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Examination of Halogen Bonding Interactions in Electronically Distinct but Structurally Related Tris(haloarenes)

F. Christopher Pigge,^{*,†} Venu R. Vangala,^{†,§} Dale C. Swenson,[†] and Nigam P. Rath[‡]

[†]Department of Chemistry, University of Iowa, Iowa City, Iowa 52242, and [‡]Department of Chemistry & Biochemistry, University of Missouri–St. Louis, One University Boulevard, St. Louis, Missouri 63121. [§]Current address: Institute of Chemical and Engineering Sciences, A*STAR, Singapore.

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ABSTRACT: Solid-state halogen bonding interactions present in four families of structurally similar tritopic halogeness were examined in an effort to identify molecular features that promote halogen...carbonyl, halogen...halogen, and/or halogen... π interactions. The substrates used in this study all featured three haloarene substituents attached to a central 1,3,5-substituted arene ring with conformationally flexible linkers (ketone or ester groups) in order to systematically vary the polarization of the aryl halogen groups. Within each individual substrate type, however, there was found to be little correlation in the halogen bonding motifs exhibited as a function of halogen present (I, Br, and Cl). In general, the iodoarene derivatives examined exhibited a greater degree of halogen bonding interactions than the bromo and chloro analogues, and a unique bifurcated $I \cdots I/I \cdots O = C$ halogen bonding synthon was identified in two substrates. Halogen bonding contacts observed in tritopic iodoarenes correlated nicely with electrostatic potentials of simpler model compounds determined using computational methods. This study highlights the difficulty in attempting to empirically correlate halogen bonding with molecular structure.

Introduction

Halogen bonding is a type of noncovalent interaction that occurs between organic, inorganic/organometallic, or diatomic halogens and Lewis basic electron pair donors.¹ Halogen bonds are primarily electrostatic attractions that are made possible by anisotropy in the electron density surrounding most halo substituents, particularly I, Br, and Cl. In organic halogens, this unequal distribution of electron density produces regions of positive electrostatic potential along the axes of C-X bonds. Approach of electron donors (N, O, or another halogen) along this vector can then result in energetically favorable interactions.² Halogen bonds are generally regarded as weak interactions (weaker than hydrogen bonds) but are highly directional. However, the strength of halogen bonding interactions can be modulated by neighboring groups, particularly functionality that serves to increase the electrophilic character of the halogen, which often leads to a corresponding increase in halogen bonding ability.³

Structurally defining halogen bonding interactions are typically manifested in the solid state, and crystal engineering studies over the past decade have demonstrated the ability of halogen bonding to influence or control the supramolecular structures of extended molecular assemblies.¹ Recent applications of solid-state halogen bonding in mediating assembly of organic conductors and magnets,⁴ chemical separation agents,⁵ NLO-active materials,⁶ liquid crystals,⁷ and porous organic solids⁸ have been reported. Additionally, evidence for solution phase halogen bonding operative in novel molecular receptors⁹ and in biological host–guest systems¹⁰ has been obtained. Despite these impressive achievements, there is still much to uncover regarding the nature of halogen bonding and the reliability of such interactions, particularly in the face of potentially competing noncovalent attractions. In turn, gain-

ing a greater fundamental understanding of solid-state halogen bonding (along with its inherent limitations) will benefit efforts in crystal engineering by ultimately allowing researchers to predictably invoke such interactions in combination with other noncovalent attractions in the rational design of functional materials.¹¹

An approach toward achieving a better understanding of halogen bonding hierarchies and the relative importance of various halogen bond types entails structurally characterizing closely related polyfunctional compounds that differ in the identity of their halogen substituents. In tandem with subtle variations in the electronic characteristics across a family of organohalogens, it may be possible to ascertain the significance of specific halogen bonding synthons as a function of molecular structure. Toward this end, we have prepared a series of tritopic haloarene derivatives designed to probe the interplay of $C=O\cdots X$ and $X\cdots X$ halogen bonding with electronic effects arising from the substitution pattern of the arene. Importantly, we have chosen to investigate conformationally flexible haloarenes in order to accommodate the significant size differences between the halogens. Our thinking is that a family of analogous organohalides will be better equipped to maintain energetically significant halogen bonding interactions if the molecular conformation can be adjusted according to the identity of the halide. This feature should attenuate the influence that large iodine substituents can sometimes exert over solid-state structures, especially in conformationally rigid molecules.12

