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Influence of substituents in aromatic ring on the strength of halogen bonding in iodobenzene derivatives

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ABSTRACT: Halogen bonding properties of 3,4,5-triiodobenzoic acid (**1**, **2**), 1,2,3-triiodobenzene (**3**), 4-iodobenzoic acid (**4**), pentaiodobenzoic acid ethanol solvate (**5**), hexaiodobenzene (**6a**, **6b**, **6c**), 4-iodobenzonitrile (**7**), 3-iodobenzonitrile (**8**), 2,4-diiidoaniline (**9**), 4-iodoaniline (**10**), 2-iodoaniline (**11**), 2-iodophenol (**12**), 4-iodophenol (**13**), 3-iodophenol (**14**), 2,4,6-triiodophenol (**15**), 4-iodoanisole (**16**), 3,4,5-triiodoanisole (**17**) have been studied. The results suggested that substituents other than halogen in the aromatic ring affect XB properties of iodide substituents in *ortho*-, *meta*- and *para*-positions. The effect depends on the electron-withdrawing/electron-donating properties of the substituent. Thus, electron-donating substituents with

1
2
3 positive mesomeric effect favor *m*-iodines to act as XB donors. By
4
5 contrast, electron substituents with negative mesomeric effect
6
7 favor *o*- and *p*-iodines to act as XB donors. Furthermore, the
8
9 stronger the mesomeric effect of the EWG or EDG substituent, the
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11 higher impact it makes on the size of the σ -hole and, consequently,
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13 on the XB donor ability of the iodide substituent.
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20 1. INTRODUCTION

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22

23 Halogen bonding (XB) can be defined as an interaction between Lewis
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25 base (electron-density donor, XB acceptor) and halogen atom
26
27 (electron-density acceptor, XB donor). Halogen bonding is
28
29 acknowledged since 1950th, when Hassel and Hvoslef discovered that
30
31 Br \cdots O bond distances in a crystal structure of Br₂/dioxane adduct
32
33 was shorter than the sum of van der Waals radii of bromine and
34
35 oxygen, indicating presence of a strong attractive interaction
36
37 between these atoms^{1,2}. Although, at that time it was called
38
39 "interaction" or "charge-transfer bonding". The term "halogen
40
41 bonding" appeared only in 1978 by Dumas and co-workers³. Over the
42
43 years, use of halogen bonding has been developed to a very powerful
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45 and useful tool in many chemical fields such as catalysis⁴⁻⁶,
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47 crystal engineering⁷⁻¹², biochemistry¹³⁻¹⁵, polymer sciences¹⁶,
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49 conductive materials^{17,18}, liquid crystals¹⁹⁻²¹ etc.
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1
2
3 Iodine, bromine, chlorine, and rarely fluorine act as XB donors.
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5 Polarizability of halogen bond donors increases in the order of F
6
7 $< \text{Cl} < \text{Br} < \text{I}^{22}$, making iodine the most favorable XB donor among
8
9 the halogens^{22,23}.

11
12
13 When an atom is involved in a covalent bond, redistribution of
14
15 electron density takes place, turning the electrostatic potential
16
17 on this atom to be anisotropic, i.e. electron density decreases
18
19 along the covalent bond extension and increases in the
20
21 perpendicular direction to it²⁴, as shown in Figure 1. This may
22
23 lead to the formation of a positive electrostatic potential along
24
25 the R-X bond and increased negative electrostatic potential in a
26
27 direction, perpendicular to the R-X bond. Politzer et. al²⁵ have
28
29 denoted the positive electrostatic potential as a "σ-hole" and
30
31 negative electrostatic potential as an "electron belt". Presence
32
33 of a positive σ-hole on the halogen atom explains its ability to
34
35 interact with nucleophiles in a "head-on" fashion. In turn, a
36
37 presence of a negative electron belt around the halogen atom allows
38
39 the interaction of the latter with electrophiles in a "side-on"
40
41 fashion. Thus, when a halogen X participates in a halogen bonding
42
43 via a σ-hole, it can be considered as an XB donor (i.e. electron
44
45 density acceptor). On the other hand, if an interaction takes place
46
47 via an electron belt, a halogen X can be considered as an XB
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49 acceptor (electron density donor).
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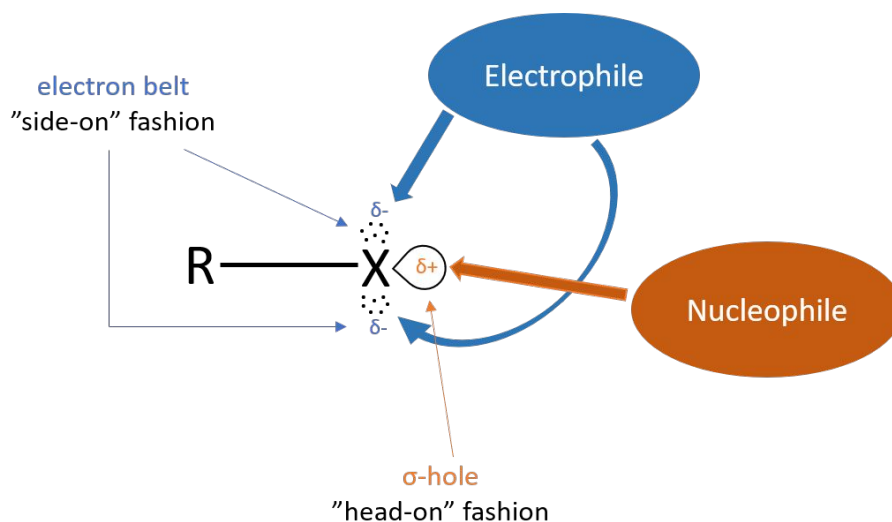


