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ARTICLE TYPE

Mechanochemical and solution-based cocrystallization of 9,10-phenanthrenequinone and thiourea

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We have synthesized the first known cocrystal of 9,10-phenanthrenequinone utilizing both liquid-assisted mechanochemical synthesis and crystallization from a solution.

In the past years, cocrystallization has become a proven and accepted way of modifying physical and chemical properties, such as colour¹, hygroscopicity², UV/Vis absorption³, thermal stability and solubility⁴, of solid materials. Cocrystals are usually obtainable by either crystallization from a solution⁵ containing the desired reactant and coformer, or, more recently, by mechanochemical methods such as neat grinding (NG) or liquid-assisted grinding (LAG).⁶ Of the two methods, mechanochemical synthesis is preferable because it sidesteps having to find a solvent or solvent mixture that can dissolve the reactants equally, is generally much shorter with very high yield, and allows for a much better scale-up without having to significantly increase the amounts of solvent used.⁷ Both NG and LAG have been established as fast and efficient screening methods for desired crystal forms: cocrystals, salts, solvates and polymorphs.⁸

The compound we were interested in is 9,10-phenanthrenequinone (**phen**), a polinuclear diketone (Fig. 1) with an intense yellow colour. Up until now, **phen** and derivative structures have mostly been studied and used as chelating agents⁹ or as a pigment.¹⁰ Generally, the quinones of polycyclic aromatic hydrocarbons are abundant in all burnt organic materials, e.g. automobile exhaust and cigarette smoke.¹¹ The title compound, **phen**, is a major quinone in diesel exhaust. In the context of biochemistry, many studies have focused on mutagenicity and the metabolic pathways of **phen**.¹² It was reported that **phen** causes oxidative protein modification in living cells and accelerates malignant progression of lung cancer cells.^{12c} A cursory search of the Cambridge Structural Database¹³ (CSD) based on the ability of the cyclic carbonyl oxygen atom (a structural motif present in **phen**) to act as a hydrogen bond acceptor has resulted in 50 000 hits. Restraining the search further, to cyclic 1,2-diketones interacting with nitrogen as a hydrogen bond donor, has resulted in 928 hits. Of those, 514 structures correspond to cocrystals. In spite of the fact that ketones are a valuable group of synthons in crystal engineering, no cocrystal structures have been published for **phen**, unlike 1,10-phenanthroline-5,6-dione, a compound that is geometrically and chemically mostly analogous to **phen**, and

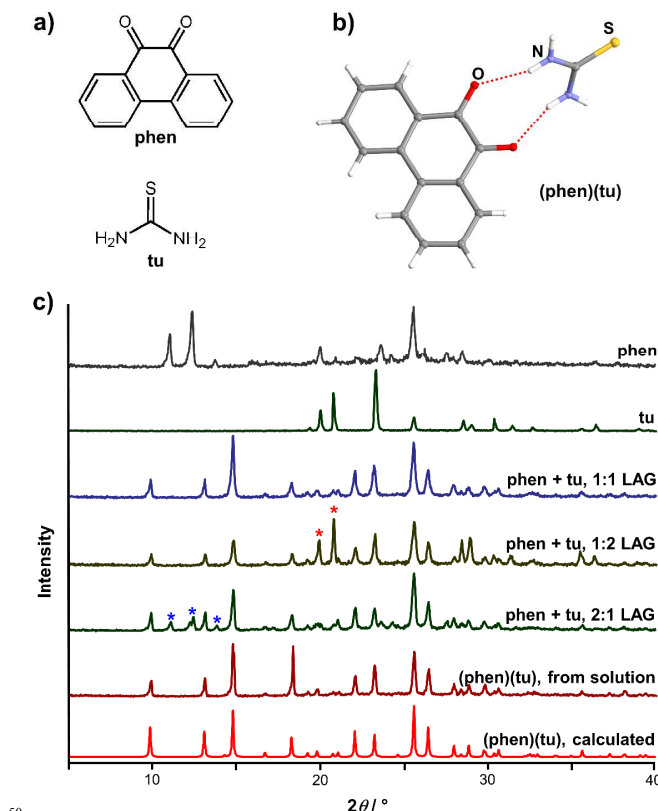


Figure 1. (a) Structures of 9,10-phenanthrenequinone (**phen**) and thiourea (**tu**), (b) The structure obtained as a result of the single crystal X-ray diffraction experiment, (c) Comparison of reactant, mechanochemical product and calculated powder patterns. Residual maxima of reactants are marked.

a reported hydrogen and halogen bond acceptor.

