Concomitant polymorphs of p-iso-propylcalix[4]arene†

Vincent J. Smith, a Charl G. Marais, a Kinga Suwińska, b Janusz Lipkowski, b Agnieszka Szumna, c Catharine Esterhuysen a and Leonard J. Barbour a

Introduction

The extensive family of calix[n]arenes have a long history as host molecules in the field of inclusion chemistry.1 For example, the cone-shaped p-tert-butylcalix[4]arene (tBc) is well known for forming solvates with many different solvents. These solvates usually crystallise to adopt one of two types of host arrangements. One of these arrangements packs according to the space group P4/n, with a host:guest ratio of 1:1, while the other crystallises in P4/mnc, with a host:guest ratio of 2:1. Both of these packing modes can be described in terms of a bilayer arrangement of alternating up-down host molecules. This is sublimed at 280 °C, resulting in a relatively low packing efficiency of 0.59. At room temperature it is clear that all four tert-butyl groups of each calixarene are rotationally disordered whereas only one of the groups is disordered at 100 K. When form IIb is heated to 130 °C it undergoes a minor and reversible phase change to a high temperature form (IIIb), which has a similar bilayer packing arrangement to that of form IIb, except that adjacent bilayers become displaced laterally.3 Despite its apparent lack of permanent channels between lattice voids, form IIb possesses transient porosity, i.e. the crystals are able absorb a variety of solvents and gases into their discrete lattice voids, often in single-crystal to single-crystal (SC-SC) fashion. This was convincingly exemplified by a guest inclusion reaction involving the uptake of vinyl bromide with a concomitant SC-SC transformation of the host packing mode. Absorption of gases such as carbon dioxide, methane and acetylene does not result in rearrangement of the host molecules.3-5

The fascinating solid-state inclusion properties of tBc prompted further studies aimed at tailoring the void space in arrangement with facing molecules slightly offset relative to one another (form IIb). The cavities of two facing molecules from adjacent layers combine to produce discrete voids of approximately 235 Å³ each, resulting in a relatively low packing efficiency of 0.59. At room temperature it is clear that all four tert-butyl groups of each calixarene are rotationally disordered whereas only one of the groups is disordered at 100 K. When form IIb is heated to 130 °C it undergoes a minor and reversible phase change to a high temperature form (IIIb), which has a similar bilayer packing arrangement to that of form IIb, except that adjacent bilayers become displaced laterally.3 Despite its apparent lack of permanent channels between lattice voids, form IIb possesses transient porosity, i.e. the crystals are able absorb a variety of solvents and gases into their discrete lattice voids, often in single-crystal to single-crystal (SC-SC) fashion. This was convincingly exemplified by a guest inclusion reaction involving the uptake of vinyl bromide with a concomitant SC-SC transformation of the host packing mode. Absorption of gases such as carbon dioxide, methane and acetylene does not result in rearrangement of the host molecules.3-5

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Scheme 1. (a) The molecular structure of p-iso-propylcalix[4]arene (iPC), (b) iPC shown in space filling representation and (c) iPC shown as a cone (iso-propyl groups are shown as spheres lining the upper rim).
apohost forms of close structural analogues. Some limited success was achieved by tetra-substitution of the tert-butyl groups with larger moieties such as tert-pentyl and tert-octyl groups. Although bilayer-type packing still occurred for the molecules with larger substituents, the more interesting guest-free offset face-to-face packing motif of IIB was not observed for these systems. It therefore appears that the host packing arrangement observed for IIB is highly sensitive to even slight addition of bulk to the upper rim of the calixarene.5,6

The present work was motivated by the observation (based on a search of the Cambridge Structural Database) that p-isopropylcalix[4]arene (iPc, Scheme 1) exhibits host packing arrangements with a variety of guests that are highly reminiscent of that of tBc with the same guests.7,8 It was therefore hoped that, under the same crystal growth conditions, a slightly less bulky group on the upper rim would produce an apohost form that is isostructural to IIB, but with slightly more void space.

A previously published apohost form of iPc (refcode YARYAR, here designated as form IIP) crystallises as interdigitated dimers and the structure is analogous to that of IIB (refcode QIGBEN).7 An overlay of individual molecules of tBc and iPc shows that they adopt highly similar conformations, as expected (Fig. 1a). However, the degree of overlap between the dimers (Fig. 1b) of IIB and IIP is less precise, implying that the slightly different upper-rim moieties would significantly affect the overall extended periodicity of the two analogous structures relative to each other.