Figure 1. Anisotropic redistribution of the electron density on the atom X, covalently bound to R, where X = Hal, R = Hal, C, N, O etc.

Halogen bonding can be classified into two groups depending on the geometry of the R1-X1...X2-R2 fragment²⁴. First group can be described by type I short contacts, in which an R1-X1...X2 angle is close or exactly the same as the R2-X2...X1 angle. It is a symmetrical interaction and is usually not considered as a true XB, because it typically arises from the close-packing requirements and minimization of repulsion²⁶ (Figure 2). Another group of XBs is represented by type II short contacts, in which R1-X1...X2 angle is close to 90°, and an R2-X2...X1 angle is close to 180°. This is a bent interaction and is a true XB according to IUPAC definition²⁷.

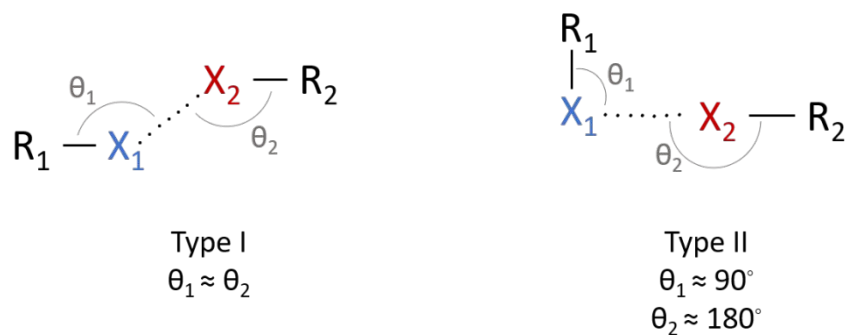


Figure 2. Types of halogen-halogen contacts.

Halogens attached to hydrocarbons are frequently used for XB investigations as in many cases they can be easily obtained and crystallized^{28,29}. In particular, halogenated benzenes are an interesting and convenient class, because halogens can be easily introduced in a benzene ring at different positions. This allows a study of structural features and energies of halogen bonding in a series of related compounds and, to a large extent, an elimination of the side effects like steric constrains etc. Besides this, halobenzenes^{28,30} provide a platform for introducing other types of substituents on the same molecule with possible interactions between the substituents. Investigation of the influence of different substituents with opposite mesomeric effects on the ability of halogens in *ortho*-, *meta*- and *para*-positions to act as XB donor or XB acceptor can contribute to better understanding of halogen bonding. Mesomeric effect can be identified as a redistribution of an electron density in an unsaturated chain due to the conjugation of a polar (electron-

1
2
3 donating or electron-withdrawing) group with the π -system of a
4 molecule. Electron-donating groups revealing a positive mesomeric
5 effect (+M) donate an electron density to a benzene ring. Due to
6
7
8 the resonance effect of conjugated double bonds in a benzene ring,
9
10 the electron density redistributes in a way that higher electron
11
12 density being localized on carbon atoms in *ortho*- and *para*-
13
14 positions and lower electron density being localized on carbon
15
16 atoms in *meta*-positions (Figure 3). In turn, such electron density
17
18 redistribution could affect the XB donor ability (i.e. an electron
19
20 density acceptor ability) of halogens, located in *ortho*-, *meta*- or
21
22 *para*-positions. This may happen because the XB donor ability of
23
24 halogens increases with the increase of the electron-withdrawing
25
26 ability of an atom Y bound to halogen atom X:



35 where Y is C, N, halogen atom etc., X is the halogen atom (electron
36
37 density acceptor, XB donor), A is an electron density donor (Lewis
38
39 base, XB acceptor) (Scheme 1)²³. Therefore, presence of electron-
40
41 donating substituents in a benzene ring should favor halogens in
42
43 *meta*-positions to act as XB donors. Electron-withdrawing groups,
44
45 revealing a negative mesomeric effect (-M), on the contrary, lead
46
47 to the opposite effect with the localization of higher electron
48
49 density on carbon atoms in *meta*-positions and lower electron
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51 density on carbon atoms in *ortho*- and *para*-positions (Figure 3).
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Therefore, halogens in *ortho*- and *para*-positions should favor XB donor behavior.

