation is in fact not the same phase for which they determined the structure. The enthalpy of transition is relatively small (Fig. 1e) for the $\beta_o' \longrightarrow \beta_o$ transition, and we suggest that it probably involves a relatively minor change in crystal symmetry, probably from the space group determined at room temperature, *P*2/*n*, to *P*4/*n*.

Scheme 1 summarizes the phase structure for the toluene compound, as determined in the experimental work reported here and elsewhere.[4–6,9] It should be noted that this behaviour is not typical of all 1:1 guest–host compounds with the *P*4/*n* structure, as guests such as benzene and acetone appear to lose their guests in a single step at heating rates of a few degrees min^{-1}.



Scheme 1 Relationship among the phases mentioned in the text. For completeness we also show the low temperature phase observed for toluene-tBC.[9]

Notes and references

† DSC and TGA measurements were performed on a TA System at scanning rates between 2 and 10 °C min^{-1}. ^{13}C NMR spectra were obtained on a spectrometer built around a Tecmag Apollo controller and using a Doty MAS probe, at a frequency of 50.3 MHz. Phase change temperatures are generally taken from peak maxima so they are not the traditionally accepted phase change temperatures, however, here they serve only to designate the approximate phase boundaries.

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