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Gauche and staggered forms of diethylamine in solvates of 1,5-dichloro-*cis*-9,10-diethynyl-9,10-dihydroanthracene-9,10-diol. A case of conformational pseudopolymorphism?

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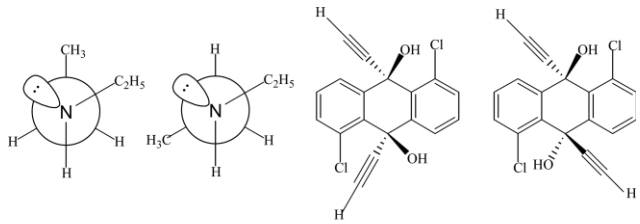
Diethylamine has been trapped in its less stable gauche conformation in a solvate of the title diol; the staggered conformation, which is *ca.* 4 kJ mol^{-1} more stable, is found in another solvate of the same host.

Solvation is an entropically disfavoured process during crystallization, being observed in only around 15% of non-ionic organic compounds in the Cambridge Structural Database.[1] More rare is when the crystal lattice of a solute molecule (host) traps a conformationally flexible solvent molecule (guest) in one of its higher energy conformations.[2] In none of these cases, however, has a solvate with the solvent in a more stable conformation in the same host ever been reported. We report here the unprecedented observation of both gauche and staggered rotamers of diethylamine, **1a** and **1b**, in two distinct 1:1 solvates, **2a** and **2b**, of the host compound 1,5-dichloro-*cis*-9,10-diethynyl-9,10-dihydroanthracene-9,10-diol, **3**. These solvates were isolated only after an analysis of the crystal structure of unsolvated **3**, which is also reported in this communication.



1a **1b** **3** **4**

2a = (**1a**).(**3**) **2b** = (**1b**).(**3**)

Isolation of single crystals of **2a**, **2b** and **3** was achieved only with careful experimentation. Hydroxy ethynylation of 1,5-dichloroanthraquinone (TMSC≡CLi, KOH) gave predominantly the *trans*-isomer, **4**, with the amount of *cis*-isomer, **3**, being so small that it could never be separated satisfactorily with chromatography. When the crude product was crystallized from 1:1 acetone–benzene, two different crystal morphologies were obtained, prisms and needles, corresponding to the *cis*- and *trans*-isomers, **3** and **4**, respectively.†

In the *cis*-diol **3** (Fig. 1), one of the hydroxyl groups forms an intramolecular O–H···Cl–C hydrogen bridge (*D* 3.04 Å, *d* 2.32 Å, θ 129°), while the other donates to an intermolecular O–H···π interaction (3.44 Å, 2.78 Å, 144°; to triple bond midpoint), with some synthon features seen previously.[3] There is an intermolecular C–H···O–H (3.08 Å, 2.13 Å, 145°), and also an intermolecular C–H···Cl–C bridge (3.67 Å, 2.72 Å, 146°). However, there is no evidence of an O–H···O–H hydrogen bond.

We had noted previously, that an awkward hydrogen bond pattern in *trans*-diol **4** results from the sterically constrained environment of hydroxyl and ethynyl groups, and that this uncomfortable pattern can relax *via* solvation.[4] Noting further that the packing in *cis*-diol **3** is reminiscent of that in **4**, we crystallized the crude mixture of isomers from Et_2NH, since organic bases were found to promote solvation very effectively.[3] Crystals with different morphologies, cuboid and plate-like, were again obtained and two different crystals from this batch with clearly different unit cells were found to correspond to the 1:1 solvates **2a** and **2b**.‡

Fig. 2 shows the conformations (**1a** and **1b**) of Et_2NH in solvates **2a** and **2b**. The dihedral angle between the two best planes in the gauche and staggered conformers is 70 and 171°, respectively. In all seven Et_2NH solvates in the Cambridge Structural Database (version 5.25, November 2003), the molecule adopts the more stable staggered conformation.[5] The energy difference between the staggered and the gauche conformations was estimated to be 3.26 kJ mol^{-1} (DFT) and 5.06 kJ mol^{-1} (HF). In order to obtain a rationale as to why the two crystal forms were obtained, the packing in these forms was examined more carefully.