We have previously reported the solid-state halogen bonding patterns found in 4-halotriaroylbenzenes 1a-1d(Scheme 1).¹³ In this family, the bromo and chloro derivatives **1b** and **1c** were found to be isostructural, and two distinct types of C=O···X halogen bonds were prominently featured in the crystalline networks. Solid solutions prepared from **1b**/ **1c** were also characterized. In contrast, the iodo analogue **1a** exhibited a different halogen bonding pattern in which one iodoarene participates as both electrophile and nucleophile in

^{*}To whom correspondence should be addressed. E-mail: chris-pigge@uiowa.edu.

a bifurcated halogen bond with C=O and ArI partners, and a second iodoarene functions solely as an electrophile in an $I \cdots I$ contact. The third iodoarene does not appear to be involved in any intermolecular associations. Not surprisingly, the fluoro analogue 1d did not exhibit any halogen bonding contacts. Our conclusions from this study are that Cl/ Br····O=C interactions are preferred over Cl····Cl and $Br \cdots Br$ in this system, but incorporation of an iodine group results in formation of I...I contacts at the expense of additional $I \cdots O = C$ bonds. In subsequent work, we prepared and characterized the tritopic iodophenoxy ester 2a that possesses more electron-rich iodoarene substituents relative to those found in **1a**.¹⁴ Triester **2a** formed an inclusion host framework mediated by a combination of symmetry, solvent templation, and bifurcated I····O=C and I··· π halogen bonding. Guest solvent molecules (CHCl₃, benzene, or pyridine) were included in nanometer-sized channels. A close packed form of 2a was also characterized and found to exhibit $I \cdots O = C$ and $I \cdots \pi$ halogen bonding interactions as well. We attribute (at least in part) the appearance of $I \cdots \pi$ interactions in 2a to the nucleophilicity of the iodophenoxy rings arising from the electron-donating oxygen atoms. Notably, such interactions were not observed in 1a. To further examine the halogen bonding patterns found in conformationally flexible carbonyl-containing haloarenes related to the compounds discussed above, we have prepared and structurally characterized tritopic bromo, chloro, and fluoro phenoxy esters 2b-2d, isomeric iodo- and bromo-esters 3a-3b, and 3-halotriaroylbenzenes 4a-4b. The results of this effort along with a comparative analysis of the relationship between molecular structure and halogen bonding interactions are reported herein.

Experimental Section

Halophenoxy Esters 2b-2d. These substrates were prepared from trimesic acid chloride and the appropriate 4-halophenol using previously reported procedures.¹⁴ Compound characterization data are given below.

Trimesic Acid Ester 2b. Mp 188–189 °C. ¹H NMR (300 MHz, CDCl₃) δ 9.21 (s, 3H), 7.59 (d, J = 8.8 Hz, 6H), 7.18 (d, J = 8.8 Hz, 6H). ¹³C NMR (75 MHz, CDCl₃) δ 163.1, 149.7, 136.4, 133.0, 131.2, 123.5, 119.8. Anal. calcd. for C₂₇H₁₅Br₃O₆: C 48.04, H 2.24. Found: C 48.02, H 2.32.

Trimesic Acid Ester 2c. Mp 194–195 °C. ¹H NMR (300 MHz, CDCl₃) δ 9.22 (s, 3H), 7.45 (d, J = 8.9 Hz, 6H), 7.24 (d, J = 8.9 Hz, 6H). ¹³C NMR (75 MHz, CDCl₃) δ 163.2, 149.2, 136.4, 132.1, 131.2, 130.0, 123.1. Anal. calcd. for C₂₇H₁₅Cl₃O₆: C 59.86, H 2.79. Found: C 59.72, H 2.74.

Trimesic Acid Ester 2d. Mp 157–158 °C. ¹H NMR (300 MHz, CDCl₃) δ 9.31 (s, 3H), 7.41–7.02 (m, 12H). ¹³C NMR (75 MHz, CDCl₃) 163.5, 162.4, 159.2, 146.5, 136.4, 131.3, 123.2, 123.1, 116.8, 116.5. Anal. calcd. for $C_{27}H_{15}F_3O_6$: C 65.86, H 3.07. Found: C 65.68, H 3.16.