Results and discussion

Perrin et al. had isolated apohost form Ip from molten menthol at 65 °C.9 Instead, inspired by our previous work on tBc, we sublimed the as-synthesised iPc (i.e. the iPc(toluene solvate) under dynamic vacuum at 260 °C. Sublimation growth resulted in the formation of crystals with two distinct morphologies (Fig. 2) and single-crystal X-ray diffraction analysis confirmed that these are indeed concomitant polymorphs (designated as forms IIp and IIIp).

For comparison, selected unit cell parameters for forms Ip, IIp, IIIp and IIP are reported in Table 1 (full crystallographic data provided in Table S1†). Forms IIp and IIIp also crystallise as interdigitated dimers while the hoped-for non-interdigitated phase (i.e. analogous to IIB) was not observed.

In the crystal structure of form Ip, the interdigitated dimers are stacked in columns parallel to [010]. In turn, these columns form layers parallel to (110) with alternating layers displaced laterally by 7.7 Å (Fig. 3a). The individual dimers (i.e. the mean plane through the eight iso-propyl groups) are inclined by approximately 32° relative to the bc plane and all the columns along a have the same orientation, as shown in Fig. 3b. In form IIP the dimers are stacked in columns parallel to [010] (Fig. 3c), which are arranged in layers parallel to [110] that stack along c. Consecutive layers have anti-parallel molecular orientations and are displaced laterally by approximately 5.0 Å (Fig. 3d). The dimers are inclined by about 6° relative to the ac plane. In form IIIp the dimers also stack in columns parallel to [010], with layers parallel to [110] and stacked along c (Fig. 3e). Alternate layers are displaced laterally by approximately 8.8 Å, with consecutive layers having an anti-parallel arrangement (Fig. 3f) and a molecular inclination angle of about 23° relative to the ac plane. It is noteworthy that the calculated densities of Ip, IIp and IIIp differ by less than 1%.

Hirshfeld surface analysis of the iPc polymorphs and of form Ip of tBc was carried out using the program CrystalExplorer.9 The Hirshfeld surfaces were mapped using dnorm, which is a normalised contact that takes into account the van der Waals radius of each atom. Although the 2D fingerprint plots for the form Ip apohost and the three polymorphs of iPc are quite different, they show strikingly similar features (Fig. 4a–d). The iPc polymorphs and form Ip experience multiple C–H⋯π interactions, as evidenced by the ‘saw-tooth’ shapes on either side of the diagonal d_e = d_i (Fig. 4e–h).

![Fig. 1 Structural overlays of tBc (blue) and iPc (red). (a) shows how closely the individual molecules of iPc and tBc overlap with each other while (b) shows the poor overlap between the dimers of iPc and tBc.](image1)

![Fig. 2 Photomicrographs of the new polymorphs of iPc: (a) form IIp and (b) form IIIp.](image2)

| Table 1 Selected unit cell parameters of tBc and the polymorphs for iPc |
|-----------------------------|-----------------|-----------------|-----------------|-----------------|
|                            | Ip              | IIp             | IIIp            | IIP             |
| Space group                | P2_1/c          | C2/c            | P2_1/n          | P2_1/c          |
| a (Å)                      | 9.432(1)        | 24.851(3)       | 17.681(1)       | 9.5878          |
| b (Å)                      | 15.349(2)       | 9.412(1)        | 9.525(1)        | 30.5003         |
| c (Å)                      | 23.578(3)       | 29.214(4)       | 19.984(2)       | 13.5412         |
| β (°)                      | 98.751(2)       | 103.211(2)      | 98.363(2)       | 109.852         |
| Dv (g cm⁻³)                | 1.167           | 1.182           | 1.184           | 1.47            |
| Temp. (K)                  | 100             | 100             | 100             | 100             |
These interactions result from the insertion of a single tert-butyl or iso-propyl moiety into its partner’s cavity by the two calixarenes comprising a dimer.

The C–H⋯π interactions for form IB contribute 20.3% to the total area of the Hirshfeld surface while those of the iPc polymorphs contribute 23.4%, 24.1% and 23.2% for forms IP, IIP and IIIP, respectively. The O⋯H(IJ) interactions, shown as short broad spikes directed towards the lower left corner of each plot, are due to the intramolecular hydrogen bonded ring formed by the hydroxyl groups on the lower rim of each calixarene (Fig. 4i–I). Interestingly, form IB also experiences weak O⋯H(IJ)C) interactions that are not present in the fingerprint plots of the iPc polymorphs – these result from interactions between hydrogen atoms belonging to tert-butyl moieties and the hydroxyl groups of neighbouring calixarenes. The total contributions of the O⋯H(O) (as well as O⋯H(C) interactions for form IB) to the Hirshfeld surfaces are 5.9, 6.3, 6.0 and 6.2% for forms IB, IP, IIP, and IIIP, respectively.