Herein we report the cocrystal of **phen** which has been synthesized by liquid-assisted grinding. We were inspired to pursue mechanochemical experiments in our study by a recent report of Bučar and co-workers,¹ who described cocrystals of fluorescein with pyridyl-based cocrystal formers. They presented proof of principle that optical properties of (poorly soluble) colourants can be altered *via* mechanochemical cocrystallisation, and described the efficiency of mechanochemistry in the screening for and preparation of cocrystals of such materials. In our work as a good counterpart to **phen** we have selected thiourea (**tu**), a

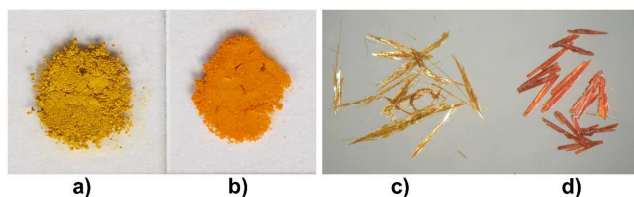


Figure 2. Photographs of **phen** and cocrystal samples: a) powder of **phen**; b) powder of **(phen)(tu)** obtained by LAG; c) crystals of **phen** and d) crystals of **(phen)(tu)**.

5 molecule with a significant propensity towards generating hydrogen bonded structures. To the best of our knowledge, this is the first structurally characterised cocrystal of **phen**. To observe LAG mechanosynthesis, as well as to facilitate the characterisation of the new cocrystal by single-crystal X-ray
10 diffraction, LAG experiments were accompanied by crystallization from the reactant solution. All reactants and products have been characterised by means of powder X-ray diffraction (PXRD), differential scanning calorimetry (DSC) and Fourier-transform infrared spectroscopy (FTIR). As a
15 means to explore the stoichiometric ratio of **phen** and **tu**, we first attempted the mechanochemical synthesis of **(phen)(tu)** by LAG of **phen** and **tu** in the stoichiometric ratio 1:1, 1:2 and 2:1, respectively, in the presence of a small amount of acetonitrile. Milling was conducted in a Retsch MM200 mill
20 using a stainless steel milling assembly (see ESI). LAG of **phen** and **tu** in a 1:1 stoichiometric ratio for 30 minutes afforded powder material of PXRD pattern identical to that of crystals prepared by the solution method. In the solution experiment, equimolar amounts of **phen** and **tu** have been
25 dissolved in a hot mixture of ethanol and benzene. The solutions were left at room temperature, and the product crystallized upon cooling. The measured PXRD patterns of **(phen)(tu)** obtained by both methods, grinding and from the solution, are in good agreement with those calculated from
30 single crystal data, thus confirming that both products were obtained as a pure single phase (Fig. 1). The powder obtained by grinding and crystals are orange, markedly different from the intensely yellow **phen** and white **tu** (Fig. 2). The other two out of three mechanochemical experiments, LAG of **phen** and
35 **tu** in the stoichiometric ratio 1:2 and 2:1, resulted in a mixture containing **(phen)(tu)** cocrystals and solid reactants, as evidenced by PXRD (Fig. 1)