Phloroglucinol Ester 3a. Phloroglucinol (0.81 g, 5.0 mmol), 4iodobenzoyl chloride (4.13 g, 15.5 mmol), Et₃N (2.2 mL, 15.5 mmol), and DMAP (0.20 g) were combined in 20 mL of CH₂Cl₂. The reaction was stirred at room temperature for 4 h. Water was then added and the layers were separated. The aqueous phase was extracted with additional CH₂Cl₂ and the combined organic layer was washed with 10% aq. HCl solution, 5% aq. NaOH solution, and brine, followed by drying over anhydrous MgSO₄. Filtration and removal of the solvent afforded a crude product that was purified by flash column chromatography (SiO₂, hexanes/EtOAc) to afford **3a** as a colorless solid (2.32 g, 57%). Mp 192–193 °C. ¹H NMR (300 MHz, CDCl₃) δ 7.86 (br. s, 12H), 7.16 (s, 3H). ¹³C NMR (75 MHz, CDCl₃) δ 164.2, 151.6, 138.3, 131.8, 128.6, 113.5, 102.3. Anal. Calcd. for C₂₇H₁₅I₃O₆: C 39.71, H 1.84. Found: C 39.45, H 1.81.

Scheme 1. Conformationally Flexible Haloarenes Examined in This Study^a



^a Structures reported in this paper are indicated with an asterisk (*).

Phloroglucinol Ester 3b. This material was prepared using the procedure given above except that 4-bromobenzoyl chloride was used in place of 4-iodobenzoyl chloride. Yield: 52%, mp 162–164 °C. ¹H NMR (300 MHz, CDCl₃) δ 8.04 (d, J = 8.6 Hz, 6H), 7.67 (d, J = 8.6 Hz, 6H), 7.17 (s, 3H). ¹³C NMR (75 MHz, CDCl₃) δ 163.9, 151.9, 132.3, 129.5, 128.3, 113.5, 107.7. Anal. Calcd. for C₂₇H₁₅Br₃O₆: C 48.04, H 2.24. Found: C 47.65, H 2.36.

3-Halotriaroylbenzenes 4a and 4b. These triaroylbenzenes were prepared from 3-iodoacetophenone and 3-bromoacetophenone, respectively, according to previously published procedures.^{13,15} **4a**: Mp 138–140 °C. ¹H NMR (300 MHz, CDCl₃) δ 8.32 (s, 3H), 8.14 (t, J = 1.7 Hz, 3H), 7.91 (m, 3H), 7.71 (m, 3H), 7.25 (t, J = 7.8 Hz, 3H). ¹³C NMR (75 MHz, CDCl₃) δ 193.1, 142.3, 138.8, 138.3, 138.0, 134.4, 130.5, 129.3, 94.8. Anal. calcd. for C₂₇H₁₅I₃O₃: C 42.22, H 1.97. Found: C 42.12, H 1.89. **4b**: Mp 140–142 °C. ¹H NMR (300 MHz, CDCl₃) δ 8.38 (s, 3H), 8.03 (t, J = 1.6 Hz, 3H), 7.70 (m, 6H), 7.44 (t, J = 9.4 Hz, 3H). ¹³C NMR (75 MHz, CDCl₃) δ 193.2, 138.3, 138.1, 136.4, 134.4, 132.9, 130.5, 128.7, 123.3. Anal. Calcd. for C₂₇H₁₅Br₃O₃: C 51.71, H 2.41. Found: C 51.55, H 2.31.

X-ray Crystallography. Single crystals of 2-4 were grown by slow evaporation of CH₂Cl₂ or CH₂Cl₂/MeOH solutions. Diffraction data were collected using either a Nonius-Kappa CCD or a Bruker APEXII CCD diffractometer. Crystallographic data are shown in Table 1. Details concerning structure solution and refinement can be found in the Supporting Information (CIF).

Computations. Electrostatic potential surfaces were generated for model iodoarenes 5-8 from DFT calculations performed at the B3LYP/6-31G (d,p) level.¹⁶ Potential surfaces were mapped by conventional molecular electron density (0.002 electron/Å³) and color-coding. Crystal structure coordinates for 1a, 2a, 3a, and 4a provided the basis for the simpler model compounds 5-8, respectively. The structures were truncated to simplify the calculations and the torsion angles of the resulting benzophenones and aryl benzoate esters were fixed to mimic the molecular conformation found in the solid state. Bond lengths and angles were not constrained so as to attain the nearest local minima.

