Structural Equivalence of Br and I Halogen Bonds: A Route to Isostructural Materials with Controllable Properties

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The structural equivalence of halogen-bonded iodine and bromine functionalities has been systematically explored as a general tool to construct isostructural cocrystal architectures with differing strengths of the constituent halogen bonds. By using acridine and phenazine as halogen bond acceptors, the structural equivalence of Br and I donors was tested for cocrystals based on discrete (0-dimensional) or infinite (1-dimensional chain) supramolecular topologies. In addition to being robust to changes in the topology of halogen-bonded assembly, this structural equivalence was also persistent in the presence of weak intermolecular hydrogen bonding of C−H···N type. The potential application of structurally equivalent I and Br donors in the design of molecular materials is illustrated by constructing pairs of solids that exhibit differing melting point, stability, and crystal morphology, although based on identical halogen-bonded architectures.

The ability to predict and control the structure of molecular crystals is key to the synthesis of functional molecular solids by design.[1] The difficulty, however, in controlling crystal structures is illustrated by the appearance of unpredictable polymorphic forms, i.e., the ability of a particular molecular species to exist in different crystalline arrangements.[2] In contrast to polymorphism is isostructurality, the occurrence of different molecular species in almost identical crystalline arrangements.[3] Whereas polymorphism is considered to be the nemesis of crystal design, isostructurality may be beneficial. In principle, the control of isostructurality would allow the assembly of different molecules in the solid state following a chosen supramolecular blueprint. With the exception of lattice inclusion compounds, isostructurality of molecular crystals is a relatively rare phenomenon,[3,4] and consequently, its applicability for the design of molecular crystals to date has been limited. Nevertheless, a significant amount of control over solid-state molecular arrangement has been demonstrated through the use of reliable supramolecular synthons for the synthesis of multicomponent crystals (cocrystals).[5] The success of cocrystals[6] as functional materials follows from their modular structure: the ability to replace each component with the purpose of fine-tuning a solid-state property.[7] Whereas the majority of cocrystals have been constructed using hydrogen bonds, the halogen bond has recently emerged as an alternative intermolecular interaction.[8,9] Halogen bond interactions, considered comparable in strength and directionality to hydrogen bonds, consist of a halogen atom as the bond donor (typically Br or I) and an electron rich atom as the bond acceptor.[9]

We have recently reported the discovery of seven isostructural cocrystals based on halogen bonds.[10] Underlying the isostructurality was the structural equivalence of donor (Br and I) and acceptor groups (NH, O, S). That the variation in thermal properties of the resulting cocrystal could be related to the different strengths of the halogen bonds involving Br and I has led us to further investigate the

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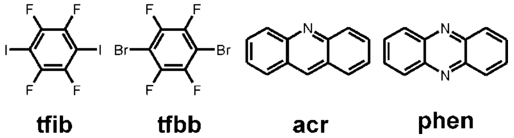
Scheme 1. Molecular Diagrams of Cocrystal Components



structural equivalence[11−14] of halogen-bonded Br and I groups[15] for the design of isostructural solids.

We now demonstrate that cocrystallization-induced structural equivalence of Br and I can be robust toward systematic modifications of cocrystal architecture. In particular, we show by constructing halogen-bonded cocrystals of 1,4-diiodotetrafluorobenzene (**tfib**) and its bromo analogue (**tfbb**) with phenazine (**phen**) and acridine (**acr**) (Scheme 1), that structural equivalence persists in solids made of discrete and infinite supramolecular motifs, based on either halogen bonds alone or a combination of halogen and hydrogen bonds.[16]

Cocrystallization of **tfib** and **phen** either from solution or by liquid-assisted grinding[17] yielded a cocrystal of composition (**phen**)$_2$·(**tfib**). The products obtained by a solution cocrystallization and by grinding were found to be identical using powder X-ray diffraction (PXRD). The cocrystal is made of inifinite chains held together by I···N halogen and C−H···N hydrogen bonds (Figure 1a).[18]

