Trimorphism in solid resorcinarenes

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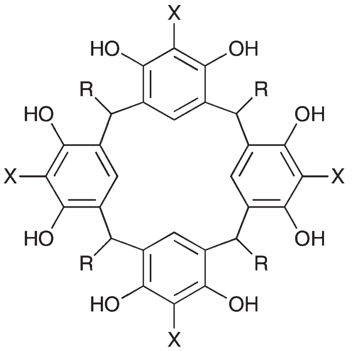
Received (in Cambridge, UK) 12th January 2007, Accepted 13th March 2007
First published as an Advance Article on the web 27th March 2007
DOI: 10.1039/b700469a

Nonylresorcinarene, in contrast to methylresorcinarene and nonylpyrogallene, exists in three isolable phases: a layer structure, a hexamer and an amorphous phase; the three are in thermal equilibrium.

Resorcinarenes,† the familiar condensation products of resorcinol and aldehydes,[1] have been subjected to considerable structural investigation. Many years ago, vapour phase osmometry measurements made by Aoyama's group[2] suggested that in benzene or chloroform undecylresorcinarene **1a** formed a hexamer or pentamer, but that in ethanol only the monomer was apparent. In 1996, Mattay *et al.*[3] reported the first X-ray crystal structure of pyrogallene **2a**, showing it to be a cubic hexamer; subsequently, Atwood and MacGillivray[4] published the snub cube crystal structure of methylresorcinarene **1b** and suggested from NMR measurements in benzene that undecylresorcinarene **1a** maintained a snub cube structure in this solvent. Later work by the Atwood,[5] Rebek[6] and Cohen[7] groups all suggests, from evidence based mainly on diffusion coefficients and NOE determinations, that resorcinarenes and pyrogallenes form hexameric capsules under appropriate conditions. However, the X-ray crystal structure[8] of nonylresorcinarene **1c**, obtained by crystallisation from ethanol, shows a layer arrangement with bowl-to-bowl hydrogen bonding and deep interdigitation of the pendant alkyl chains. This combination of interactions also leads to the spontaneous multilayering of **1c** from solution onto planar surfaces.[9] We were prompted to enquire whether the intermolecular association between alkyl chains observed in the layer structure of resorcinarenes such as **1c** could also be seen with a simple straight-chain alkane, *i.e.* whether van der Waals' interactions at the lower rim would lead to binding of small alkyl guest molecules. Although the molecular recognition properties of the aromatic bowl region have been widely investigated, binding to the lower rim has so far not been explored.

To facilitate observation of any such interactions by ^1H NMR spectroscopy, we used oct-1-ene and nonylresorcinarene **1c**, obtained by crystallisation from methanol to give the layer structure. A 10% w/v suspension of **1c** in hot oct-1-ene was taken into solution using THF (one drop per ml). It was planned to allow the solution to evaporate and to check for the incorporation of oct-1-ene using ^1H NMR spectroscopy. However, upon heating the solution close to its boiling point, copious precipitation occurred; on cooling the suspension to room temperature, the precipitate redissolved to give a clear, mobile *solution*. When this solution was again heated to *ca.* 100 °C, precipitation once more occurred and the precipitate again redissolved on cooling. This cycle could be repeated several times. Evaporation of the cold solution at atmospheric pressure gave a solid that we assign the hexamer structure frequently observed by others in related systems. In contrast to the original (layer) material, this solid was freely soluble in octane and chloroform. The ^1H NMR spectrum was identical with that of the original material and no incorporation of either oct-1-ene or THF was detected. Ether, dichloromethane or chloroform could also be used, albeit less effectively, for solubilisation and reversible precipitation, but the phenomenon was not seen with methanol, dioxane, acetone or acetonitrile. These observations suggest that resorcinarenes can exist in a hitherto undetected three-phase system.



1a X = H, R = $(CH_2)_{10}CH_3$
1b X = H, R = CH_3
1c X = H, R = $(CH_2)_8CH_3$
2a X = OH, R = $CH_2CH(CH_3)_2$
2b X = OH, R = $(CH_2)_8CH_3$

In our efforts to characterise the system, neither temperature variable ^1H NMR spectroscopy in CCl_4 nor GPC measurements yielded any coherent information concerning aggregation in solution, and neither electrospray nor MALDI‡ MS on the octene-soluble material showed any evidence of aggregates that survive into the gas phase (Mattay *et al.*[3] had earlier reported the same frustration with these techniques in attempting to identify hexameric structures). However, four further techniques provide useful data concerning our observations. (1) The X-ray powder diffraction pattern of **1c** obtained as the layer structure by crystallisation from methanol (Fig. **1**, top trace) is similar but not identical to that of the octene-soluble material (Fig. **1**, middle trace). In contrast, the X-ray powder photograph of the material which separates when the octene solution is heated (Fig. **1**, bottom trace) clearly shows that it is amorphous. (2) Solid state infrared spectra show striking similarity in the O–H stretching region between the layer material and the amorphous material, but that of the hexamer is substantially different (Fig. **2**). In the hexamer

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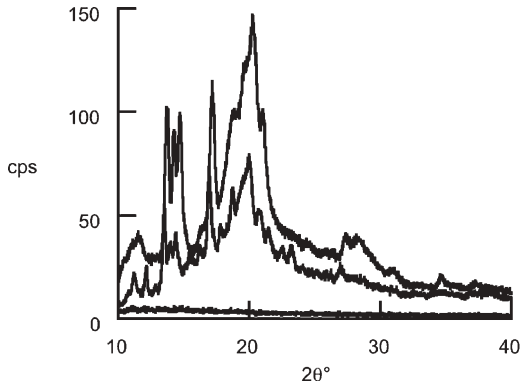


Fig. 1 X-Ray powder diffraction data for solid forms of **1c**. Top line: layer; middle line: hexamer; bottom line: amorphous.