Results and Discussion

Our previous study of solid-state halogen bonding patterns in 4-halotriaroylbenzenes 1 revealed significant differences

	$\begin{array}{c} 2b \cdot (CH_2 Cl_2)_{0.43} \cdot \\ (CH_3 OH)_{0.26} \end{array}$	$\begin{array}{c} 2c \!\cdot\! (CH_2Cl_2)_{0.34} \cdot \\ (CH_3OH)_{0.09} \end{array}$	2d	3a · CH ₂ Cl ₂	3b	4a	4b
cryst syst	monoclinic	monoclinic	monoclinic	monoclinic	monoclinic	monoclinic	monoclinic
space group	C2/c	$P2_1/n$	$P2_1/c$	$P2_1/n$	$P2_1/c$	$P2_1/c$	$P2_1/c$
a/Å	46.434(5)	3.8968(5)	19.872(2)	4.2535(3)	3.8321(5)	11.9616(13)	11.6382(13)
b/Å	3.9139(5)	21.877(3)	3.8652(5)	41.981(3)	27.975(3)	14.2501(15)	14.1355(15)
$c/\text{\AA}$	34.656(4)	29.152(3)	28.764(3)	15.1423(12)	23.031(3)	14.9466(16)	14.9051(16)
α/°	90	90	90	90	90	90	90
β'°	120.273(5)	91.083(5)	90.584(5)	97.928(4)	90.108(6)	106.816(5)	109.070(5)
$\gamma/^{\circ}$	90	90	90	90	90	90	90
$V/Å^3$	5439.4(11)	2484.8(5)	2209.2(4)	2678.1(3)	2469.0(5)	2438.8(5)	2317.5(4)
Ż	8	4	4	2	4	4	4
$D_{\rm calc}$	1.758	1.532	1.480	2.129	1.816	2.092	1.797
$\mu (\text{mm}^{-1})$	4.576	0.485	0.121	3.643	4.944	3.872	5.250
T/K	210(2)	190(2)	210(2)	100(2)	100(2)	150(2)	190(2)
no. of reflns	53881	15103	41938	49424	34122	55068	40352
no. of unique reflns	6183	4191	4997	5182	4308	5589	5308
no. of reflns with $I > 2\sigma(I)$	4717	2777	4080	4598	3281	4907	4200
no. of params	389	367	325	331	326	303	298
$R1 \left[I \ge 2\sigma(I)\right]$	0.0378	0.0551	0.0353	0.0736	0.1618	0.0225	0.0325
wR2 (all reflns)	0.0886	0.1189	0.0918	0.1698	0.3691	0.0498	0.0739

between the iodo-substituted compound as compared to the bromo/chloro analogues.¹³ Given this observation we were interested in examining the effect of perturbing the electronics of the haloarene substituents while nominally preserving the gross molecular structures. Consequently, the trimesic acid esters **2** and the phloroglucinol benzoates **3** were prepared and characterized. In **2**, the haloarene rings are now more electron rich due to the presence of electron donating ester oxygen atoms. This feature should attenuate the electrophilicity of the para-halogen atoms while also rendering the ester carbonyl groups less Lewis basic than the ketone functional groups found in **1**. Conversely, in **3** electron withdrawing groups remain positioned para with respect to the halogens but in the form of an ester linkage rather than a ketone carbonyl.

Several solid-state inclusion compounds and a nonsolvated close-packed structure of iodo-substituted trimesic acid ester 2a were reported previously.¹⁴ Both types of structures exhibited a combination of $I \cdots O = C$ and $I \cdots \pi$ interactions. Hexagonal nanoporous inclusion complexes with pyridine, CHCl₃, and benzene solvates were further mediated by symmetry and solvent templation. The preparation of similar inclusion complexes from the bromo congener 2b was attempted, but crystallization from the solvents listed above failed to produce single crystals. Slow evaporation of a CH₂Cl₂/MeOH solution of 2b, however, afforded X-ray quality crystals and a view of the structure illustrating the principal intermolecular interactions is shown in Figure 1. Individual molecules of **2b** adopt an approximately C_3 symmetrical orientation and form discrete supramolecular dimers mediated by a pair of type II $Br \cdots Br$ halogen bonds.¹⁷ Disordered CH₂Cl₂ solvate molecules are housed within the macrocycles formed as a consequence of this dimerization, while methanol solvates (also disordered) reside in channels between supramolecular macrocycles. There appear to be no significant Br····O=C or Br··· π interactions, unlike the situation encountered in structures of 2a. Dimeric arrays of **2b** stack in superimposed sheets along the *b* axis.