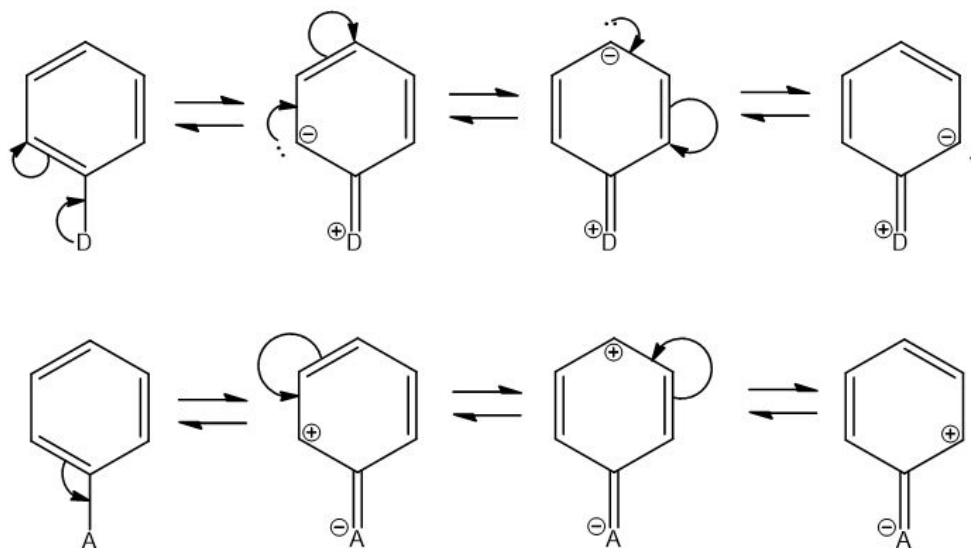


Figure 3. Redistribution of an electron density in a benzene ring by the electron-donor group (D) and the electron-acceptor group (A).

In the present work, we crystallized and studied the X-ray structures of commercially available 3,4,5-triiodobenzoic acid (**1**) and 3,4,5-triiodobenzoic acid with a solvate (ethanol) molecule (**2**). Also, we have compared structures of **1** and **2** with the structures of similar substituted iodobenzene derivatives: 1,2,3-triiodobenzene (**3**)³¹, 4-iodobenzoic acid (**4**)³², pentaiodobenzoic acid ethanol solvate (**5**)³³, hexaiodobenzene (**6a**, **6b**, **6c**)^{34,35}, 4-iodobenzonitrile (**7**)³⁶, 3-iodobenzonitrile (**8**)³⁷, 2,4-diiodoaniline (**9**)³⁸, 4-iodoaniline (**10**)³⁹, 2-iodoaniline (**11**)⁴⁰, 2-iodophenol

(12)⁴¹, 4-iodophenol (13)³⁷, 3-iodophenol (14)³⁷, 2,4,6-triiodophenol (15)⁴², 4-iodoanisole (16)⁴³, 3,4,5-triiodoanisole (17)⁴⁴ (Figure 4) found in literature.