The **(phen)(tu)** cocrystal crystallizes in the orthorhombic system with four formula units per unit cell. The molecular
40 structure of cocrystal with the atom numbering scheme is given in Fig. S1 (see ESI). Each **phen** molecule is associated with a **tu** molecule *via* a N-H...O hydrogen bond (N...O distance: 3.044 Å, N-H...O angle 154°; $1/2 - x, y - 1/2, z$) forming a 1:1 molecular complex through the $R^2_2(9)$ hydrogen
45 bond motif,¹⁴ Fig. 1. Geometry of **phen** is not consistent with that normally observed for the pure **phen** crystal.¹⁵ The normally planar structure of **phen** gets twisted about 13 degrees around the least torsionally restricted central ring. The crystal structure of **(phen)(tu)** can be described by
50 association of 1:1 molecular complexes to hydrogen bonded chains, assisted by N-H...S hydrogen bonds (N...S distance: 3.403 Å; $x, 1 - y, z - 1/2$) between **tu** molecules forming a $R^2_2(8)$ motif. Also, 1:1 molecular complexes are associated

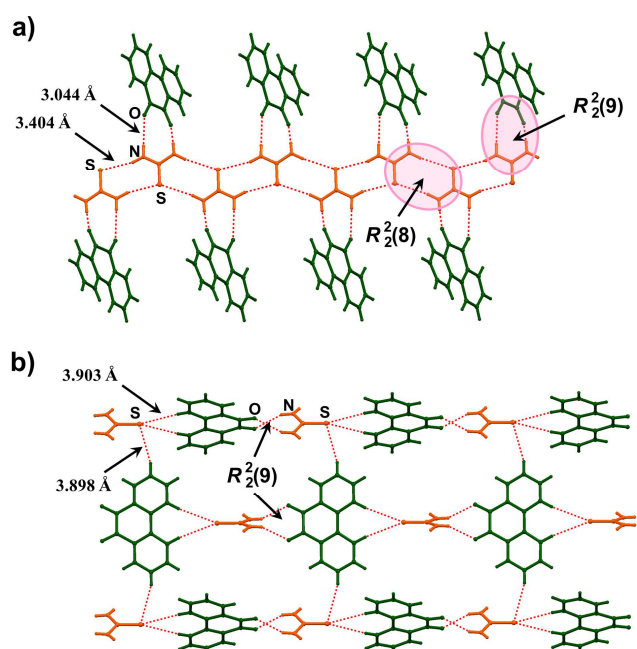


Figure 3. The crystal structure of **(phen)(tu)**: (a) chains of hydrogen bonded molecules, *via* N-H...O and N-H...S interactions, and (b) C-H...S interactions and N-H...O hydrogen bond motifs that give rise to the two-dimensional network.

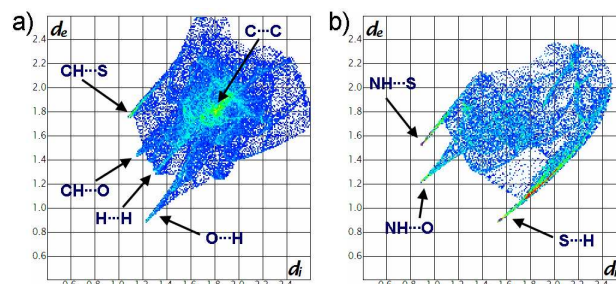


Figure 4. Two-dimensional fingerprint plot derived from the Hirshfeld surface of the **phen** molecule (a) and **tu** molecule (b) in the **(phen)(tu)** cocrystal.

into a 2-dimensional network *via* C-H...S interactions (C...S distance: 3.898 Å and 3.903 Å; $1 - x, 1 - y, 1 - z$ and $x + 1/2, y - 1/2, 3/2 - z$) between aromatic carbon atoms of **phen** and sulfur in **tu** (Fig. 3). The overall structure results from the combination of such interactions and it is additionally
70 stabilized with C-H...O hydrogen bonds (C...O distance: 3.439 Å; $3/2 - x, y - 1/2, z$), Fig. 5. Also, the described interactions can be observed by close analysis of the two-dimensional fingerprint plot derived from the Hirshfeld
75 surface¹⁶ of the **(phen)(tu)** cocrystal components (Fig. 3). The cocrystal as a whole is densely packed (Fig. 5) and a notable detail of the cocrystal structure is the fact that each sulfur is a hexafurcated hydrogen bond acceptor.

