ORIGINAL ARTICLE

# A self-assembling hexameric spheroid with variable degrees of hydration

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**Abstract** The V-shaped racemic compound 4,12-dinitro-6,7,14,15-tetrahydro-6,14-methanocycloocta[1,2-*b*:5,6-*b'*]diquinoline **2** crystallises from solvents of differing water content as a centrosymmetric spheroidal hexamer in the form of a series of isostructural clusters $(2)_6 \cdot (water)_x$ X-ray structures of these crystals in space group $R\bar{3}$ show that they can exhibit an extent of hydration anywhere throughout the composition range $x = 0$ to 1.

**Keywords** Inclusion compounds · Hydrate · X-ray crystal structures · Spheroidal structure · Variable composition

## Introduction

For some time we have been investigating the chemistry of racemic V-shaped diheteroaromatic compounds and, in particular, their inclusion properties [1–6]. Characteristic aspects of this study are our deliberate design strategy for obtaining these host molecules and their normal use of only weak supramolecular synthon attractions [7, 8] (rather than more commonly used strong hydrogen bonding) in their crystal packing arrangements. These studies have been reviewed recently [9, 10].

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One of the less expected outcomes of our investigation was encountered when the derivative **1** was crystallised from methanol or benzene containing traces of water. These experiments yielded the compounds $(1)_6 \cdot (CH_3OH)$ or $(1)_6 \cdot (H_2O)$, respectively [11, 12]. The isostructural crystals formed in the trigonal space group $R\bar{3}$ have a repeat unit comprising an assembly of six host molecules surrounding a small cavity of $\bar{3}$ symmetry in which the guest is located (Fig. 1).

The racemic dinitrodiquinoline **2** can also crystallise in $R\bar{3}$ by formation of a hexameric cluster with concomitant guest inclusion. It does so, however, by using a different mode of assembly and which results in the unusual structural and inclusion properties described in this paper.
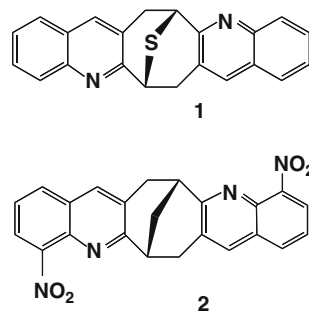


## Experimental

### Structure determination

4,12-Dinitro-6,7,14,15-tetrahydro-6,14-methanocycloocta-[1,2-*b*:5,6-*b'*]diquinoline **2** [13] was crystallised in turn from anhydrous toluene, commercial toluene, commercial dimethyl sulfoxide (DMSO), and acetonitrile–water mixture to yield crystals of $(2)_6 \cdot (H_2O)_x$, where $x = 0.00, 0.48,$

**Fig. 1** Space-filling and framework representations of $(1)_6 \cdot (CH_3OH)$ showing the methanol guest enclosed at a $\bar{3}$ site and surrounded by six host molecules. Host atom code: C *green*, H *light blue*, N *dark blue*, S *yellow*. Only one disorder component of the guest is illustrated for clarity. Both its heavy atoms are coloured *red* and its hydrogens are omitted [11]
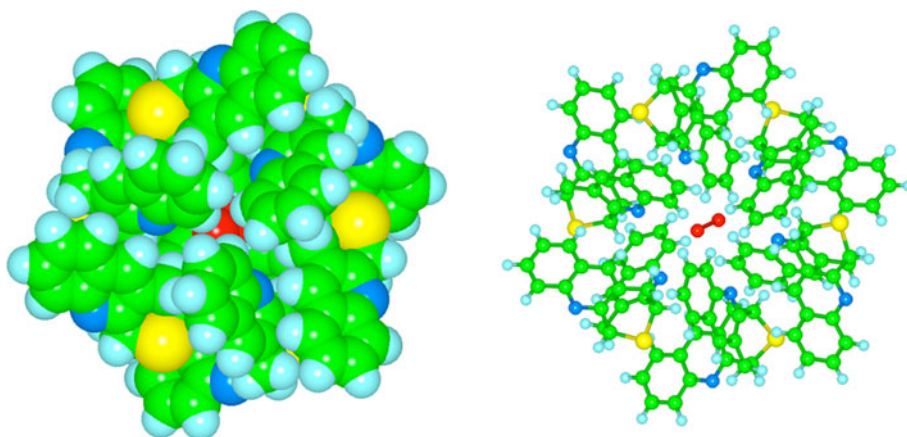