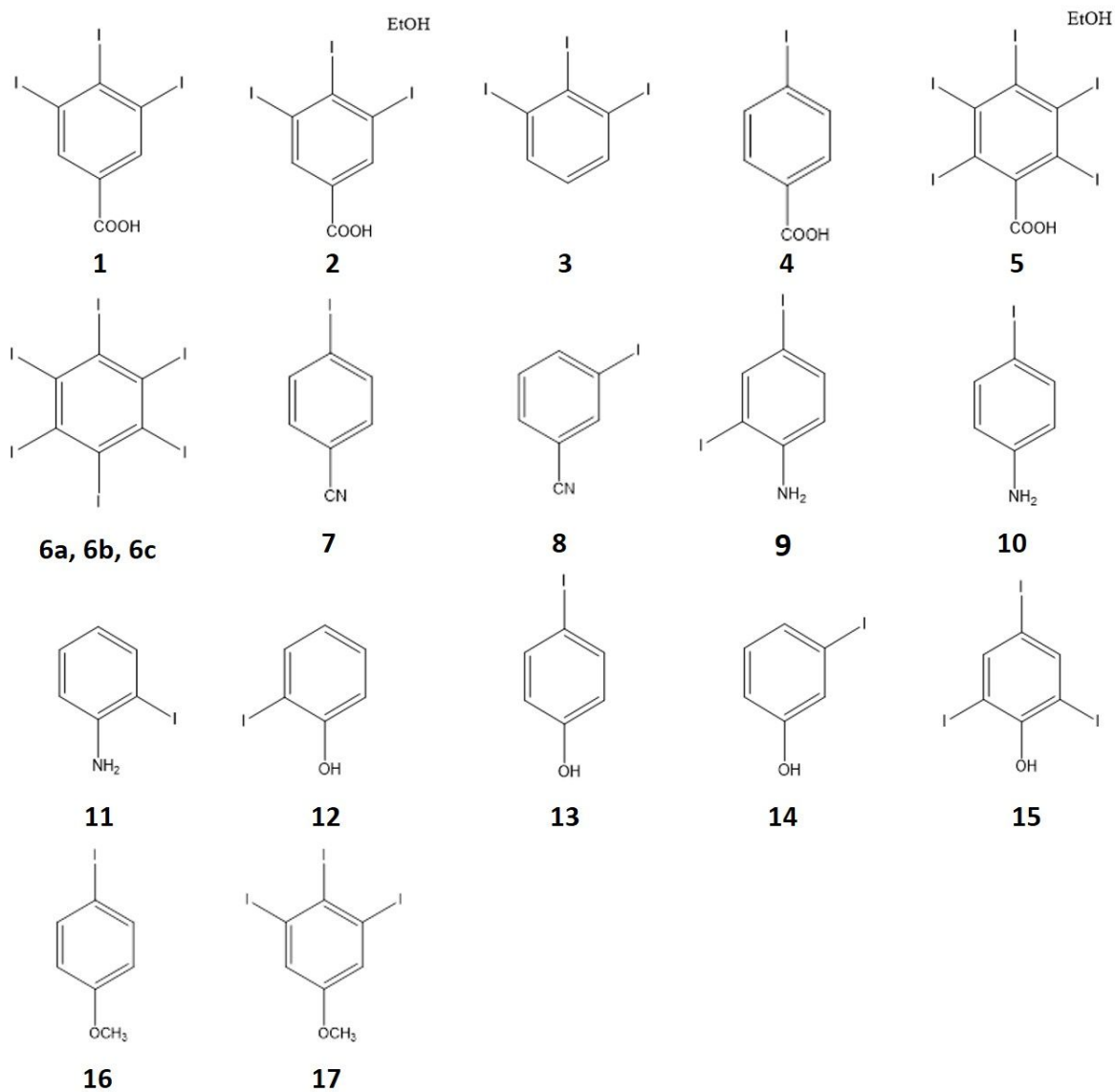


Figure 4. Schematic representation of the molecules, chosen for the investigation.

In this work we focused especially on the carboxyl -COOH, nitrile -CN, amino -NH₂, hydroxy -OH and methoxy -OCH₃ substituents as

1
2
3 potential halogen bond modifiers on *ortho*-, *meta*- and *para*-
4 positions in relation to the halogen atoms. Iodine was chosen as
5 the XB active atom due to its higher polarizability in comparison
6 with other halogens. This feature makes it easier to study the
7 possible mesomeric effects on its XB properties. The studied
8 systems **1-17** are summarized in Fig 4.
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17 The studied compounds have also many practical applications.
18 Halogenated derivatives of benzoic acids, anilines and phenols can
19 be found in various biological applications⁴⁵⁻⁵⁵, pharmacy⁵⁶,
20 biochemistry⁵⁷⁻⁵⁹, electrochemistry⁶⁰, catalysis⁶¹⁻⁶⁷ etc.⁶⁸⁻⁷².
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22 Therefore, the investigation of the XB behavior of this type of
23 molecules may also shed light on details on these processes.
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32 2. RESULTS AND DISCUSSION