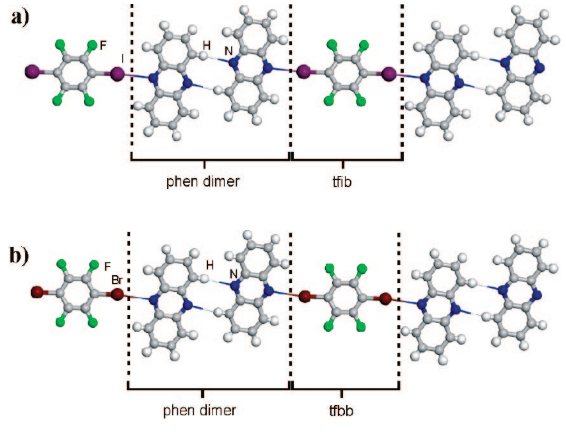


Figure 1. Supramolecular chains in (a) (**phen**)$_2$·(**tfib**), halogen and hydrogen bond parameters (Å): N···I = 2.97, C···N = 3.48; (b) (**phen**)$_2$·(**tfbb**), halogen and hydrogen bond parameters (Å): N···Br = 2.99, C···N = 3.49.

Table 1. Unit-Cell Parameters, Calculated Densities, and Melting Points for Isostructural Cocrystals of Acr and Phen

	(**acr**)$_2$·(**tfbb**)	(**acr**)$_2$·(**tfib**)	(**phen**)$_2$·(**tfbb**)	(**phen**)$_2$·(**tfib**)
space group	$P2_1/c$	$P2_1/c$	$P2_1/c$	$P2_1/c$
a (Å)	9.9607(2)	10.4907(2)	5.6897(1)	5.6639(2)
b (Å)	5.6734(1)	5.5679(1)	13.6631(3)	14.3240(4)
c (Å)	23.0529(3)	23.0787(4)	16.5159(4)	16.5730(6)
β (deg)	91.118(1)	90.765(1)	99.566(1)	102.224(1)
ρ_c (g cm^{-3})	1.70	1.87	1.75	1.93
T_m (°C)	81	153	107	174

In the chains, each molecule of **tfib** is involved in two I···N halogen bond interactions with neighboring molecules of **phen**. In turn, each **phen** molecule is a part of a dimer formed by a pair of C−H···N bonds. The structure of the chains thereby enabled us to test the structural equivalence of halogen-bonded I and Br groups in the presence of intermolecular hydrogen bonds.[15,16] Cocrystallization of **phen** and **tfbb** from solution or via liquid-assisted grinding,[17] provided cocrystals of (**phen**)$_2$·(**tfbb**). As evidenced by structure determination and PXRD, the resulting (**phen**)$_2$·(**tfbb**) cocrystal is isostructural to (**phen**)$_2$·(**tfib**) (Table 1) and displays analogous hydrogen- and halogen-bonded chains. Whereas the Br···N bonds are longer than the I···N bonds in (**phen**)$_2$·(**tfib**), no significant changes were observed in the C−H···N bond distances (Figure 1b).

That **phen** in both cocrystals acts as a monovalent halogen bond acceptor[18] provided an opportunity to investigate whether Br/I structural equivalence is tolerant to "switching off" intermolecular hydrogen bonding. For that purpose, we used **acr** as an analogue of **phen** that would likely form discrete halogen-bonded assemblies with **tfib** and **tfbb**. We expected that the discrete ternary assemblies would be similar to halogen-bonded sections of supramolecular chains in **phen** cocrystals, but would not associate via hydrogen bonds. Indeed, cocrystallization of **acr** with **tfbb** and **tfib** provided cocrystals composed of the expected discrete assemblies (**acr**)$_2$·(**tfbb**) and (**acr**)$_2$·(**tfib**), respectively. The cocrystals could be obtained either by cocrystallization from solution or via liquid-assisted

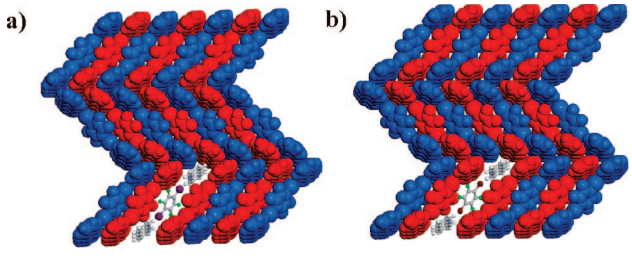


Figure 2. Crystal packing of assemblies in (a) (**acr**)$_2$·(**tfib**), (b) (**acr**)$_2$·(**tfbb**).

