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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 few years, cocrystallization has become a proven and accepted way of modifying the physical and chemical properties, such as colour,[1] hygroscopicity,[2] UV/Vis absorption,[3] thermal stability and solubility,[4] of solid materials. Cocrystals are usually obtainable by either crystallization from a solution[5] 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 amount of solvent used.[7] Both NG and LAG have been established as fast and efficient screening methods for desired crystal forms such as 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 agents[9] or as pigments.[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 the mutagenicity and 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 in the Cambridge Structural Database[13] (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.
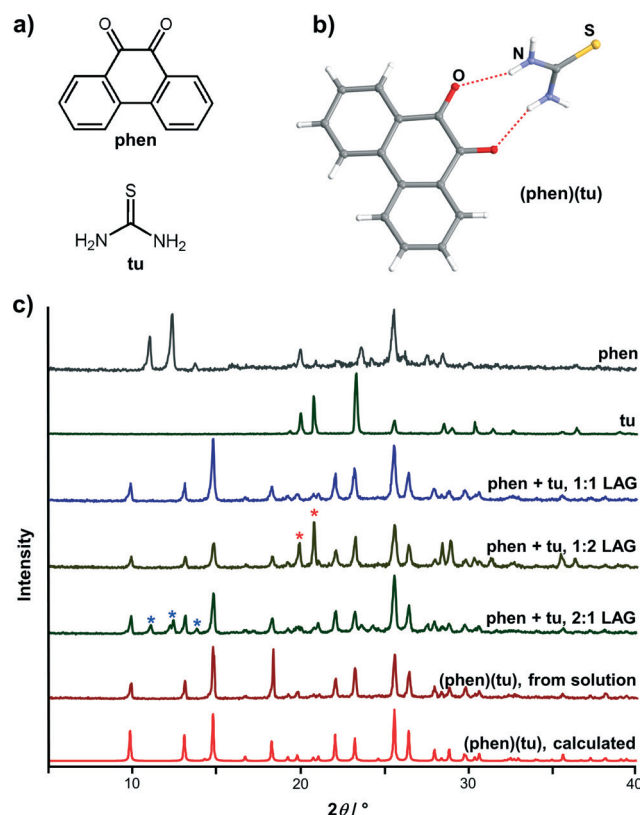

Fig. 1 (a) Structures of 9,10-phenanthrenequinone (phen) and thiourea (tu), (b) the structure obtained as a result of the single crystal X-ray diffraction experiment, (c) comparison of reactant, mechanochemical product and calculated powder patterns. Residual maxima of the reactants are marked.

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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 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 a proof of principle which states that the 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 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 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 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 stoichiometric ratios 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 using a stainless steel milling assembly (see the ESI†). LAG of **phen** and **tu** in a 1:1 stoichiometric ratio for 30 minutes afforded a powder material with a PXRD pattern identical to that of the crystals prepared by the solution method. In the solution experiment, equimolar amounts of **phen** and **tu** have been 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 single crystal data, thus confirming that both products were obtained as a pure single phase (Fig. 1). The powder obtained by grinding and the crystals are orange, markedly different from the intensely yellow **phen** and white **tu** (Fig. 2). The other two out of the three mechanochemical experiments, LAG of **phen** and **tu** in stoichiometric ratios 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 structure of the cocrystal with the atom numbering scheme is
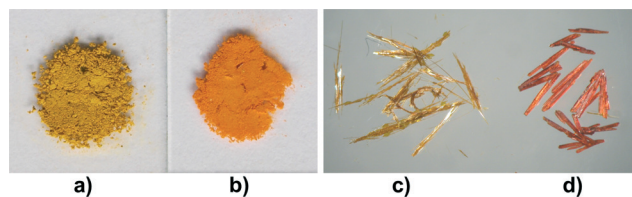

Fig. 2 Photographs of **phen** and cocrystal samples: a) powder of **phen**; b) powder of (**phen**)(**tu**) obtained by LAG; c) crystals of **phen** and d) crystals of (**phen**)(**tu**).