The crystal structure of chloro analogue 2c (also obtained as a channel-type inclusion complex with disordered CH₂Cl₂ and MeOH solvates) differs markedly from both 2a and 2b. In this structure, molecules of 2c are connected via Cl···O=C halogen bonds to form undulating ribbon-like chains (Figure 2). Additional solid-state C-H···O hydrogen bonds (not shown in Figure 2) appear to further reinforce this ribbon



Figure 1. View of Br····Br interactions in **2b**. Halogen bonding metrics: $d_{\text{Br}...\text{Br}} = 3.78 \text{ Å}$, C–Br···Br angles = 142.6°, 83.7°. Halogen bonding is indicated by dashed lines; CH₂Cl₂ and MeOH solvates are omitted for clarity.

motif and there are no significant $Cl \cdots Cl$ close contacts. Thus, the crystal structures of **2a** (nonsolvated), **2b**, and **2c** each exhibit distinct and nonidentical halogen bonding interactions that vary as a function of halogen identity.

Not surprisingly, the 4-fluorophenoxy trimesic acid ester does not exhibit any contacts that can be categorized as halogen bonding interactions, and this reflects the general



Figure 2. Ribbon motif maintained by C=O···Cl halogen bonds in **2c**. Relevant distances and angles: d_{C1} ... $_{O=C}$ = 3.23 Å, C-Cl···O = 154.3°, C=O···Cl = 111.5°. Solvate molecules omitted for clarity.

correlation between halogen bonding ability and halogen polarizability.^{1,2} The structure of **2d** does display several types of weak hydrogen bonding contacts, however, including examples of C–H···F hydrogen bonds.¹⁸ These hydrogen bonds serve to connect individual molecules to give rise to helical chains as shown in Figure 3. Given the lack of halogen bonding evident in the structure of **2d** and the absence of meaningful halogen bonding interactions in the 4-fluoro-(triaroylbenzene) **1d**,¹³ characterization of the fluoro derivatives of **3** and **4** was not pursued.

The trimesic acid esters described above feature halophenoxy rings arrayed about a central arene core. The 4-halobenzoate esters prepared from phloroglucinol (**3a** and **3b**) represent topologically similar tritopic haloarenes in which the electronic effects of the ester linkage are reversed relative to **2**. Consequently, we anticipated a priori that the para electron withdrawing carbonyl group would increase the electrophilicity of the halogen substituents, resulting in a corresponding increase in the likelihood of halogen bond formation relative to what we observed in **2a**-**2c**.

Crystals of $3a \cdot CH_2Cl_2$ were obtained from slow evaporation of a CH_2Cl_2 solution. Individual molecules were found to stack in layers connected by a helical chain of halogen bonding interactions. A partial view of the structure is shown in Figure 4 that illustrates the major intermolecular solid-state attractions. Two of the three iodo-arene units in molecules of 3a are engaged in halogen bonding. One iodo group forms bifurcated contacts with another iodine substituent and a carbonyl oxygen atom. Thus, this iodine functions as a



Figure 3. Helical chains exhibiting C-H···F hydrogen bonding in the structure of **2d**. C-H···F hydrogen bonds indicated by dashed lines: $d_{\text{H}...\text{F}} = 2.75 \text{ Å}$, C-H···F = 153.7°, C-F···H = 152.5°.



Figure 4. View of halogen bonding interactions in **3a**. CH₂Cl₂ solvates omitted for clarity. Relevant distances and angles: $d_{I...I} = 3.89$ Å, $d_{I...O} = 3.07$ Å, C–I···I angles = 163.8° and 94.7°, C–I···O = 163.7°, C=O···I = 143.2°.

halogen bond donor (electrophile) toward the Lewis basic carbonyl group and a halogen bond acceptor (nucleophile) toward neighboring electrophilic iodoarenes. The third iodoarene moiety does not appear to be involved in any non-covalent interactions. Notably, the halogen bonding motif operative in the structure of **3a** closely resembles the halogen bonding pattern identified in 4-iodotriaroylbenzene **1a**.¹³ Crystals of **3a** were obtained as an inclusion complex with CH_2Cl_2 . The solvates reside in channels oriented down the *a* axis and are disordered about an inversion center. A view of the extended packing is shown in Figure 5.

