

# Relative importance of $X\cdots O=C$ vs. $X\cdots X$ halogen bonding as structural determinants in 4-halotriaroylbenzenes†

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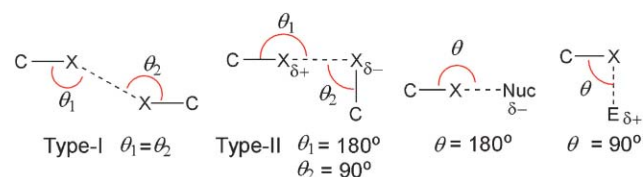
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The structures of 4-chloro- and 4-bromotribenzoylbenzene, as well as a solid solution prepared from these two components, are isomorphous and dominated by  $C-X\cdots O=C$  interactions, whereas type-II  $I\cdots I$  interactions are important in the 4-iodo derivative.

The structure-determining influence that halogen bonding can exert during the course of crystallization has attracted considerable interest within the crystal engineering community.<sup>1</sup> Organic and inorganic halide building blocks are readily available, potentially facilitating the construction of functional solid-state materials *via* the controlled manipulation of halogen bonding synthons. Indeed, halogen bonding has been successfully exploited in the design and synthesis of inclusion hosts,<sup>2</sup> in the preparation of ordered solids capable of undergoing topochemical reactions,<sup>3</sup> for the construction of conducting and NLO active materials,<sup>4</sup> and in the assembly of heteroditopic host–guest complexes.<sup>5</sup>

A straightforward approach to achieving a better fundamental understanding of the relative importance of solid-state halogen bonding entails examining the structures of closely related compounds that differ only in the identity of the halogen substituent. Recent studies along these lines further substantiate the computational finding that halogens possess an anisotropic distribution of electrostatic potential that enables them to enter into energetically significant, directional, non-covalent interactions.<sup>6</sup> Halogen substituents, especially the heavier halogens (Cl, Br and I), exhibit electrophilic character along the axes of  $C-X$  (or metal–X) bonds and nucleophilic character along vectors perpendicular to these bonds. Hence, halogen bonding interactions with nucleophiles (*e.g.*, O, N) display roughly linear geometries with respect to the halogens, whereas interactions with electrophiles (*e.g.*, hydrogens, as encountered in  $D-H\cdots X$  hydrogen bonding) occur in a side-on fashion (Scheme 1).<sup>7</sup> As a consequence of the



**Scheme 1** Schematic of idealized halogen bonding interactions.

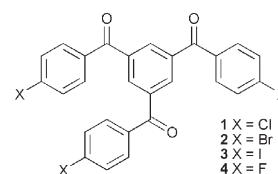
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† Electronic Supplementary Information (ESI) available: DSC, powder XRD and compound characterization data, and tabular listing of relevant intermolecular contacts. See DOI: 10.1039/b603110b

spatially segregated regions of complementary electrostatic potential, inter-halogen bonding is also observed, with halogen groups acting as both nucleophiles and electrophiles. Such directional halogen–halogen interactions are referred to as type-II halogen bonds.<sup>8</sup> The halogen trimer synthon is a further example of this phenomenon.<sup>2,7a,d</sup> In contrast, computational and empirical studies have shown that fluorine substituents do not participate in halogen bonding interactions due to a combination of extreme electronegativity and limited polarizability.<sup>6,7b,g,9</sup>

In order to fully utilize halogen bonding as a design element in crystal engineering, it is important to have insight into the relative strengths of the various non-covalent interactions involving halogens and to identify preferred halogen bonding partners. Solid-state studies of polyfunctional organohalogens can provide valuable information in this regard by presenting possibilities for several types of competitive halogen bonding interactions, only a subset of which might actually be observed. In this way, a hierarchical ordering of different interactions may be determined. An important consideration when designing experiments of this type concerns mitigating the size differences among the halogens. Obviously, iodine is much larger than the other halogens, and this physical feature can influence solid-state structure, especially in rigid molecules.<sup>10</sup> Conformationally flexible compounds, however, should be able to better accommodate substituents of different sizes while maintaining energetically favorable interactions.

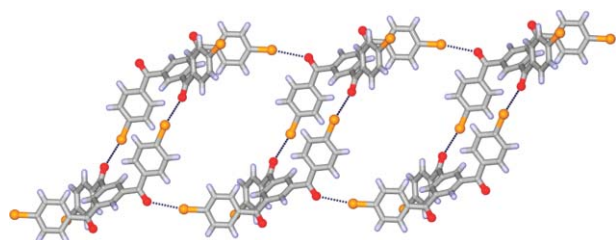
The 1,3,5-triaroylbenzene (TAB) molecular framework combines synthetic accessibility and conformational flexibility to afford an attractive platform for the systematic study of solid-state supramolecular interactions such as halogen bonding. In a previous study, we reported the characterization of concomitant dimorphs of (4-chloro)TAB **1**.<sup>11</sup> Significantly, various halogen bonding interactions were observed in the structures of both modifications, most notably type-II  $Cl\cdots Cl$  interactions of form A and  $Cl\cdots O=C$  interactions of form B. Consequently, we initiated a study aimed at defining the relative importance of  $C-X\cdots O=C$  vs.  $X\cdots X$  interactions as a function of halide through the structural characterization of (4-halo)TABs **2–4**.