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[11] The ability to exchange groups in a molecule without affecting its crystal packing has been designated structure mimicry,[12] group isostructurality,[13] supramolecular equivalence,[14] and structural equivalence.[10] We use the term structural equivalence[10] to describe functional groups that are exchangeable without affecting the crystal structure and the term supramolecular equivalence[14] to describe functional groups that are exchangeable without affecting the pattern of noncovalent bonds.

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[19] The analysis of the disorder using solid-state ^{13}C CP-MAS NMR was unsuccessful, due to the overlap of signals in (**acr**)$_2$·(**tfbb**) and (**acr**)$_2$·(**tfib**). Low-temperature (−60 °C) DSC thermograms are featureless for both cocrystals, indicating that the disorder is independent of temperature (see the Supporting Information).

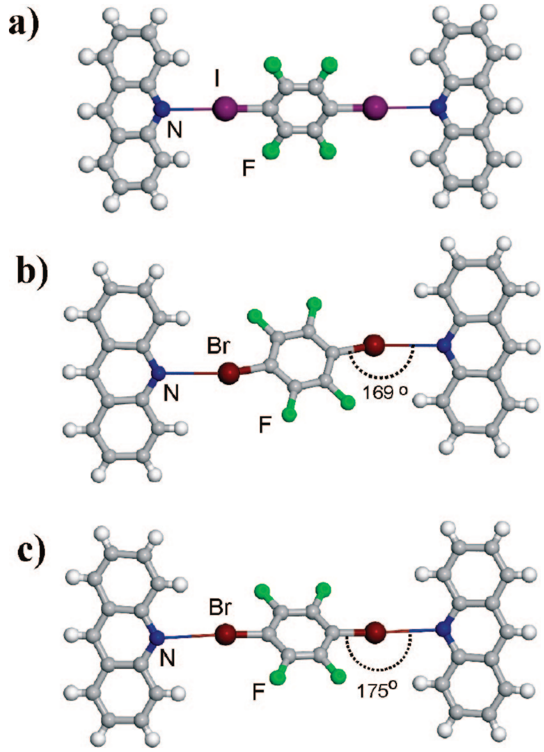
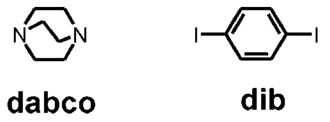


Figure 3. (a) Single molecular assembly in (**acr**)$_2$•(**tfib**); (b, c) two disordered forms of the (**acr**)$_2$•(**tfbb**) assembly in the solid state.

grinding.[17] In both cocrystals the assemblies pack into a herringbone pattern via edge-to-face C−H•••π contacts (Figure 2).

While (**acr**)$_2$•(**tfbb**) and (**acr**)$_2$•(**tfib**) are essentially isostructural (Table 1), their crystal structures are not completely identical. In (**acr**)$_2$•(**tfbb**), the **acr** molecules are disordered over two closely related positions that differ largely in the angle formed between the halogen bond interaction and the corresponding carbon−iodine bond. Despite this disorder, absent in (**acr**)$_2$•(**tfib**), the overall shape and packing of (**acr**)$_2$•(**tfbb**) assemblies resemble those in (**acr**)$_2$•(**tfib**) (Figure 3). Consequently, the structural equivalence of halogen-bonded Br and I atoms can be achieved in solids based on infinite, as well as discrete supramolecular motifs.

Scheme 2. Molecular Diagrams of Dabco and Dib



The potential for using structurally equivalent functional groups in materials design lies in the ability to modify solid-state properties of a solid without changing its supramolecular architecture. This is illustrated by the thermal properties of the synthesized cocrystals. Isostructural replacement of Br with I should increase the thermal stability of a halogen-bonded structure, as I•••N bonds are expected to be stronger than the Br•••N ones.[20] This is confirmed by differential scanning calorimetry (DSC): the melting point of (**phen**)$_2$•(**tfib**) is 67 °C higher than for (**phen**)$_2$•(**tfbb**).[20] Similarly, (**acr**)$_2$•(**tfib**) melts 72 °C above the melting point of (**acr**)$_2$•(**tfbb**). Consequently, for both **acr** and **phen** the structural equivalence of Br and I enabled the construction of two materials with identical architectures, but with ~70 °C difference in melting point (Figure 4a,b). This difference is surprisingly similar to the one in isostructural cocrystals of **tfib** and **tfbb** with aliphatic acceptors.[10] In contrast, the smaller melting point difference between pure **tfib** and **tfbb** (ΔT = 20 °C) supports the view that melting points of isostructural cocrystals largely reflect the relative strengths of the N•••I and N•••Br halogen bonds, rather than the differences in relative molecular weight. Furthermore, the replacement of N•••Br with N•••I halogen bond interactions leaves a significant mark on the chemical stability of isostructural frameworks. Whereas (**acr**)$_2$•(**tfib**) is stable on standing in open air, (**acr**)$_2$•(**tfbb**) readily loses the halogen bond donor and converts to **acr** with the retention of particle shape (Figure 4c,d). In a similar way, melting of (**phen**)$_2$•(**tfbb**) is accompanied by the loss of **tfbb** to form **phen**, identified using PXRD.