Crystals of the tris(bromobenzoate) ester of phloroglucinol (**3b**) were also obtained from a CH_2Cl_2 solution; however, these crystals proved to be quite fragile and diffracted poorly.



Figure 5. View of extended packing (down a) in $3a \cdot CH_2Cl_2$. Solvate molecules shown in blue.



Figure 6. Extended packing in 3b viewed down a.

Consequently, diffraction data could only be refined to an Rvalue of $\sim 16\%$ and so discussions concerning specific noncovalent attractions must be approached with caution. The poor quality of the diffraction data notwithstanding, examination of the extended network present in 3b reveals no significant halogen bonding interactions. Indeed, 3b crystallizes as a close-packed structure seemingly mediated by various C-H···O and perhaps C-H···Br hydrogen bonds. The structure is composed of two-dimensional sheets that stack directly on top of each other down the a axis as shown in Figure 6. Within each layer individual molecules are aligned in vertical rows in a "head-to-tail" fashion, with adjacent vertical rows running in antiparallel directions. The extended packing in the ac plane shows the presence of distinct and noninterpenetrated layers. Thus, the network assemblies found in 3a and **3b** differ significantly, not just in their overall topology but also (somewhat surprisingly) by the presence of multiple halogen bonding interactions in 3a and the complete absence of such interactions in 3b. The tris(4-chlorobenzoate) phloroglucinol ester was prepared as well, but unfortunately efforts to secure X-ray quality crystals of this material have failed.

A final molecular scaffold examined in this study is based on the 1,3,5-triaroylbenzene framework and so is directly structurally related to 1. In 4a and 4b, however, the halogen substituents have been moved to meta positions relative to the ketone carbonyls, and this positioning is expected to diminish the halogen bonding activating effect of these electron withdrawing groups. The iodo, bromo, and chloro analogues of 4 have all been prepared using established procedures, but



Pigge et al.



Figure 7. Four-point C-H···O hydrogen bonding interaction observed in 4a and 4b (structure of 4a illustrated). See text for Hbonding metrics.

single crystals of this last derivative have not been successfully obtained. X-ray quality crystals of both iodo (4a) and bromo (4b) analogues, however, were grown from CH₂Cl₂ solution and diffractometry revealed these two crystals to be isostructural. Iodo derivative 4a, however, exhibits minor rotational disorder ($\sim 2\%$) about one of the aryl – C=O bonds. Rather than halogen bonds, the dominant intermolecular interaction present in these structures appears to be centrosymmetric four-point recognition patterns involving two unique C-H···O hydrogen bonds (Figure 7). The "outer" H-bonding interactions are longer and more distorted from ideal geometry ($d_{H...O} = 2.69$ Å, C–H···O = 132.4°) compared to the two equivalent "inner" hydrogen bonds $(d_{\rm H...O} =$ 2.46 Å, $C-H\cdots O = 160.3^{\circ}$), but both contacts fall within the range of attractive interactions. Similar distances and angles were found in the structure of bromo derivative 4b $(d = 2.60, 2.42 \text{ Å}, 133.8, 167.7^{\circ})$. Notably, a similar four-point hydrogen bonding motif (exhibiting comparable H-bond distances and angles) was encountered in a nonsolvated structure of a triaroylbenzene derivative that possessed NO2 groups in place of the halogen substituents.¹⁹

Halogen bonding interactions are nominally present in the structures of 4a and 4b, although in these instances arene π systems function as the halogen bond acceptors. These $X \cdots \pi$ interactions (X = I, Br) serve to connect the discrete dimeric supramolecular assemblies of the type illustrated in Figure 7 to adjacent H-bonded dimers resulting in generation of supramolecular columns aligned down the *a* axis.²⁰ The association of two such dimers via $I \cdots \pi$ interactions is illustrated in Figure 8 in which halogen bonds have been drawn to the centroids of the arene acceptors. Two distinct types of I $\cdots \pi$ contacts are observed to converge upon a single arene ring, and both exhibit relatively short I $\cdots \pi_{centroid}$ distances (3.57 and 3.61 Å) and near linear C–I \cdots $\pi_{centroid}$ angles (150.6 and 157.0°). The bromo analogue 4b displays comparable halogen bonding angles about the relevant aryl



Figure 8. Linking of hydrogen bonded dimers in 4a via putative $I \cdots \pi$ interactions (shown in blue).