33 2.1. Analysis of crystal structures of **1** and **2**

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36 In the structure of **1**, the I...I distances are in the range of 3.7323
37 (7) - 3.8791 (7) Å, while the sum of Bondi's van der Waals (vdW)
38 radii is 3.96 Å⁷³. Therefore, these interactions are expected to
39 be quite weak. There is also another intermolecular XB between
40 *para*-iodine of one triiodobenzoic acid (TIBA) molecule and the
41 double bonded oxygen atom O1 of a carboxyl group of another TIBA
42 molecule (I...O=C = 3.031 (6) - 3.138 (5) Å, Figure 5). This
43 interaction is already somewhat stronger based on the donor-
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3 acceptor distance (sum of vdW radii is 3.5 Å). It should be noted
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5 that *meta*-iodines participate in a halogen bonding both as XB
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7 donors and XB acceptors, while *para*-iodines act only as XB donors
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9 and interact only with the double bonded oxygen atom of the
10
11 neighboring molecule.
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15 The I atoms in *meta*-position relative to the -COOH substituent (I1
16
17 and I3) adopt different types of XB geometries. I1 is bound to two
18
19 I3B of two adjacent molecules providing a non-linear C4-I1...I3B-
20
21 C6B fragment with the C-I...I angles close to 90 ° (C4-I1...I3B =
22
23 99.4 (2) and C6B-I3B...I1 = 88.9 (2) °) and close to 180 ° (C6B-
24
25 I3B...I1 = 158.8 (2) and C4-I1...I3B = 169.2 (2) °). Therefore,
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27 this contact can be considered as type II XB (Figure 5), in which
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29 one angle in the R-X...X-R fragment is close to 90 ° and another
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31 angle is close to 180 °.
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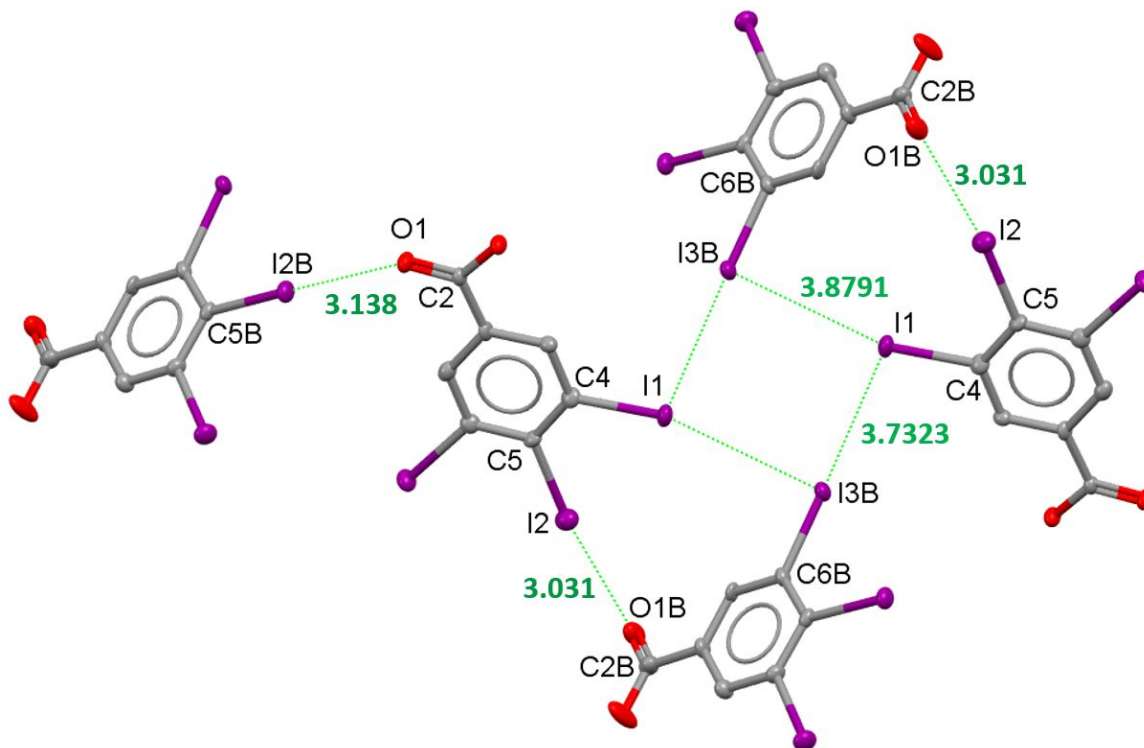


Figure 5. Halogen bonds in **1**. Type II contacts. Hydrogens are omitted for clarity. Selected bond lengths (Å) and angles (°): I1-I3B⁽ⁱ⁾ 3.8791 (7), I1-I3B⁽ⁱ⁾ 3.7323 (7), I2B-O1 3.138 (5), I2-O1B⁽ⁱ⁾ 3.031 (6), C4-I1-I3B⁽ⁱ⁾ 99.4 (2), C4-I1-I3B⁽ⁱ⁾ 158.8 (2), C6B⁽ⁱ⁾-I3B⁽ⁱ⁾-I1 88.9 (2), C6B⁽ⁱ⁾-I3B⁽ⁱ⁾-I1 169.2 (2), C5-I2-O1B⁽ⁱ⁾ 171.5 (2), C2B⁽ⁱ⁾-O1B⁽ⁱ⁾-I2 111.3 (5), C5B-I2B-O1 178.8 (2), C2-O1-I2B 143.8 (5). Equivalent positions: (i) $x, -1+y, z$.

In contrast, the I1B (Figure 6) is connected to the I1B of the adjacent molecule in such a way that the C4B-I1B \cdots I1B-C4B fragment is almost linear with equal angles (C4B-I1B \cdots I1B = I1B \cdots I1B-C4B = 152.3 (2) °, I1B \cdots I1B = 3.7598 (6) Å). Therefore, this contact is an example of a type I halogen bonding (Figure 6). Despite type

I XB is quite typical for Cl and Br, only few compounds are known in which structures I is involved in this type of interactions²⁴. Therefore, **1** is a rare example of the substances of this class.

