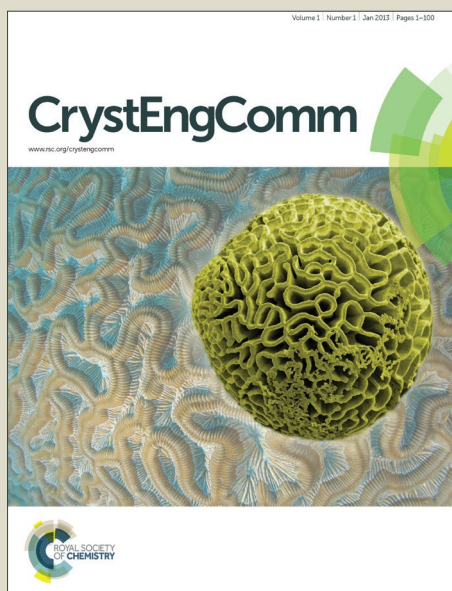


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COMMUNICATION

Halogen bonding of *N*-bromosuccinimide by grinding†

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Two halogen bonded cocrystals of *N*-bromosuccinimide and 4,4'-bipyridine, with stoichiometric ratios 1:1 and 2:1, have been synthesized and characterized. We present the first mechanochemical cocrystallization of *N*-bromosuccinimide.

Halogen bonds are non-covalent interactions that form between polarisable and electron-deficient halogen atoms (Br, I) and electron-rich Lewis bases (nucleophilic atoms such as O, N, S, etc.).¹ They have been utilised as alternatives to hydrogen bonds in crystal engineering of organic and metal-organic materials.² An overview of the currently available literature reveals that studies of halogen bonding have largely focused on cocrystals of perfluorohalocarbons as classic halogen bond donors.³ Numerous reports have been published over the past decade dealing with crystal engineering and synthesis of multicomponent materials containing iodo-substituted perfluorinated donors.⁴ Recently, Rissanen and Raatikainen have introduced a new family of halogen bond donors.⁵ They have demonstrated how *N*-halosuccinimides can be used for constructing halogen bonded molecular crystals. Also, in a recent study Fourmigué and Espinosa described *N*-iodoimide derivatives as strong halogen bond donors.⁶ *N*-halosuccinimides are commercially available inexpensive compounds, commonly used as halogenation agents in organic synthesis.⁷ They possess an extremely polarised halogen atom but have not yet been fully recognized and studied as potential halogen bond donors.⁸ A cursory search of the Cambridge Structural Database^{8b} (CSD) based on the ability of *N*-halosuccinimides to act as a halogen bond donor has resulted in 13 hits; 10 of those have been derived from *N*-iodosuccinimide (**nis**) and 3 from *N*-bromosuccinimide (**nbs**).

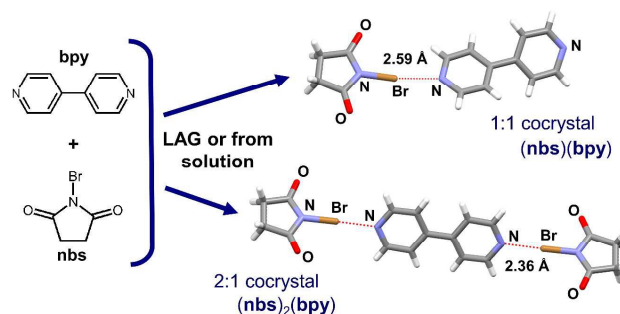


Figure 1. Structures of reactants, *N*-bromosuccinimide (**nbs**) and 4,4'-bipyridine (**bpy**), and cocrystal structures obtained as a result of the single crystal X-ray diffraction experiment.

Herein we report a mechanochemical approach⁹ to the construction of halogen-bonded cocrystals of **nbs**. We have selected 4,4'-bipyridine (**bpy**) as a good counterpart to **nbs**, a molecule that is a commonly used ditopic hydrogen or halogen bond acceptor (Fig 1). Compared to the traditional cocrystallization method, synthesis from a solution, mechanochemical synthesis has proven superior and is preferable because it sidesteps having to find an appropriate solvent or solvent mixture.^{10,11} In general it is much faster, therefore, unexpected products resulting from unwanted reactions such as oxidation, halogenation or solvolysis are avoided. To the best of our knowledge, this is the first mechanosynthesis of multicomponent halogen-bonded solids using **nbs** via neat grinding (NG) and liquid-assisted grinding (LAG).¹² However, numerous reports have been published dealing in mechanochemical approaches to halogenation using **nbs** and **nis** compounds.¹³