Figure 9. View of **4a** down *b*. Hydrogen bonding shown as dashed lines, $I \cdots \pi$ interactions from Figure 8 shown as solid black lines, $I \cdots \pi$ interactions connecting adjacent rows shown in green.

bromines (150.4 and 161.5°) with somewhat shorter Br $\cdots \pi_{\text{centroid}}$ distances (3.47 and 3.49 Å).

A view of the extended packing observed in **4a** (as well as **4b**) is shown in Figure 9 to illustrate the arrangement of hydrogen/halogen bonded ribbons in parallel rows. Interestingly, close contacts between an arene π system in one row and a halogen in an adjacent row are present; however, the arene involved possesses a 1,3,5-tricarbonyl substitution pattern and so is extremely deactivated toward participation in halogen bonding. This contact, then, may arise simply as a consequence of other crystal packing forces. Indeed, all the halogen $-\pi$ interactions found in **4a**,**b** involve deactivated arenes substituted with inductively electron withdrawing

 Table 2. Summary of Solid-State Halogen Bonding Interactions

 Observed in 1–4

interaction	1	2	3	4
I···I	+++		+++	
I····O=C	+++	+++	+++	
$I \cdots \pi$		+++		+++
Br⋅⋅⋅Br		+++		
Br····O=C	+++			
$Br \cdots \pi$				+++
Cl···Cl			nc ^a	nc
Cl···O=C	+++	+++	nc	nc
$Cl\cdots\pi$			nc	nc

^a No crystals were obtained.

Scheme 2. Halogen Bonding Synthons Exhibited in 1–4 along with Idealized Geometries^{*a*}



 $^a\mathrm{Bifurcated}$ interaction IV was observed exclusively in iodoarene derivatives 1a and 3a.

halogen atoms as well as carbonyl groups. Given the presence of multiple and seemingly mutually reinforcing four-point hydrogen bonding interactions in this system, the $X \cdots \pi$ interactions observed may represent secondary contacts that support the supramolecular network but do not exert directing effects upon its formation. While the contacts in question certainly meet the distance and angle criteria established for $X \cdots \pi$ halogen bonding, electronic factors in the molecular building blocks should attenuate the energetic significance of these putative interactions.

The substrates examined in this study were designed to probe the interplay between specific types of halogen bonding interactions $(X \cdots X, X \cdots O = C, and X \cdots \pi)$ in structurally similar but electronically distinct systems (Scheme 2). At the outset we were hopeful that clear trends in halogen bonding behavior would emerge, but this has largely proved not to be the case. A summary of halogen bonding interactions observed across all four substrate families is provided in Table 2. The most meaningful comparisons can be drawn between the iodo- and bromo-substituted derivatives as crystal structures of 1a-4a and 1b-4b were successfully obtained. The only instance in which similar halogen bonding interactions are evident is found in 4a and 4b as crystals of these two compounds are isostructural. The significance of the putative halogen bonding contacts in **4a** and **4b** (I $\cdots \pi$ and Br $\cdots \pi$, respectively), however, is tempered by the presence of seemingly more significant $C-H\cdots O$ hydrogen bonds and the recognition that the close $X \cdots \pi$ contacts may well be a consequence of lattice-imposed proximity. In contrast, the halogen bonding interactions in 1-3 do appear to be energetically significant, but the patterns present in I/Br substrate pairs 1a/1b, 2a/2b, and 3a/3b have little in common. It is

Table 3. Electrostatic Potential Maps of Model Iodoarenes 5-8^a



^{*a*} Blue represents areas of positive electrostatic potential and red represents areas of negative electrostatic potential. Relative electrostatic potential values were determined on a scale of -25 to +25 kcal mol⁻¹.