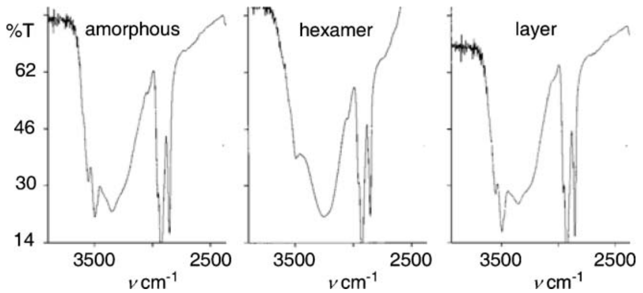
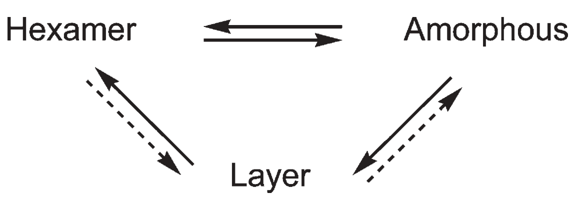


Fig. 2 OH stretching region of infrared spectra (KBr disc) of solid forms of **1c**.

structure the OH groups are all hydrogen bonded, and so this signal is a broadened band centred at a reduced frequency. It appears that the layer and amorphous material have a significant proportion of free OH groups, as shown by the sharper signals at $\sim$3500 cm^{-1}. (3) Differential scanning calorimetry with dual heat–cool cycles from 40 °C to 350 °C on all three samples show no significant differences, although for the amorphous material, a structural change just below the melting point is apparent. (4) Temperature variable quasi-elastic dynamic light scattering measurements on octane solutions of **1c** in its hexameric phase show that at room temperature the hydrodynamic radii of the majority of the particles present is about 2 nm. This dimension is congruent with a hexameric structure with extended pendant chains and is consistent with earlier assignments[2,4–7] of hexameric structures in appropriate solvents. When these octane solutions are heated, much larger particles, with hydrodynamic radii up to 1 μm, appear and precipitation of amorphous material occurs as before. Finally, when these hot solutions are distilled to remove all of the solubilising solvent, the precipitate formed no longer redissolves on cooling and the X-ray powder diffraction pattern shows it to have the crystalline layer structure.

We suggest the following interpretation of these findings. There are three solid phases in thermal equilibrium: the most stable is the layer structure to which the other two revert under appropriate thermal protocols. The hexameric structure is moderately stable for resorcinarenes when long pendant alkyl chains present a non-polar exterior to non-polar solvents. On heating in a non-polar solvent, however, the hexamer dissociates to give the insoluble amorphous phase which is randomly held together by inter-bowl hydrogen bonding and van der Waals' interactions between the pendant chains. In a non-polar solvent, the amorphous phase reverts to the ordered hexamer at lower temperature. When heating is prolonged, the amorphous phase is ultimately converted to the layer phase. The amount of THF needed to cause the phase change from layer to hexamer is less than 1 mol per mol and suggests that hexamer formation is promoted by way of an unstable THF aggregate.

This general behaviour is also observed when the pendant chain is decyl and undecyl but not methyl (**1b**). Much more THF co-solvent is required to dissolve **1b** in octane; this solution does not form a precipitate at high temperature, and subsequent cooling only leads to simple precipitation in direct contrast to the behaviour of **1c**. When the pendant chains are very short as in **1b**, the exterior surface of the hexamer is now much more polar, and this phase is observed only in special conditions.[4] In contrast, we find that pyrogallenes such as **2b** (investigated by others[5–7] as well as by ourselves) are freely soluble in octane and no precipitation occurs on heating. Evidently, the four additional hydroxyl groups stabilise the hexameric structure sufficiently to prevent significant partitioning into the amorphous phase.



We conclude that the layer structure produced by crystallisation from a hydrogen bonding solvent is the most stable for any resorcinarene. In a non-hydrogen bonding solvent, the hexamer becomes the most stable solution structure for resorcinarenes with long pendant chains. The structure is stabilised by 60 internal hydrogen bonds[4] in the absence of competition from a hydrogen bonding solvent. Presentation of 24 pendant alkyl chains in a spherical architecture to a non-polar solvent evidently promotes solution. Atwood has suggested that the network of hydrogen bonds holding the hexamer together relies on the presence of protic solvent molecules to occupy some sites, which in our experiments may be provided by adventitious water. Solvent molecules are also incorporated into the bowl-to-bowl region of the layer structure, and presumably could also be part of the amorphous structure. Formation of the most stable layer structure is clearly slow in a non-polar solvent and the hexamer form is readily isolated at low temperature. However, it is fragile even in a non-polar solvent, and thermal dissociation leads rapidly and reversibly to the amorphous structure stabilised by random hydrogen bonding and van der Waals' interactions. At high temperature, prolonged heating leads to conversion of the amorphous phase to the layer structure. Conversion of the layer form to the hexamer occurs readily in the presence of low concentrations of THF, but it is not clear whether there is direct conversion of hexamer to layer without passing through the amorphous phase (in non-polar solvents) or the monomeric species (in hydrogen bonding solvents).[10]

We thank the University of Sheffield for support.

Notes and references

† In this communication, resorcinarenes are those macrocycles derived from aldehydes and resorcinol; pyrogallenes, from aldehydes and pyrogallol. For clarity, each is named according to the length of alkyl chain pendant from the macrocycle.

‡ Determined directly on the solid; no solvent used.

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