In addition to thermal stability and density (Table 1), isostructurality of Br with I also provides an opportunity to control crystal morphology. Specifically, crystallization from acetonitrile yields (**acr**)$_2$•(**tfbb**) as isometric crystals, whereas

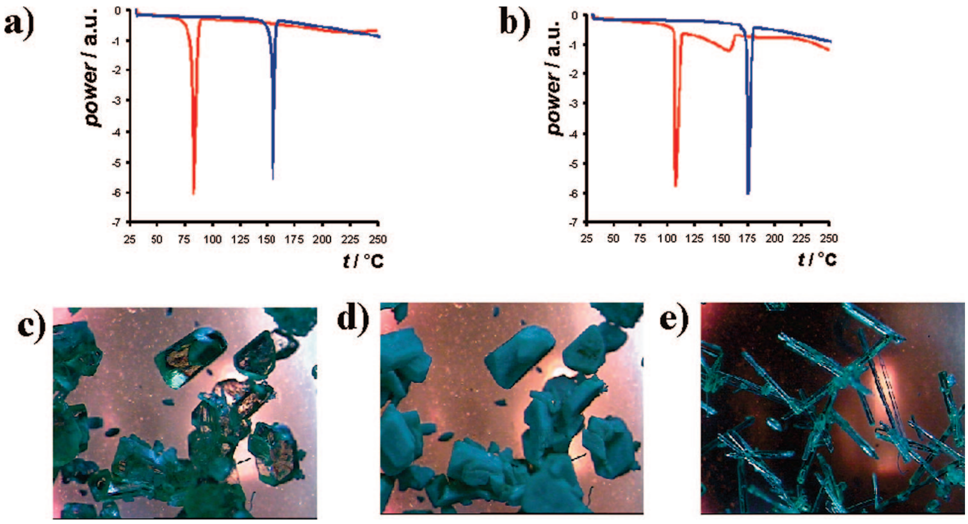


Figure 4. Differences in thermal stability and crystal morphology for isostructural cocrystals. DSC thermograms for isostructural cocrystals of (a) **acr** and (b) **phen**. Thermograms for iodine- and bromine-based cocrystals are traced in blue and red, respectively. Isostructural cocrystals grown from acetonitrile: (c) (**acr**)$_2$•(**tfbb**), (d) (**acr**)$_2$•(**tfbb**) after overnight standing in air, and (e) (**acr**)$_2$•(**tfib**).

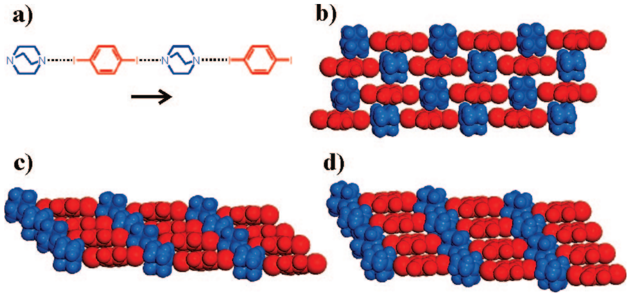


Figure 5. (a) diagram of expected halogen-bonded chain in **dabco** cocrystals; packing of halogen-bonded chains in (b) (**dabco**)·(**dib**), (c) (**dabco**)·(**tfib**), and (d) (**dabco**)·(**tfbb**). Molecules of **dabco** and halogen bond donor are shown in blue and red, respectively.