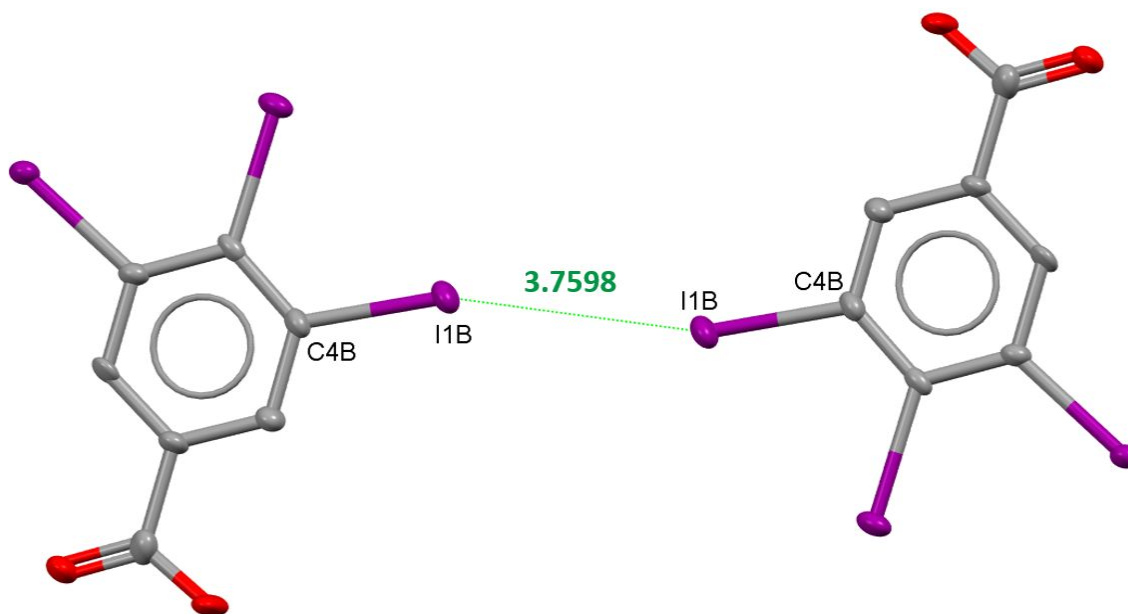
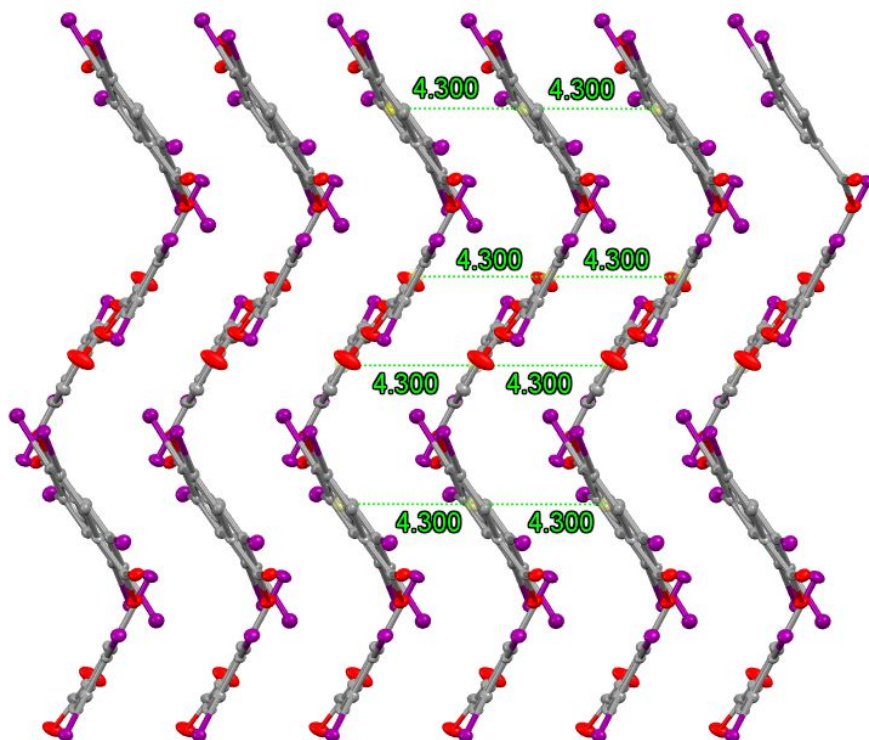


Figure 6. Halogen bonds in **1**. Type I contacts. Hydrogens are omitted for clarity. Selected bond lengths (Å) and angles (°): I1B-I1B⁽ⁱ⁾ 3.7598 (6), C4B-I1B-I1B⁽ⁱ⁾ 151.3 (2), C4B⁽ⁱ⁾-I1B⁽ⁱ⁾-I1 151.3 (2). Equivalent positions: (i) 1-x, 1-y, 1-z.

Hydrogen bonding (Table 1) between two carboxyl groups is rather strong in the structure of **1** being 1.806 Å and 1.811 Å (sum of vdW radii of H and O is 2.62 Å). It clearly shows that the HB is the key structural factor in this structure (see Figure S1).