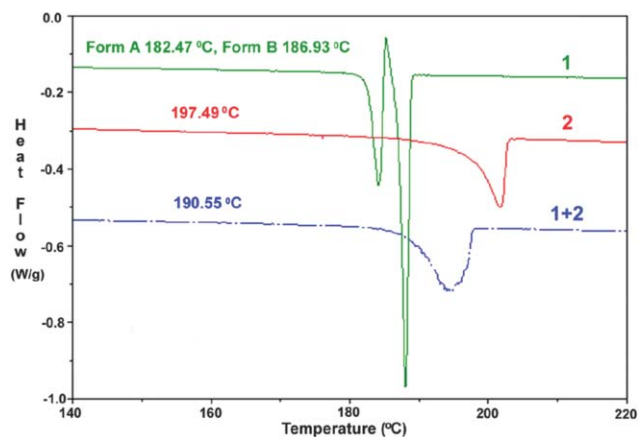
Substrates **2–4** were prepared from the corresponding 4-haloacetophenones according to literature procedures.<sup>12</sup> X-Ray quality crystals of **2**, **3** and a **1 + 2** solid solution were obtained by the slow

evaporation of acetone solutions.‡ The structure of **2** was found to be isomorphous with the form B modification of (4-chloro)TAB **1** ( $I = 0.0085$ ).<sup>13</sup> Specifically, a halogen bonding network consisting of two slightly different types of  $\text{Br}\cdots\text{O}=\text{C}$  interactions mediates the assembly of an approximately 2D square grid-like architecture, as shown in Fig. 1. The majority of these contacts (two-thirds) exhibit relatively short  $\text{Br}\cdots\text{O}$  distances (3.105 Å) and near linear angles about the halogen (166.9°). The angle about the carbonyl oxygen (138.5°) is also close to the expected value of 120°. The remaining  $\text{Br}\cdots\text{O}$  contacts are slightly longer but directional ( $\text{Br}\cdots\text{O} = 3.190$  Å,  $\text{C}-\text{Br}\cdots\text{O} = 166.5^\circ$ ,  $\text{C}=\text{O}\cdots\text{Br} = 134.7^\circ$ ). Parallel square grids are connected through inversion-related  $\text{Br}\cdots\text{Br}$  contacts (type-I halogen bonds, Scheme 1). While short ( $d = 3.496$  Å), halogen interactions of this type are generally attributed to crystal packing effects rather than energetically attractive associations.<sup>7b,14</sup> Close packing is achieved by interpenetration of a second square grid network.

Isostructurality between **1** and **2** is not surprising, as many organohalogens (at least for  $\text{X} = \text{Cl}, \text{Br}$  and  $\text{I}$ ) display similar or identical solid-state structures.<sup>15</sup> Furthermore, Moorthy and co-workers have shown that robust  $\text{Cl}(\text{Br})\cdots\text{O}=\text{C}$  interactions mediate the formation of isostructural crystals in aromatic aldehydes.<sup>16</sup> It is noteworthy, however, that unlike chloro derivative **1**, bromo analogue **2** does not exhibit any indications of polymorphism.§ The bulk crystalline sample of **2** was found to be homogeneous, as determined by powder X-ray diffraction (PXRD) and differential scanning calorimetry (DSC) (see ESI†). In the case of **1**, form B was always obtained, along with non-centrosymmetric form A as a mixture of concomitant polymorphs.<sup>11</sup> However, a microcrystalline sample of **1**, obtained after purification by column chromatography, was found to be exclusively form A according to DSC and PXRD. A solid solution prepared from equimolar amounts of this material (*i.e.*, **1**, form A) and **2** was also found to be homogeneous, yielding a structure isomorphous to that of **2** ( $I = 0.0054$ ).<sup>13,17</sup> Individual molecules of **1** and **2** within the solid solution possess an occupancy factor of  $\sim 50\%$ , mirroring the composition of the crystallization mixture. DSC of the solid solution revealed a single endotherm corresponding to the melting point of the sample at an onset temperature intermediate between the melting points of pure **1** (dimorphic mixture) and **2** (Fig. 2). Thus, the tendency of **1** to crystallize as concomitant polymorphs is completely suppressed upon admixture with the bromo analogue, and a single crystalline network mediated by  $\text{X}\cdots\text{O}=\text{C}$  halogen bonding is observed. The structural features present in crystals of **1**, **2** and the **1** + **2** solid solution highlight the architecturally defining role that halogen-carbonyl interactions can play, particularly when compared to



**Fig. 1** Halogen bonding network in **2**; O = red, Br = orange,  $\text{C}=\text{O}\cdots\text{Br}$  interactions indicated by dashed lines.