The role of solvent in improving the hydrogen bond arrangement in **3** is without doubt. In solvate **2a** (Fig. 3), the (gauche) Et_2NH

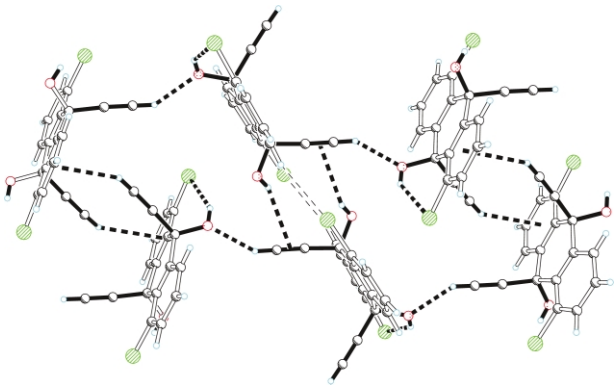


Fig. 1 Crystal structure of *cis*-diol **3**. Notice the absence of O–H···O interactions.

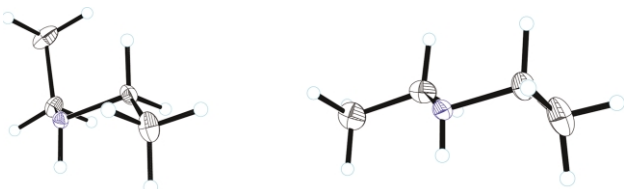


Fig. 2 Gauche, **1a**, (left) and staggered, **1b**, (right) conformations of Et_2NH in solvates **2a** and **2b**.

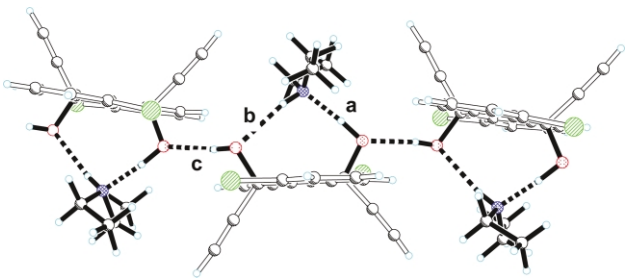


Fig. 3 Crystal structure of solvate **2a**. Notice how the solvent enters the space between hydroxyl groups in the same molecule. Notice also the infinite cooperative arrangement of O–H···N–H···O–H···O interactions (**a**, **b**, **c** respectively in the figure) that is formed thereby.

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molecule links the intramolecular hydroxyl groups of the diol and there is an infinite cooperative array of O–H···N (2.677 Å, 1.70 Å, 172.5°), N–H···O (3.178 Å, 2.19 Å, 166.4°) and O–H···O (2.782 Å, 1.81 Å, 170.5°) interactions. In solvate **2b** too, the (staggered) Et_2NH molecule performs the same function (Fig. 4). The cooperative array is topologically the same but the metrics are different: O–H···N (2.709 Å, 1.72 Å, 175.5°); N–H···O (3.350 Å, 2.39 Å, 156.8°); O–H···O (2.764 Å, 1.78 Å, 173.9°). While the O–H···N and O–H···O interactions are comparable in **2a** and **2b**, the N–H···O bridge is distinctly longer in **2b** (interaction **e** is longer than interaction **b**). This lengthening of the N–H···O interaction seems to arise from steric hindrance between one of the ethyl groups of the solvent and the aromatic ring of the diol. When the methyl fragment in this ethyl group swings away from the ring in the gauche conformation, steric hindrance is reduced and the N–H···O bridge can become shorter. We suggest that the N–H···O lengthening in **2b** is balanced by the solvent being in its most stable staggered conformation. Alternatively, one might say that the more energetic gauche conformation is stabilized in solvate **2a** by a better N–H···O hydrogen bond. All other packing features in the two solvates are nearly comparable and we feel that it is reasonable to equate the energy difference between rotamers of *ca.* 4 kJ mol^{-1} with a difference of around 0.3 Å in an N–H···O hydrogen bond.[6]

Finally, can one refer to these solvates as pseudopolymorphs? The term *pseudopolymorph* was originally suggested by McCrone[7] and it has become standard in the pharmaceutical literature.[8] However, it is not generally favoured in the chemical literature.[9] Its usage suggests that there are two structures, the unsolvated and solvated forms with different crystal structures but that because the systems being considered are different chemical entities, the 'polymorphism' is not real but 'pseudo'. However, a compound and its solvate must necessarily have different crystal structures, and since they are not chemically identical it is argued that there is no question of polymorphism, pseudo or otherwise.[10]