Each molecule of **1** is bound to two adjacent molecules by π - π interactions with the corresponding distance between the

1
2
3 calculated centroids of benzene rings 4.300 Å. Such stacking
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5 together with other described non-covalent interactions lead to a
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7 zig-zag packing of the molecules (Figure 7).
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37 **Figure 7.** Zig-zag layers of **1**. Hydrogens are omitted for clarity.
38
39 Distance is measured between the calculated centroids of benzene
40
41 rings.
42
43

44
45 The presence of a solvent molecule in the structure of **2** changes
46
47 drastically the whole arrangement of molecules as well as their
48
49 interaction modes (Figures 8 and 9). Thus, the I...I distance is
50
51 3.7851 (8) and 3.8165 (9) Å for *meta*- and *para*-iodines,
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53 correspondingly, which is relatively close to I...I distance in **1**
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1
2
3 and is again less than the sum of vdW radii (3.96 Å)⁷³. However,
4
5 in **2** there are no type I contacts. Instead, all iodines interact
6
7 with iodines of the adjacent molecules via type II contacts.
8
9

10
11 Iodine atoms in *meta*-position relative to the -COOH substituent
12
13 (I1 and I3) show different XB behavior than the corresponding atoms
14
15 in **1** (Figure 8). I1 is bound to I3 of an adjacent molecule providing
16
17 a non-linear C4-I1...I3-C6 fragment with C4-I1...I3 = 120.0 (3)
18
19 and C6-I3...I1 = 169.9 (3) °. The second *meta*-iodine atom, I3,
20
21 forms XBs with two adjacent molecules giving a C6-I3...I1-C4
22
23 fragment and a C6-I3...I2-C5 fragment with C6-I3...I2 = 99.3 (3)
24
25 fragment and a C6-I3...I2-C5 fragment with C6-I3...I2 = 99.3 (3)
26
27 and C5-I2...I3 = 169.8 (2) °. Thus, I1 behaves as an XB acceptor
28
29 and I3 shows both XB donor and XB acceptor properties. The *para*-
30
31 iodine I2 participates in a halogen bonding with one adjacent
32
33 molecule and behaves as an XB donor, resulting in a close to linear
34
35 C5-I2...I3-C6 fragment with C5-I2...I3 = 169.8 (2) ° and C6-I3...I2
36
37 = 99.3 (3) °.
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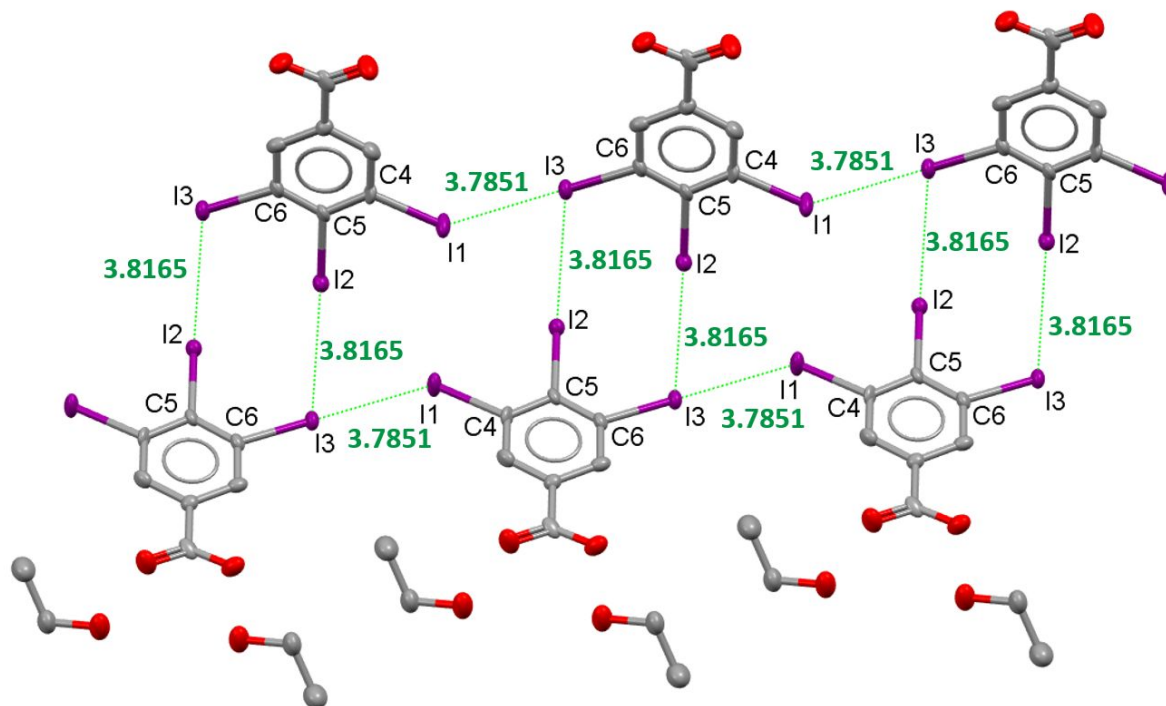


Figure 8. Structure of **2**. Hydrogens are omitted for clarity.