0.78 and 1.00, respectively. Reflection data were measured in $\theta/2\theta$ scan mode with an Enraf–Nonius CAD-4 diffractometer and Mo-K$\alpha$ radiation ($\lambda = 0.7107$ Å). The positions of all atoms in the asymmetric unit were determined by direct phasing (SIR92) [14] with hydrogen atoms included in calculated positions. The occupancy of the water in the structures $x = 0.48$ and 0.78 was refined. Thermal motion of the water was described anisotropically with cross terms U13 and U23 set to zero as required by symmetry. The thermal motion of groups of adjacent atoms was refined as 15 parameter TLX thermal groups (where T is the translation tensor, L is the libration tensor and X is the origin of libration). For all determinations, T = 297 K. There was no crystal decay, and no corrections were applied for absorption. Full details of refinement [15] can be found in the supplementary information.

Crystallographic data (cif) have been deposited with the Cambridge Crystallographic Data Centre (deposition numbers CCDC 680471–680474). Copies can be obtained, free of charge, from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

## Results

Racemic samples of the dinitrodiquinoline derivative **2** can crystallise from anhydrous toluene in two concomitant crystal forms [16, 17]: the lattice inclusion compound $(2)_2 \cdot$(toluene) which is a layer structure in the monoclinic space group $P2_1/n$ [13], and the solvent-free compound **2** in $R\bar{3}$. The structure of the latter comprises hexameric spheroidal assemblies of **2**. If recrystallisation solvents that contain differing amounts of water are used instead, then only a range of isostructural $R\bar{3}$ crystals of composition $(2)_6 \cdot (H_2O)_x$ is produced (where $x$ lies between 0 and 1). Single crystal X-ray determinations for the $x = 0.00$, 0.48, 0.78 and 1.00 compounds were found to only differ significantly in their water occupancy. The spheroidal cluster of **2** lacks sufficient internal void space to enclose the guest, which instead associates at a surface location. The numerical details of the solution and refinement of these four X-ray crystal structures are presented in Table 1.

The hexameric spheroidal assembly of **2** in the compound $(2)_6 \cdot (H_2O)$ is illustrated in Fig. 2. This reveals that three nitro groups (subtended by three molecules of **2** of the same handedness) are proximal at the top, and three others of molecules with opposite handedness at the bottom, of each spheroid. These nitro-rich zones form N–O···H–O hydrogen bonds (O···O distance 3.54 Å) with the water molecules, which can occupy the $\bar{3}$ sites at the top of one spheroid and the bottom of the next along $c$. Complete occupancy ($x = 1$) is achieved if all these sites are used, but partial ($x$ = intermediate) or complete absence ($x = 0$) of water requires essentially no structural alteration to the packing of **2**. We found no evidence for the inclusion of alternative guest types in these tiny void spaces between the nitro groups. Larger potentially hydrogen bonding guests (such as chloroform) may be included by **2** but this requires a completely different host arrangement [13].

If the spheroid assembly is hypothetically sliced in half across the $ab$ plane, and through its inversion centre, then it can be seen (Fig. 3) that there are three identical offset face-face (OFF) interactions [18] present between the *endo-exo* aromatic wing surfaces belonging to pairs of opposite enantiomers. There is also a triplet of identical aryl edge-face (EF) interactions [19] between like enantiomers.

The spheroids $(2)_6$ pack as layers along the $c$ direction. Each layer is made up of a combination of spheroids indicated by pink, blue, and green colours in Fig. 4. Adjacent layers are offset to allow close packing, with three such layers making up the repeat. There are OFF interactions between surfaces of adjacent spheroids. Where two spheroids abut along $c$, and surrounding the six (nitro) N–O···H–O (water) interactions, there are six bifurcated (nitro) O···H–C interactions (d = 2.58 and 2.83 Å) [20, 21]. In addition, there are two different interactions of this type (d = 2.61, 3.15 and d = 2.73, 2.75 Å) that occur between spheroids in adjacent layers.