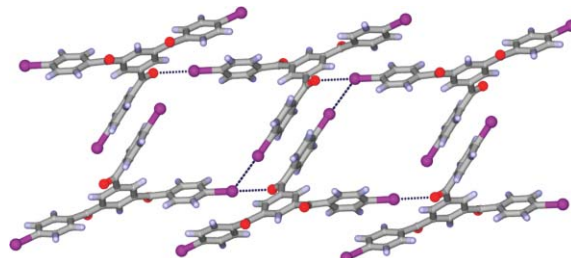


**Fig. 2** DSC trace of **1** (dimorphic mixture, green), **2** (red) and **1** + **2** solid solution (blue).

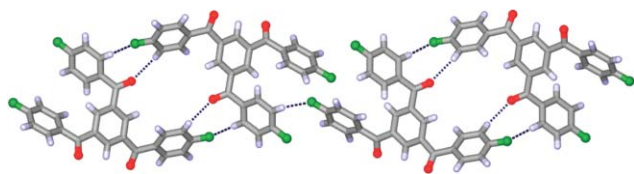
other possible halogen bonding interactions either not observed (*e.g.*, type-II  $\text{Br}\cdots\text{Br}$  contacts) or observed only in certain polymorphic modifications (*cf.* **1**, form A).<sup>18</sup>

The crystal packing of (4-iodo)TAB (**3**) is not isostructural with the chloro and bromo derivatives, instead exhibiting a solid-state pattern formed through a combination of  $\text{I}\cdots\text{O}=\text{C}$  and type-II  $\text{I}\cdots\text{I}$  interactions (Fig. 3). Individual molecules of **3** are arranged in parallel linear chains *via* what appears to be significant (based on distance and angle criteria) iodine-carbonyl halogen bonding ( $d_{\text{IO}} = 3.072$  Å,  $\text{C}-\text{I}\cdots\text{O} = 179.0^\circ$ ,  $\text{C}=\text{O}\cdots\text{I} = 138.4^\circ$ ). The short  $\text{I}\cdots\text{O}$  distance presumably reflects the greater polarizability (and hence electrophilicity) of iodine relative to the other halogens.<sup>6</sup> The electron-withdrawing carbonyl groups *para* to the iodine substituents would be expected to further heighten this effect.<sup>19</sup> Each linear chain is connected to two adjacent chains *via* type-II  $\text{I}\cdots\text{I}$  interactions ( $d = 4.075$  Å,  $\text{C}-\text{I}\cdots\text{I}$  angles = 153.1 and 108.8°). Similar  $\text{X}\cdots\text{X}$  interactions are absent in the structures of **1** (form B) and **2**. Bulk crystalline homogeneity was confirmed through PXRD and DSC.

Of the three iodine substituents present in each molecule of **3**, one participates in bifurcated halogen bonding (acting as both nucleophile and electrophile) and one participates as an electrophile in an  $\text{I}\cdots\text{I}$  contact. The third iodine, however, does not appear to participate in any significant intermolecular interactions. This contrasts with the other structures described above, in which all halogen substituents were engaged in mediating supramolecular assembly. The differences between the two types of crystalline assembly are perhaps even more significant when one considers the conformational mobility of the TAB framework—a molecular



**Fig. 3** Packing in (4-iodo)TAB **3**; O = red, I = violet,  $\text{I}\cdots\text{O}=\text{C}$  and  $\text{I}\cdots\text{I}$  interactions indicated by dashed lines.



**Fig. 4** The C–H···F and C–H···O hydrogen bonding network in **4**; O = red, F = green, hydrogen bonds indicated by dashed lines. C–H···F metrics ( $d/\text{Å}$ ,  $\theta/^\circ$ ): 2.32, 162.0; 2.34, 177.9.

feature deemed important in order to facilitate approximate isostructurality within this family of organohalogens, if such similarity is energetically advantageous. Therefore, we tentatively assign the structural differences observed as arising (principally) from differences among the various halogen bonding interactions. In the case of **1** (form B) and **2**, the numerous halogen–carbonyl interactions that serve to define the solid-state network are of greater significance than any alternative halogen bonding array involving type-II X···X interactions. In **3** however, the combination of one I···O=C contact and a type-II I···I contact is sufficient to mediate solid-state assembly, at the expense of additional I···O=C interactions (even though additional iodine and carbonyl substituents are available).