In order to explore the stoichiometric ratio of **nbs** and **bpy** as well as reactivity in the solid state, we first attempted the mechanochemical synthesis of cocrystals by NG and LAG of **nbs** with **bpy** in the stoichiometric ratio 1:1 and 2:1, respectively. Milling was conducted in a Retsch MM200 mill using a stainless steel milling assembly (see ESI) under normal laboratory conditions (temperature ca. 25 °C, 40–50% RH). To observe grinding experiments, as well as to facilitate the

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† Electronic Supplementary Information (ESI) available: experimental details for solution-based synthesis, instrumental experimental details and PXRD, and DSC data. CCDC 1465378 and 1465379 contain the supplementary 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/

characterisation of the new cocrystals by single-crystal X-ray diffraction, mechanochemical experiments were accompanied by crystallization from the solution. All reactants and products have been characterised by means of powder X-ray diffraction (PXRD) and differential scanning calorimetry (DSC). NG of **nbs** with **bpy** in a stoichiometric ratio 1:1 for 15 min afforded (**nbs**)(**bpy**) cocrystal, as proven by PXRD, but the NG experiment in a stoichiometric ratio 2:1 for 15 min afforded a mixture of products, where the (**nbs**)(**bpy**) cocrystal was present as a major product and the (**nbs**)₂(**bpy**) cocrystal only in traces (see ESI). When the same NG experiment was carried out for 80 min, the reaction was still not quantitatively complete – this time the experiment resulted in a mixture with the (**nbs**)₂(**bpy**) cocrystal as major product (see ESI). Considering that a liquid phase can significantly enhance the scope and rate of the mechanochemical experiment^{12,14} we turned to LAG. An addition of a small quantity of acetonitrile to the reaction mixtures,¹⁵ followed by grinding for 15 min, quantitatively provided both 1:1 and 2:1 cocrystals of PXRD pattern identical to that of cocrystals prepared by the solution method (Fig. 2). In the solution experiments, **nbs** and **bpy** have been dissolved in a hot acetonitrile. The solutions were left at room temperature, and the products, 1:1 and 2:1 cocrystals crystallized upon cooling. Single crystals of both cocrystals suitable for X-ray diffraction were obtained by concomitant crystallization from acetone. The measured PXRD patterns of (**nbs**)(**bpy**) and (**nbs**)₂(**bpy**) obtained by both methods, grinding and from solution, are in good agreement with those calculated from single crystal data (Fig. 2, see ESI). The (**bpy**)(**nbs**) and (**nbs**)₂(**bpy**) cocrystals crystallize in the monoclinic system with four formula units per unit cell. The molecular structures of cocrystals with the atom numbering

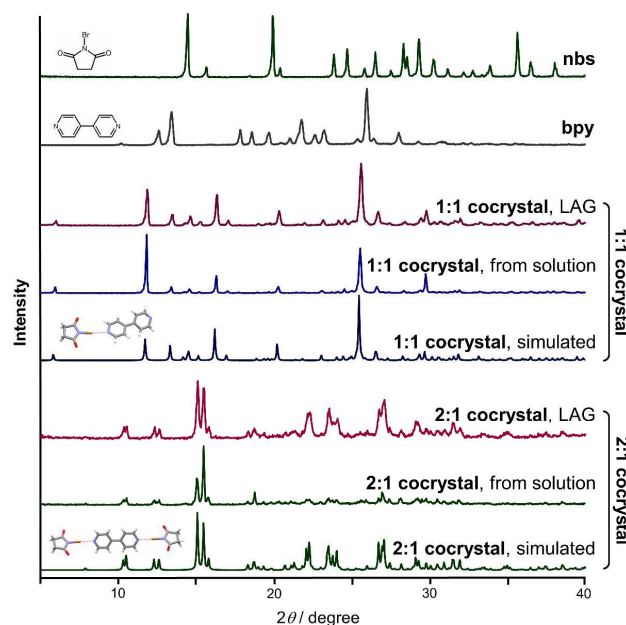


Figure 2. Comparison of reactants, mechanochemical products, crystallization products and calculated powder patterns.