**Table 1** Numerical details of the solution and refinement of the X-ray structures

| Compound | $(2)_6$ | $(2)_6 \cdot (H_2O)_{0.48}$ | $(2)_6 \cdot (H_2O)_{0.78}$ | $(2)_6 \cdot (H_2O)$ |
|---|---|---|---|---|
| Formula | $C_{23}H_{16}N_4O_4$ | $C_{23}H_{16}N_4O_4(H_2O)_{0.08}$ | $C_{23}H_{16}N_4O_4(H_2O)_{0.13}$ | $C_{23}H_{16}N_4O_4(H_2O)_{0.17}$ |
| Formula mass | 412.4 | 413.8 | 414.7 | 415.5 |
| Space group | $R\bar{3}$ | $R\bar{3}$ | $R\bar{3}$ | $R\bar{3}$ |
| $a, b/\text{Å}$ | 25.983(4) | 26.054(4) | 26.020(4) | 25.994(4) |
| $c/\text{Å}$ | 14.729(4) | 14.740(3) | 14.730(3) | 14.733(4) |
| $V/\text{Å}^3$ | 8612(3) | 8665(2) | 8637(2) | 8621(2) |
| $T/$ °C | 21(1) | 21(1) | 21(1) | 21(1) |
| $Z$ | 18 | 18 | 18 | 18 |
| $D_{calc.}/\text{g cm}^{-3}$ | 1.43 | 1.43 | 1.44 | 1.44 |
| Radiation, $\lambda/\text{Å}$ | MoKα, 0.7107 | MoKα, 0.7107 | MoKα, 0.7107 | MoKα, 0.7107 |
| $\mu/\text{mm}^{-1}$ | 0.099 | 0.094 | 0.100 | 0.100 |
| Scan mode | $\theta/2\theta$ | $\theta/2\theta$ | $\theta/2\theta$ | $\theta/2\theta$ |
| $2\theta_{max.}/°$ | 50 | 46 | 50 | 50 |
| No. of intensity meas. | 3370 | 2691 | 3383 | 3375 |
| Criterion for obs. ref. | $I/\sigma(I) > 2$ | $I/\sigma(I) > 2$ | $I/\sigma(I) > 2$ | $I/\sigma(I) > 2$ |
| No. of indep. obsd. ref. | 1870 | 1466 | 2138 | 1817 |
| No. of reflections ($m$), | 1870 | 1466 | 2138 | 1817 |
| Variables ($n$) in final ref. | 165 | 148 | 169 | 167 |
| $R = \sum^m |\Delta F| / \sum^m |F_o|$ | 0.054 | 0.066 | 0.056 | 0.051 |
| $R_w = [\sum^m w |\Delta F|^2 / \sum^m w |F_o|^2]^{1/2}$ | 0.058 | 0.072 | 0.067 | 0.055 |
| $s = [\sum^m w |\Delta F|^2 / (m-n)]^{1/2}$ | 1.55 | 1.49 | 1.79 | 1.47 |
| Crystal decay | none | none | none | none |
| Min., max. trans. coeff. | – | – | – | – |
| $R$ for mult. meas. | 0.015 | 0.072 | 0.029 | 0.016 |
| Largest peak in final diff. map/e $\text{Å}^{-3}$ | 0.51 | 0.53 | 0.34 | 0.45 |
| CCDC no. | 680471 | 680472 | 680473 | 680474 |



**Fig. 2** X-ray crystal structure of the spheroid $(2)_6 \cdot (H_2O)$ projected in the *ab* (*left*) and *ac* (*right*) planes. The carbon atoms of the two enantiomers are coloured *green* or *orange*. Atom code: H *light blue*, N *dark blue*, O *red*. The water molecule is shown as a *black sphere*
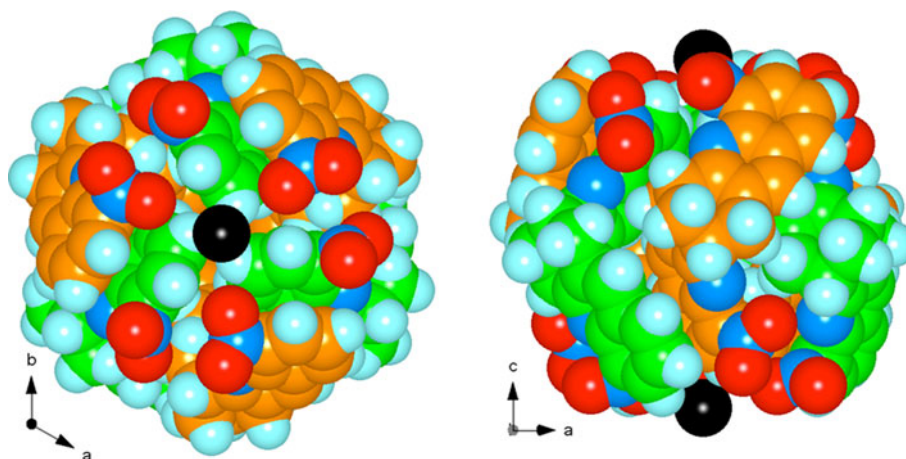
## Discussion

It is a most unusual event for an inclusion host to retain the same packing arrangement with, and without, the presence of its guest molecules. It is also rare for a small inclusion host to include guests in variable proportions from zero- to full-occupancy [22–25]. We are unaware of any prior instance where both these conditions have been observed for a lattice inclusion host over its entire range of zero- to full-occupancy.