given in Fig. S1 (see the 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 bond motif[14] (Fig. 3). The geometry of **phen** is not consistent with that normally observed for the pure **phen** crystal.[15] The normally planar structure of **phen** gets twisted by about 13 degrees around the least torsionally restricted central ring. The crystal structure of (**phen**)(**tu**) can be described by association of 1:1 molecular complexes with 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 with 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 the 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 stabilized by C–H···O hydrogen bonds (C···O distance: 3.439
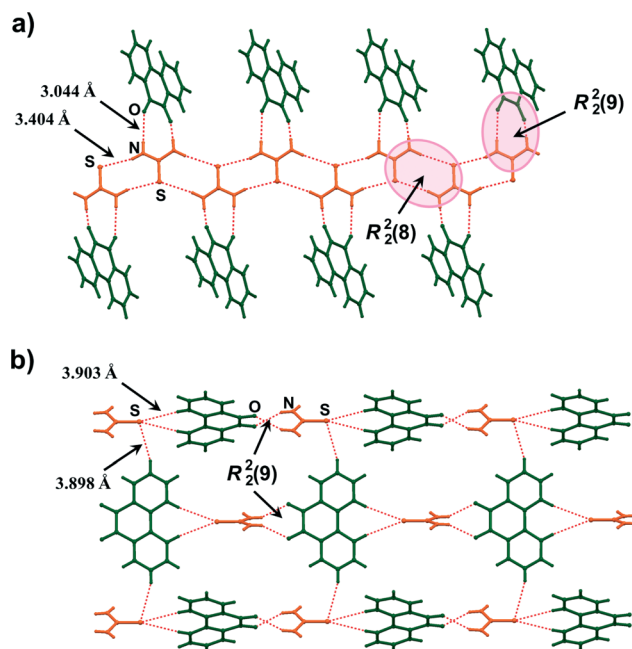

Fig. 3 The crystal structure of (**phen**)(**tu**): (a) chains of hydrogen-bonded molecules *via* N–H···O and N–H···S interactions, and (b) C–H···S interactions and N–H···O hydrogen bond motifs that give rise to the two-dimensional network.
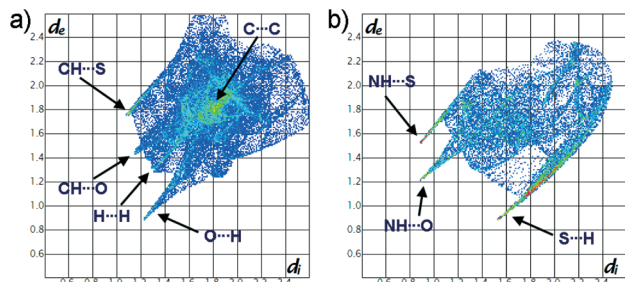
Fig. 4 Two-dimensional fingerprint plot derived from the Hirshfeld surface of the **phen** molecule (a) and **tu** molecule (b) in the (**phen**)(**tu**) cocrystal.
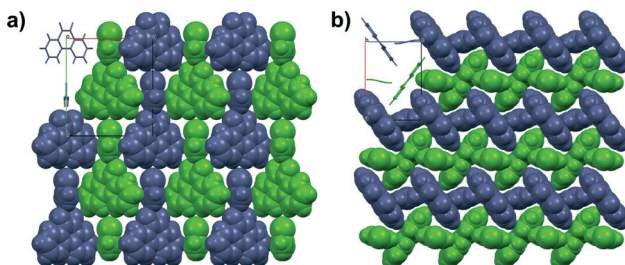

Fig. 5 Assembly of hydrogen-bonded chains of (**phen**)(**tu**) into layers viewed along the *c* axis (a) and *b* axis (b). For clarity, adjacent chains are colour-coded blue and green.

Å; 3/2 − *x*, *y* − 1/2, *z*) (Fig. 5). Also, the described interactions can be observed by a close analysis of the two-dimensional fingerprint plot derived from the Hirshfeld surface[16] of the (**phen**)(**tu**) cocrystal components (Fig. 4). 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, the FTIR spectra of pure **phen** and (**phen**)(**tu**) were recorded (see the ESI†). Their spectra show strong bands corresponding to the C–O stretching of the **phen** carbonyl group at about 1670 cm^{-1} (1676 cm^{-1} for **phen** and 1650 cm^{-1} for the cocyrstal). The C–O stretching for (**phen**)(**tu**) is expectedly at a lower frequency than that for pure **phen** due to the 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 the 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 $R_2^2(9)$ 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 an orange

colour, markedly different from the intensely yellow **phen**. Crystal structure analysis demonstrates that the 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, and 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 implications for the future design and optimization of colourants, dyes and pigments *via* mechanochemical cocrystallization.

Acknowledgements

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