interesting to note, however, that the bifurcated $I \cdots I$ and $I \cdots O = C$ synthon observed in 4-iodo(triaroylbenzene)¹³ derivative 1a is also present in phloroglucinol iodobenzoate 3a and that both of these substrates feature an iodoarene activated for enhanced halogen bonding by the presence of an electron withdrawing group at the para position. While analogous I····O=C interactions have been observed in inter alia structurally simpler p-iodophenyl aldehydes, ketones and esters,²¹ incorporation of an additional iodo group to form a three-centered halogen bonding chain does not appear to be common. The presence of multiple iodoarene units within individual molecular building blocks and conformational flexibility may facilitate this interaction. The $I \cdots I/I \cdots O = C$ bifurcated synthon features an iodo group that functions as both electron donor and acceptor and in this regard resembles the halogens found in cyclic halogen bonding trimers reported by Nangia²² and Bosch.²³ In 1a and 3a, however, halogen bonded chains rather than cyclic supramolecular constructs are produced.

In an effort to better understand how the substitution pattern of the haloarene units in 1-4 affects halogen polarization, electrostatic potential maps were generated from DFT calculations performed on simpler model compounds.¹⁶ Specifically, four iodoarenes 5-8 representing truncated versions of 1a-4a, respectively, were modeled. The molecular conformation in each model compound was taken directly from relevant crystal structure coordinates of 1a-4a in order to approximate the empirically observed solid-state conformation. Torsion angles about the ketone and ester linkages were then fixed. The results of this computational study are presented in Table 3. In each case a region of positive electrostatic potential (blue) is located on the iodine substituent along the axis of the C-I bond; however, qualitative differences in the degree of polarization as a function of arene substitution pattern are also apparent. These differences are quantified in a relative sense by the calculated potentials shown at the bottom of Table 3. As can be seen, the iodoarenes possessing electron withdrawing carbonyl groups at the para

positions (5 and 7) exhibit the greatest polarization and so would be expected to be better halogen bond donors than the iodo groups in 6 and 8. This feature is borne out experimentally in that triaroylbenzene 1a and phloroglucinol ester 3a seemingly exhibit more halogen bonding contacts than 2a and **4a**. Moreover, the bifurcated $I \cdots I/I \cdots O = C$ interactions in both 1a and 3a appear to constitute the principal mode of noncovalent bonding in the respective crystals. In contrast, the halogen bonding interactions in solvated forms of 2a $(I \cdots \pi \text{ and } I \cdots O = C)$ occur in combination with solvent templating and symmetry effects to produce metastable hexagonal nanoporous structures,¹⁴ while those in 4a (I $\cdots \pi$) appear to be a consequence of crystal packing. In line with these observations, model compounds 6 and 8 reveal a lesser degree of iodine polarization due to an electron donating para substituent (ester linkage) in 6 and a meta-oriented substituent in 8. Thus, computational results performed on simpler analogues accurately reflect the relative halogen bonding abilities of tritopic iodoarenes 1a-4a.

Conclusions

This study probed the propensity of structurally related but electronically differentiated tritopic haloarenes to engage in various types of solid-state halogen bonding. While only a small number of structures were examined, the lack of correlation between halogen bonding interactions among conformationally flexible substrates that differed only in the identity of the halogen highlights the difficulty in predicting the occurrence and topology of these interactions, even in organic molecules devoid of strong hydrogen bonding functionality. The generally weak nature of many halogen bonding interactions may contribute to this lack of predictability as solid-state self-assembly processes that maximize alternative noncovalent attractions (e.g., C-H···O hydrogen bonds, van der Waals attractions) may offer greater energetic advantages.²⁴ In contrast, the iodoarene derivatives 1a, 2a, and 3a all gave rise to structures in which halogen bonding seemingly plays a

Article

central role. Both $1a^{13}$ and 3a exhibit similar $I \cdots I/I \cdots O = C$ bifurcated motifs assisted by the electronic activation of the iodine substituents by electron withdrawing *para*-carbonyl groups, while trimesic acid ester $2a^{14}$ assembles via $I \cdots O = C$ and $I \cdots \pi$ interactions to form nanoscale channel-type inclusion complexes in the presence of suitable solvent templates. Future studies will examine the occurrence of similar interactions in more highly functionalized substrates.

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Supporting Information Available: X-ray data with details of refinement procedures (CIF). This material is available free of charge via the Internet at http://pubs.acs.org.

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