For example, β-cyclodextrin crystallises in space group $P2_1/c$ containing variable numbers of disordered water molecules, such as (host)·(water)$_{11.56}$, (host)·(water)$_{11.89}$, and (host)·(water)$_{12.26}$ [26], but the anhydrous crystal
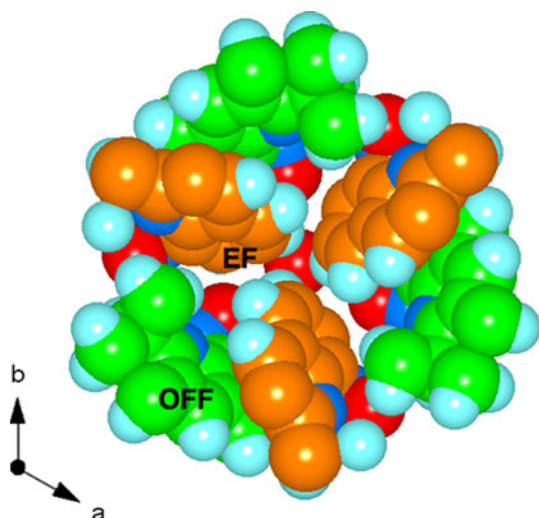
**Fig. 3** One spheroid assembly with its top half sliced off horizontally. The aromatic OFF and EF interactions present between the six half-molecules of **2** are clearly visible. Equivalent interactions are also present in the removed top half of the spheroid
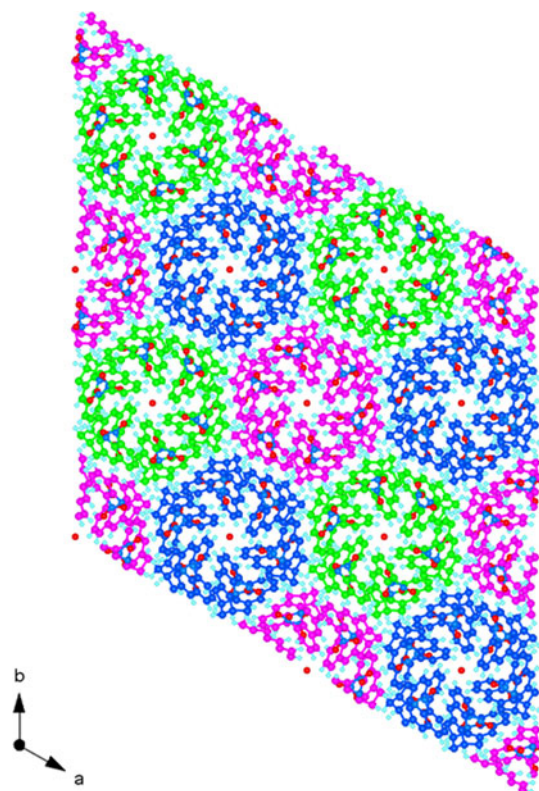


**Fig. 4** The crystal structure of **2** projected in the *ab* plane to show the packing of the spheroid assemblies. Layers of spheroids (comprising a combination of close-packed *pink*, *blue*, and *green* spheroids) repeat along the *c* direction

structure is unknown. In addition, Stezowski et al. have reported isostructural crystals of a substituted β-cyclodextrin that contain 1.08 or zero water molecules [27]. In both these instances, however, the cyclodextrin host is a permanently bonded receptor unit, rather than being a self-assembling cluster.

Deoxycholic acid forms variable composition lattice inclusion compounds with acetophenone in space group $P2_12_12_1$:(host)·(acetophenone)$_{0.4}$ and (host)·(acetophenone)$_{1.0}$ [28], but perhaps the closest analogues are the tunable clathrates described by Caira and Nassimbeni [29]. When a certain diol was exposed to mixtures of dimethylformamide (DMF) and dimethyl sulfoxide (DMSO), they found that the stepwise series of five stoichiometric inclusion compounds of composition (host)·(DMF)$_n$·(DMSO)$_{4-n}$ was produced in space group $P\bar{1}$ (where $n$ = integral values between 0 and 4).