Table 2. Unit-Cell Parameters of Dabco Cocrystals

	(**dabco**)·(**tfbb**)[a]	(**dabco**)·(**tfib**)[a]	(**dabco**)·(**dib**)
space group	$P\bar{1}$	$P\bar{1}$	$P\bar{1}$
a (Å)	6.0248(1)	6.8112(1)	6.2077(2)
b (Å)	10.3547(2)	10.8944(2)	9.5818(4)
a (Å)	12.2080(3)	11.4157(2)	12.7244(5)
α (deg)	102.983(1)	107.263(1)	104.361(3)
β (deg)	102.568(1)	92.854(1)	97.004(2)
γ (deg)	105.033(1)	105.076(1)	107.591(2)

[a] Reference 23.

(**acr**)$_2$·(**tfib**) from the same solvent and at the same concentration forms needles elongated along the crystallographic *x*-axis (images c and e in Figure 4).

In the studied cocrystals, the atoms of Br and I participate in halogen bonds that define a supramolecular motif in each cocrystal.[21] Because halogen bonds are robust to differences between Br and I, the observed isostructurality must depend on the ability of other crystal packing forces to accommodate Br/I exchange and direct the packing of these halogen-bonded fragments. Presumably, in the **phen** and **acr** cocrystals described here this is achieved either by "soft" C−H···N bonds that link hydrogen-bonded assemblies into chains or C−H···π contacts between halogen-bonded assemblies. Consequently, isostructurality through I/Br exchange would be less likely in cocrystals composed of rigid molecules connected by highly directional intermolecular interactions.

To test this hypothesis, we have compared the structures of cocrystals of 1,4-diazabicyclo[2.2.2]octane (**dabco**) with **tfib**, **tfbb** and 1,4-diiodobenzene (**dib**) (Scheme 2) as rigid halogen bond acceptors and donors.[22] All three cocrystals are composed of chains (Figure 5a), demonstrating halogen bonding as a motif-defining interaction. However, the cocrystals are not isostructural, as evidenced by a comparison of crystallographic parameters (Table 2) and crystal packing of the halogen-bonded chains (Figure 5b−d).

Therefore, I and Br groups now exhibit supramolecular, rather than structural, equivalence.[11] Presumably, this is due to the rigidity of the halogen-bonded chains and the lack of a common "soft" interaction that would direct an identical arrangement of rigid chains in all three cocrystals. The packing of chains in (**dabco**)·(**tfib**) and (**dabco**)·(**tfbb**) is similar, but it is noticeably different for (**dabco**)·(**dib**). This can be attributed to C−H···π interactions between **dabco** and **dib** molecules in neighboring chains. These interactions are not observed in (**dabco**)·(**tfbb**) or (**dabco**)·(**tfib**), presumably due to the electron-withdrawing fluorine substituents on **tfbb** and **tfib** weakening possible C−H···π interactions.

In summary, we have demonstrated that the formation of halogen bonds can result in cocrystallization-induced structural equivalence of I and Br halogen bond donors. This structural equivalence was explored as a means of constructing solids with controllable properties by duplicating a given cocrystal architecture. In particular, we have applied the isostructural replacement of Br with I to rationally modify the properties of solids based on discrete and infinite molecular assemblies. Replacement of Br and I increased the thermal stability of a given supramolecular architecture by increasing the strength of supramolecular links that hold it together.[10,20] Consequently, when cocrystal formation is possible, cocrystallization-induced isostructurality may be an attractive alternative to traditional approaches that pursue different materials properties by alternate supramolecular architectures.[24] We note that the differences in melting points between bromine- and iodine-based isostructural cocrystals are surprisingly similar for solids based on discrete and infinite supramolecular motifs, suggesting a possibility to quantify structure−property relationships. We are currently exploring further structurally equivalent groups to expand the scope of our approach.[10,21]

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Supporting Information Available: Measured and simulated XRPD patterns, solid-state ^{13}C CP-MAS NMR, and low-temperature DSC data for (**acr**)·(**tfbb**) and (**acr**)·(**tfib**) (PDF). CIF files for (**acr**)$_2$·(**tfbb**), (**acr**)$_2$·(**tfib**), (**phen**)$_2$·(**tfbb**), (**phen**)$_2$·(**tfib**), and (**dabco**)·(**dib**). This material is available free of charge via the Internet at http://pubs.acs.org.

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