To investigate the non-covalent interactions within the cocrystal, FTIR spectra of pure **phen** and **(phen)(tu)** were recorded (see ESI). Their spectra show strong bands corresponding to the C-O stretching of **phen** carbonyl group
80 at about 1670 cm⁻¹ (1676 cm⁻¹ for **phen** and 1650 cm⁻¹ for cocrystal). The C-O stretching for **(phen)(tu)** is expectedly at a lower frequency than that in pure **phen** due to the

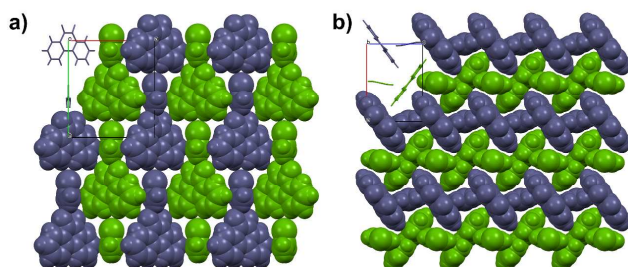


Figure 5. Assembly of hydrogen-bonded chains of **(phen)(tu)** into layers viewed along the *c* axis (a) and *b* axis (b). For clarity, adjacent chains are colour-coded blue and green.

involvement of C–O groups in strong intermolecular hydrogen bonds. The DSC curve of **(phen)(tu)** shows one endothermic peak at 175 °C (34 kJ mol⁻¹), which corresponds to the cocrystal melting point (see ESI). It is at a lower temperature than that of pure reactants, **phen** (206 °C) and **tu** (179 °C).

In summary, we have presented the first example of a **phen** cocrystal obtained from the reaction of **phen** and **tu** in a 1:1 molar ratio by solid-state synthesis. Also, the **(phen)(tu)** cocrystal has been prepared by crystallization from a solution, despite the low solubility of **phen** in most organic solvents. Single-crystal X-ray analysis of **(phen)(tu)** revealed an interesting *R*₂²(9) hydrogen bond motif formed between **phen** and **tu** molecules *via* N–H···O hydrogen bonds. Besides exploring synthetic routes we have also found that the resulting powder material and crystals exhibit orange colour, markedly different from the intensely yellow **phen**. Crystal structure analysis demonstrates that introduction of **tu**, as a cocrystal former, can change the molecular structure of **phen** as well as the geometric arrangement of the chromophore in the cocrystal. A number of recently reported cocrystallizations of organic solid chromophores^{1,3} suggest that cocrystallization provides a facile way to develop and design new types of solid organic materials with desirable optical properties, *e.g.* luminescence, emission, colour, UV/VIS absorption. The described results are important in the context of supramolecular synthesis, as well as solid-state and materials chemistry, and could have significant implication for the future design and optimization of colourants, dyes and pigments, *via* mechanochemical cocrystallization.

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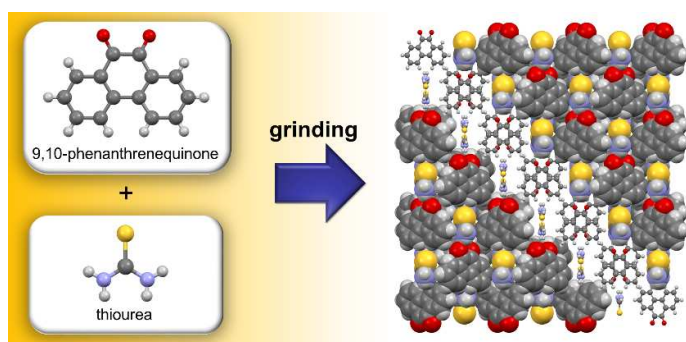
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‡ Electronic Supplementary Information (ESI) available: details of mechanochemical and solution syntheses, instrumental analysis, PXRD, FTIR, DSC data. CCDC 1409744 contains crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif. See DOI: 10.1039/b000000x/

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