scheme are given in Fig. S1 (see ESI). In the crystal structure of (**bpy**)(**nbs**) each **nbs** molecule is associated with a **bpy** molecule *via* an N...Br halogen bond. The Br...N distance of 2.586(2) Å is 23.9 % less than the sum of the van der Waals (VDW) radii of nitrogen and bromine (3.4 Å) and almost linear, with an N–Br...N angle of 171.20(6)°. Only one of the two nitrogen atoms in each **bpy** molecule is involved in bonding with an **nbs** molecule (Fig. 3). Furthermore, crystal structure determination of (**nbs**)₂(**bpy**) revealed two pairs of symmetry equivalent (CO)₂N–Br...N halogen bonds with contact distances of 2.358(3) and 2.374(2) Å which are 30.6 and 30.2 % less than the sum of the VDW radii, respectively. Both contacts are highly linear, with an N–Br...N angle of 176.5(1)° and 179.0(1)°. For both cocrystals the N–Br bond in **nbs** molecules is extended compared to that observed for the pure **nbs** crystal¹⁶ (0.03 Å for 1:1 cocrystal; 0.07 Å and 0.08 Å for 2:1 cocrystal). All these observations indicate the presence of a strong halogen bond with partially covalent character and with charge transfer from the N–Br bond to the Br...N contact.¹⁷ Considering that an **nbs** molecule possesses carbonyl groups and is also a strong hydrogen bond acceptor, components in both cocrystals create a specific halogen and hydrogen bonding pattern. The crystal structure of (**nbs**)(**bpy**) can be described by the association of 1:1 halogen bonded complexes into a hydrogen bonded 3D network *via* C–H...O hydrogen bonds between **nbs** and **bpy** (C9...O1 contact of 3.542(3) Å, C14...O2 contact of 3.342(3) Å and C11...O2 contact of 3.356(3) Å) and *via* C–H...O hydrogen bonds between **nbs** molecules (C3...O1 contact of 3.412(3) Å and C2...O1 contact of 3.384(3) Å). A notable detail of the cocrystal structure is the fact that each **nbs** molecule is connected to seven neighbouring molecules (three **nbs** and four **bpy**) as a halogen bond donor, ditopic hydrogen bond donor and ditopic hydrogen bond acceptor (Fig. 3). As in the 1:1 cocrystal, the crystal structure of (**nbs**)₂(**bpy**) can be described by the association of 2:1 halogen

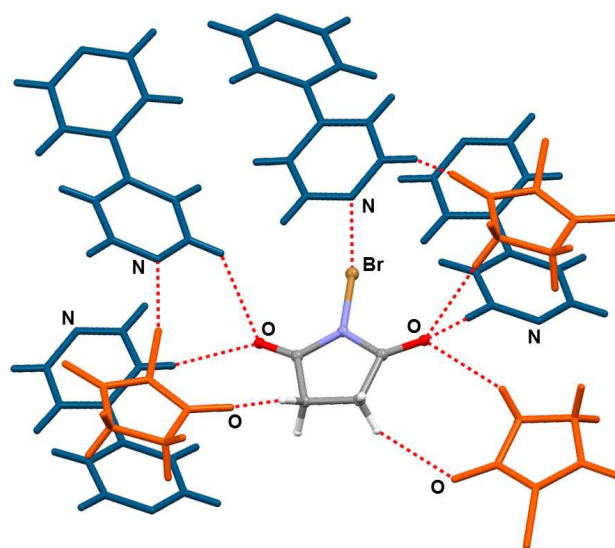


Figure 3. Halogen and hydrogen bonding of **nbs** molecule with neighbouring molecules in the crystal structure of (**nbs**)(**bpy**).