Melting temperatures and enthalpies (T_on, T_peak, ΔH_fus and ΔH_des) were determined for the three polymorphs of iPc and iPc⊂toluene using differential scanning calorimetry (DSC) and these values are reported in Table 2. DSC thermograms for the phases IP, IIP and IIIP are shown in Fig. 5; each thermogram displays a single thermal event corresponding to the melt endotherm of each phase.

The iPc⊂toluene solvate (Fig. S1†) undergoes two thermal events that are related to desolvation and subsequent melting of the apohost. The observed melting point of the desolvated material corresponds to the melting point of form IP (Table 2). From the thermal data for the three apohost forms of iPc it appears that the highest melting phase (form IP) also has the highest heat of fusion. Indeed, the heats of fusion can be arranged in the order ΔH_fusIP > ΔH_fusIIP > ΔH_fusIIIP.

Table 2 Thermoanalytical results for the different phases of iPc as determined from DSC measurements (an average of two measurements in each case)

| Phase      | T_on (°C) | T_peak (°C) | ΔH_fus (J g⁻¹) | ΔH_des (J g⁻¹) |
|------------|-----------|-------------|----------------|----------------|
| Desolvation | 133.1     | 159.3       | —              | 53.4           |
| Melt       | 293.5     | 295.2       | 76.4           | —              |
| IP         | 294.3     | 296.1       | 75.3           | —              |
| IIP        | 289.9     | 292.4       | 62.1           | —              |
| IIIP       | 277.3     | 284.8       | 37.1           | —              |
Furthermore, we believe that the higher melting phase IP is also the thermodynamically most stable of the three forms since it can be crystallized from a saturated solution. According to the heat of fusion rule proposed by Burger et al. the three forms are monotropes (or monotropically related to one another).10

In order to understand the relationships between forms IP, IIIP, and IIIIP, temperature-cycled DSC (TC-DSC) experiments were carried out by heating each sample in the range 25 to 315 °C, followed by cooling to 25 °C and then reheating to 315 °C. The TC-DSC experiments were carried out at different heating rates, ranging from 10 to 20 K min$^{-1}$ at 5 K min$^{-1}$ increments (Fig. S2†). Since the toluene solvate was used to generate the new phases IIIP and IIIIP in the sublimation experiment, it was also used as the starting phase for the TC-DSC experiments. The first TC-DSC experiment, which was carried out at a scanning rate of 10 K min$^{-1}$ resulted in form IIIIP, while a scanning rate of 15 K min$^{-1}$ yielded a mixture of phases IIIP and IIIIP. From the ratio of the corresponding enthalpies we determined that more of form IIIIP was produced than of form IIIP (Fig. S3†). A rate of 20 K min$^{-1}$ also resulted in a mixture of forms IIIP and IIIIP, but in this case the ratios were more evenly distributed. Powder X-ray diffraction (PXRD) was used to characterise the pure phases (Fig. 6) and also to confirm the identity of the phases obtained from DSC (calculated PXRD profiles Fig. S4†). The TC-DSC experiments imply that the cooling rate influences which phases are produced, and that forms IIIP and IIIIP are kinetic products, whereas IP is the thermodynamic product.

**Conclusions**

We have described the concomitant isolation and characterisation of two new polymorphs (IIIP and IIIIP) of iPc grown by sublimation. Similar to the known form IP, the two new forms consist of interdigitated calixarene dimers. Thermoanalytical measurements of all three forms imply that none of them interconvert to one another prior to their melting. Moreover, the higher melting form IP has the highest enthalpy of fusion and is most likely the thermodynamically stable form since it can be crystallized from solution. Forms IIIP and IIIIP appear to be kinetic forms since they can be isolated upon rapid cooling of the melt. We conclude that forms IP, IIIP and IIIIP are monotropes while IIIP and IIIIP can more specifically be considered *kinetic* monotropes of form IP. A temperature gradient within the glass oven used for the sublimation experiments could explain the origin of the concomitant forms since IIIP and IIIIP can be generated based on different cooling rates that only differ marginally.

The original objective of this work was to establish whether iPc could fully mimic the highly interesting transient porosity of tBc. Unfortunately iPc does not appear to form an apohost form that is analogous to IIIP. Although only one interdigitated form of pure tBc apohost is known (form Ib), iPc yields three such forms as monotropic polymorphs of one another. This study demonstrates that, despite several marked similarities in their inclusion behaviour, tBc and iPc show very different packing trends in the manifestations of their apohost forms.
Acknowledgements

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