The self-assembly of the spheroid $(2)_6$ from its individual building blocks is shown diagrammatically in Fig. 5. Each arrow represents a $\bar{3}$ symmetry operation (a 120° rotation, combined with inversion provided by the opposite enantiomer). Assembly of this novel centrosymmetric spheroid $(2)_6$ is very different from that normally encountered in our diquinoline studies [1–6]. It employs three molecules of each enantiomer of **2**, and uses only aryl-aryl synthons in its formation.

It is notable that two concomitant crystal forms were obtained when **2** was crystallised from anhydrous toluene [13] but that only one was produced in the presence of small quantities of water. Thus, although inclusion of the guest water molecule is not obligatory ($x = 0$), its partial ($x$ = intermediate) or complete ($x = 1$) occupancy provides additional stabilisation of the inter-spheroid packing by means of the strong hydrogen bonding. In contrast, the cluster formed by **1** is only stabilised by means of weaker C–H···O hydrogen bonding between the host and the guest species.

In anhydrous solution there will be competing equilibria between the various very weak intermolecular attractions. Thus solvated versions of the monomer, adducts such those shown in Fig. 5, and the alternative crystal nucleation assemblies, are in competition. When traces of water are present, these guest molecules are sequestered by the low concentration of host hexamers to form hydrated crystals involving stronger attractive forces and this results in compounds with a slightly lower lattice energy. A switch to just one crystal form therefore takes place.

The host cluster formed by **2** shows structural similarity to the host capsule formed by **1**. The latter also self-assembles into a hexameric spheroid structure involving three (+)-molecules on one side, and three (−)-isomers on the opposite side, of the spheroid. In the case of host **1** these two trimers associate, leaving a small central cavity, by means of a sixfold phenyl embrace [11, 30]. For **2**, the two trimers interdigitate much more fully and thereby produce a cluster with no void space, rather than a capsule.

**Fig. 5** Diagrammatic representation of the assembly of the (**2**)₆ spheroidal cluster from its two enantiomeric components (*green* or *orange* carbons)
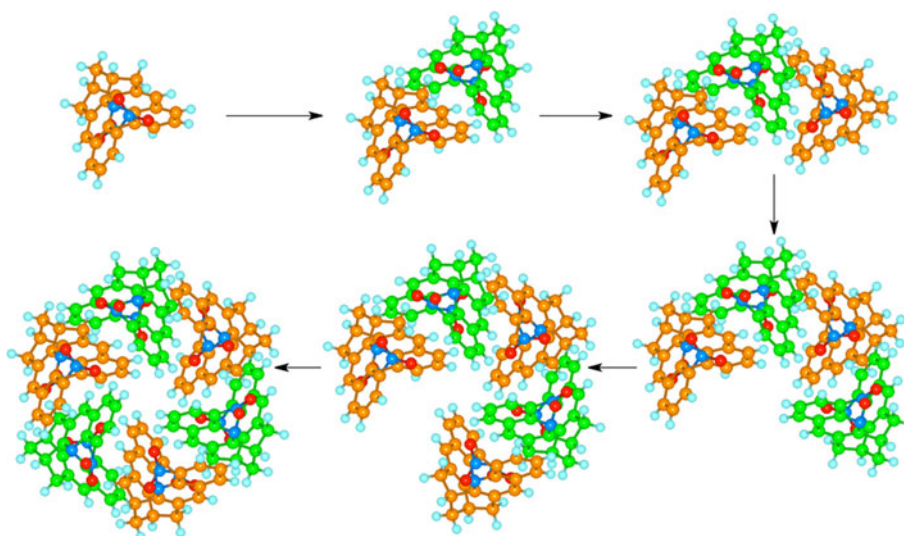


The self-assembly process of complementary molecular building blocks into molecular capsules and spheroidal aggregates is generally driven by carefully chosen and positioned hydrogen bonding, ionic, or metal coordination functionalities [31, 32]. The behaviour of the diquinolines **1** and **2** demonstrates that the use of weaker supramolecular interactions can also succeed. With our current level of prediction of weak interaction behaviour, however, any such successes are likely to be serendipitous rather than designed.

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