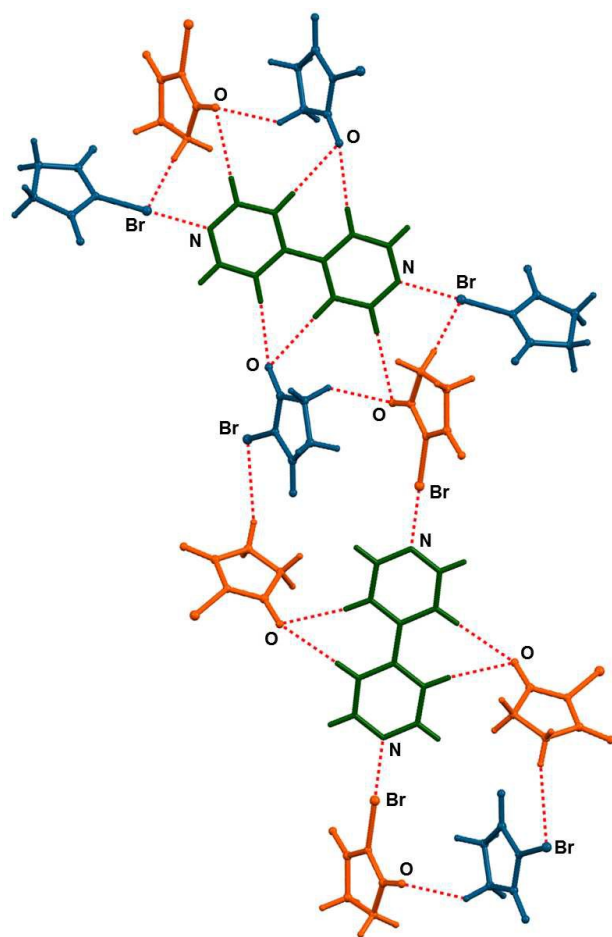


Figure 4. Network of halogen and hydrogen bonded molecules in the crystal structure of $(\text{nbs})_2(\text{bpy})$.

bonded complexes into a hydrogen bonded 3D network *via* C–H...O hydrogen bonds. The crystal structure contains two symmetrically nonequivalent **nbs** and **bpy** molecules (Fig. 4). One **bpy** molecule is connected with four neighbouring **nbs** molecules *via* the described halogen bond and bifurcated C–H...O hydrogen bonds (C15...O3 contact of 3.477(4) Å and C17...O3 contact of 3.341(5) Å). The second **bpy** molecule is connected with six neighbouring **nbs** molecules *via* the described halogen bond, C–H...O hydrogen bonds (C9...O4 contact of 3.515(4) Å), and *via* bifurcated C–H...O hydrogen bonds (C10...O2 contact of 3.403(4) Å and C12...O2 contact of 3.434(4) Å). The overall structure results from the combination of such interactions and it is additionally stabilized by C–H...O hydrogen bonds between **nbs** molecules (C3...O4 contact of 3.406(5) Å). Furthermore, the described interactions in both cocrystals can be observed by close analysis of the two-dimensional fingerprint plot derived from the Hirshfeld surface¹⁸ of the cocrystal components (see ESI). Thermal analysis of prepared cocrystals by DSC reveals that both compounds are of similar thermal stability. The DSC curves of both cocrystals have the same profile and show one weak endothermic change peak and one strong exothermic change peak. They occur for $(\text{nbs})(\text{bpy})$ at 116 °C (3.5 kJ mol^{−1}) and 131

°C (58.4 kJ mol^{−1}), and for $(\text{nbs})_2(\text{bpy})$ at 103 °C (3.7 kJ mol^{−1}) and 136 °C (114.6 kJ mol^{−1}) (see ESI). For both cocrystals the exothermic change peak corresponds to the cocrystal decomposition and is at a lower temperature than that of the pure **nbs** reactant (208 °C, 42.9 kJ mol^{−1}).

Conclusions

In summary, we have demonstrated how **nbs**, a commercially available compound commonly used as a brominating agent in organic synthesis, can be used in cocrystal synthesis. To the best of our knowledge, this is the first demonstration of mechanosynthesis of multicomponent halogen-bonded solids using **nbs** as a halogen bond donor. The mechanochemical approach exhibits notable advantages over conventional solution-based synthesis of such compounds, not only through reducing the time of preparation and isolation, but also by evading of the formation of potentially unwanted halogenation products. Crystal structure analysis of $(\text{nbs})(\text{bpy})$ and $(\text{nbs})_2(\text{bpy})$ demonstrated that the presence of a polarised halogen atom and two carbonyl groups on the **nbs** molecule leads to a specific halogen and hydrogen bonding pattern in their crystal structure. The high stability of both materials, as a result of halogen and hydrogen bonding patterns, was proven by a relatively high decomposition temperature. Also, crystal structure analysis revealed indications of a very strong halogen bond with partially covalent character and with charge transfer from the N–Br bond to the Br...N contact. We believe that the described results will have significant impact on the design and synthesis of future halogen-bonded materials containing *N*-haloimides as well as on halogen bond-driven crystal engineering in general.

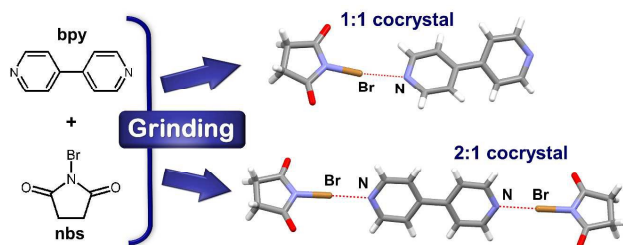
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