The structure of the 4-fluoro derivative (**4**), crystallized from chloroform, was also determined (Fig. 4). As expected, the solid-state network observed with this substrate has little in common with analogues **1–3**. Rather than engaging in halogen bonding interactions, the fluorine substituents in **4** participate in various C–H···F interactions, leading to the ribbon motif evident in Fig. 4.<sup>20</sup> Aside from relatively short H···F hydrogen bonding distances, the structure is unremarkable (see ESI†).

In conclusion, the structurally defining role exerted by halogen bonding interactions between Cl, Br, I and carbonyl groups has been probed using the triarylbenzene molecular framework. Structural comparisons reveal that Cl···O=C and Br···O=C interactions are preferred over type-II Cl···Cl and Br···Br contacts in the structures of **1** (form B), **2** and a **1** + **2** solid solution. However, in the case of iodo derivative **3**, I···I interactions are formed in preference to additional I···O=C bonds, resulting in a unique solid-state architecture. Structural studies of related organohalogens are under way to determine the generality of these observations.

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## Notes and references

† Crystallographic data. **2**:  $C_{27}H_{15}Br_3O_3$ ,  $M = 627.12$ , triclinic,  $P\bar{1}$ ,  $a = 8.7341(9)$ ,  $b = 11.0843(11)$ ,  $c = 12.6991(13)$  Å,  $\alpha = 95.413(5)$ ,  $\beta = 98.622(5)$ ,  $\gamma = 107.017(5)^\circ$ ,  $V = 1149.8(2)$  Å<sup>3</sup>,  $Z = 2$ ,  $D_c = 1.811$  g cm<sup>-3</sup>,  $\mu = 5.291$  mm<sup>-1</sup>, 9937 reflections collected, 5256 unique, 3221 observed ( $I > 2\sigma(I)$ ) reflections, 298 refined parameters, GOF = 1.017,  $R_1 = 0.0410$ ,  $wR_2 = 0.0874$ . CCDC 600573. **1** + **2** solid solution:  $[(C_{27}H_{15}Br_3O_3)_{0.552}][C_{27}H_{15}Cl_3O_3]_{0.448}$ ,  $M = 567.37$ , triclinic,  $P\bar{1}$ ,  $a = 8.6566(9)$ ,  $b = 11.0606(11)$ ,  $c = 12.6155(13)$  Å,  $\alpha = 95.743(5)$ ,  $\beta = 98.372(5)$ ,  $\gamma = 106.709(5)^\circ$ ,  $V = 1131.7(2)$  Å<sup>3</sup>,  $Z = 2$ ,  $D_c = 1.665$  g cm<sup>-3</sup>,  $\mu = 3.161$  mm<sup>-1</sup>, 9664 reflections collected, 5174 unique reflections, 3889 observed ( $I > 2\sigma(I)$ ) reflections, 308 refined parameters, GOF = 1.019,  $R_1 = 0.0374$ ,  $wR_2 = 0.0849$ . CCDC 600574. **3**:  $C_{27}H_{15}I_3O_3$ ,  $M = 768.09$ , monoclinic,  $P2_1/c$ ,  $a = 7.3649(7)$ ,  $b = 13.8815(13)$ ,  $c = 24.580(2)$  Å,  $\beta = 92.966(5)^\circ$ ,  $V = 2509.6(4)$  Å<sup>3</sup>,  $Z = 4$ ,  $D_c = 2.033$  g cm<sup>-3</sup>,  $\mu = 3.763$  mm<sup>-1</sup>, 20899 reflections

collected, 5758 unique reflections, 4354 observed ( $I > 2\sigma(I)$ ) reflections, 298 refined parameters, GOF = 1.044,  $R_1 = 0.0328$ ,  $wR_2 = 0.0799$ . CCDC 600575. **4**:  $C_{27}H_{15}F_3O_3$ ,  $M = 444.39$ , monoclinic,  $P2_1/c$ ,  $a = 22.757(2)$ ,  $b = 8.7286(9)$ ,  $c = 10.5930(11)$  Å,  $\beta = 101.174(5)^\circ$ ,  $V = 2064.3(4)$  Å<sup>3</sup>,  $Z = 4$ ,  $D_c = 1.430$  g cm<sup>-3</sup>,  $\mu = 0.111$  mm<sup>-1</sup>, 15622 reflections collected, 4691 unique reflections, 3469 observed ( $I > 2\sigma(I)$ ) reflections, 298 refined parameters, GOF = 1.075,  $R_1 = 0.0385$ ,  $wR_2 = 0.1060$ . CCDC 600576. For crystallographic data in CIF or other electronic format, see DOI: 10.1039/b603110b

§ Crystals of **2** obtained from THF and THF/acetone were found to be identical with those obtained from acetone.

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