We note that difficulties arise when the term *polymorph* is applied to crystals that contain more than one chemical component.[11] This is because there are too many structural variations in mixed crystals ranging from a situation wherein one of the components is an innocuous bystander in the packing to one wherein both components are essential to the crystal packing. In the present case, **2a** and **2b** may be called polymorphs according to currently accepted definitions. But the major features in the packing of the major component are virtually the same. Does the term *polymorph* do full justice to the chemical situation encountered? Another possibility for **2a** and **2b** is to call them *conformational polymorphs*.[12] But is this term appropriate when the major component has the same conformation in both forms? Any discussion of nomenclature is, in the end, subjective but if we refer to **2a** and **2b** as pseudopolymorphs of **3**, a way of sharpening this definition, given that it is the minor component in these solvates that has the conformational variations, is to refer to them as *conformational pseudopolymorphs*.[13]

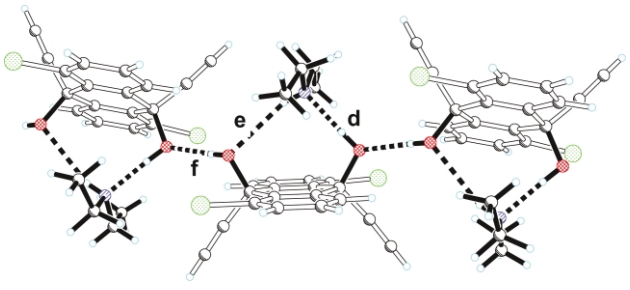

Fig. 4 Crystal structure of solvate **2b**. Compare this with Fig. 3. The cooperative array is formed with interactions, **d**, **e** and **f**.

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Notes and references

† Data were collected using a Bruker SMART 1K-CCD area detector. *Crystal data*: for **2a**: $(C_{18}H_{10}Cl_2O_2)\cdot(C_4H_{11}N)$, M = 402.30, monoclinic, a = 8.1794(2), b = 13.6483(4), c = 18.0272(5) Å, α = 90, β = 96.984(1), γ = 90°, V = 1997.53(9) Å^3, T = 120(2) K, space group $P2_1/n$, Z' = 1, μ(Mo-Kα) = 0.342 mm^{-1}, size 0.26 × 0.20 × 0.10 mm. 19 907 total reflections of which 3925 were independent, 3353 observed [$I > 2\sigma(I)$]. Refinement against F^2 with 328 parameters, R_1 [$I > 2\sigma(I)$] = 0.0460. For **2b**: $(C_{18}H_{10}Cl_2O_2)\cdot(C_4H_{11}N)$, M = 402.30, orthorhombic, a = 14.955(3), b = 13.659(3), c = 19.433(4) Å, α = 90, β = 90, γ = 90°, V = 3969.4(14) Å^3, T = 95(2) K, space group $Pbca$, Z' = 1, μ(Mo-Kα) = 0.344 mm^{-1}, size 0.22 × 0.18 × 0.06 mm. 41 925 total reflections of which 4557 were independent, 3539 observed [$I > 2\sigma(I)$]. Refinement against F^2 with 328 parameters, R_1 [$I > 2\sigma(I)$] = 0.0656. For **3**: $C_{18}H_{10}Cl_2O_2$, M = 329.16, monoclinic, a = 7.4731(2), b = 12.5163(3), c = 16.2952(5) Å, α = 90, β = 100.565(1), γ = 90°, V = 1498.34(7) Å^3, T = 120(2) K, space group $P2_1/n$, Z' = 1, μ(Mo-Kα) = 0.436 mm^{-1}, size 0.24 × 0.22 × 0.14 mm. 16 656 total reflections of which 3431 were independent, 2430 observed [$I > 2\sigma(I)$]. Refinement against F^2 with 239 parameters, R_1 [$I > 2\sigma(I)$] = 0.0460. CCDC 225589–225591. See http://www.rsc.org/suppdata/cc/b3/b316270b/ for crystallographic data in .cif or other electronic format.

‡ The Et_2NH solvate of **4** was also isolated in this experiment: $(C_{18}H_{10}Cl_2O_2)\cdot(C_4H_{11}N)$, M = 402.30, triclinic, a = 8.8625(4), b = 8.8881(5), c = 9.5190(5) Å, α = 109.609(2), β = 116.003(2), γ = 90.739(2)°, V = 623.39(6) Å^3, space group $P\bar{1}$, Z' = 0.5 and the O–H···N–H···O–H hydrogen bond pattern is similar to that in the aminophenols. See V. R. Vangala, B. R. Bhogala, A. Dey, G. R. Desiraju, C. K. Broder, P. S. Smith, R. Mondal, J. A. K. Howard and C. C. Wilson *J. Am. Chem. Soc.*, 2003, **125**, 14 495. The crystal structure of this solvate will be published elsewhere.

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