Selected bond lengths (Å) and angles (°): I1-I3⁽ⁱ⁾ 3.7851 (8), I2-I3⁽ⁱⁱ⁾ 3.8165 (9), C4-I1-I3⁽ⁱ⁾ 120.0 (3), C6⁽ⁱ⁾-I3⁽ⁱ⁾-I1 169.9 (3), C5-I2-I3⁽ⁱⁱ⁾ 169.8 (2), C6⁽ⁱⁱ⁾-I3⁽ⁱⁱ⁾-I2 99.3 (3). Equivalent positions: (i) $1/2+x, -1/2+y, z$; (ii) $1/2-x, 1/2+y, 1/2-z$.

In **2**, ethanol molecules form strong hydrogen bonds (Table 1) with carboxyl groups of the adjacent TIBA molecules ($H1\cdots O3 = 1.670$ Å, $H3A\cdots O2 = 1.862$ Å). The $H\cdots O$ distance is again much shorter than the sum of vdW radii (2.62 Å). This indicates that HB plays a central role also in the crystal structure of **2** (see FigureS2).

Table 1. Hydrogen bond parameters in **1** and **2**.

	D-H	d(D-H)	d(H...A)	<DHA	d(D...A)	A	Equivalent positions of (i-iii)
1	O2-H2	0.840	1.811	177.8	2.650 (7)	O1 ⁽ⁱ⁾	2-x, 1-y, -z
	C7-H7	0.950	3.0558	160.9	3.966 (8)	I2	
	O2B-H2B	0.841	1.806	165.0	2.63 (1)	O1B ⁽ⁱⁱ⁾	-1-x, 2-y, 1-z
2	O1-H1	0.884	1.670	171.3	2.55 (1)	O3 ⁽ⁱⁱⁱ⁾	1-x, -y, 1-z
	O3-H3A	0.939	1.862	145.7	2.69 (1)	O2	

The incorporation of the ethanol molecule into the crystal structure of 3,4,5-triiodobenzoic acid does not break the π - π stacking of the aromatic rings, although the distance between them is slightly longer than in the case of **1** (distance between the calculated centroids of benzene rings is 4.470 Å). Like in **1**, the molecules of **2** are organized in a zig-zag layout (Figure 9).

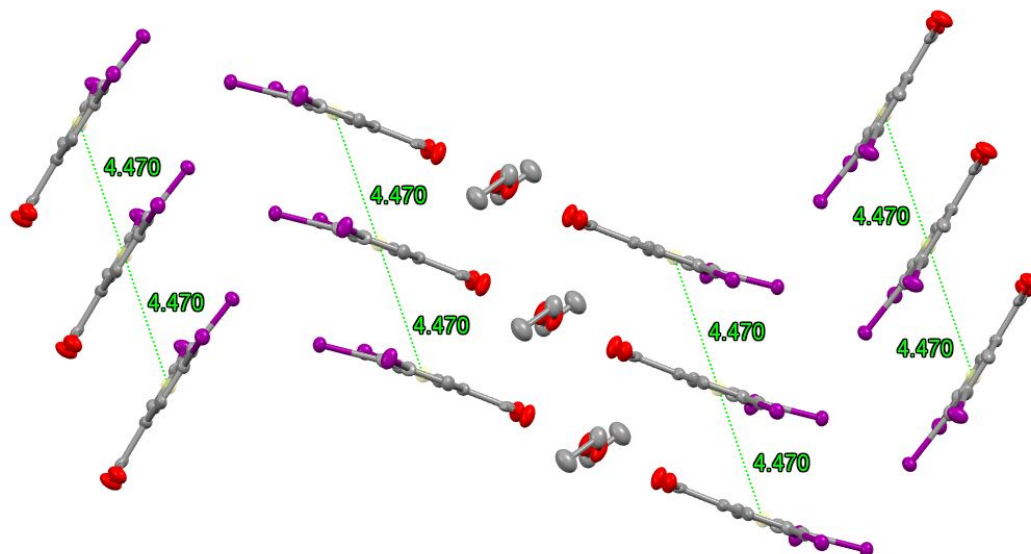


Figure 9. Layers of **2**. Hydrogens are omitted for clarity. Distance is measured between the calculated centroids of benzene rings.

In addition to the intermolecular halogen bonding, there is also an intramolecular XB present in the structures of **1** and **2** with the I...I distances equal to $I1 \cdots I2 = 3.5479 (8) \text{ \AA}$, $I2 \cdots I3 = 3.6256 (9) \text{ \AA}$, $I1B \cdots I2B = 3.6045 (7) \text{ \AA}$, $I2B \cdots I3B = 3.6464 (6) \text{ \AA}$ for **1** and $I1 \cdots I2 = 3.6126 (8) \text{ \AA}$ and $I2 \cdots I3 = 3.620 (1) \text{ \AA}$ for **2**.

2.2. Influence of the substituent on the XB behavior of halogens in substituted iodobenzenes

A carboxyl group present in TIBA is a substituent with -M effect. Therefore, it is expected to decrease the electron density on the carbon atoms in *ortho*- and *para*-positions of the ring and to increase the electron density on the carbon atom in *meta*-position. Because of this phenomenon, in **1** and **2** C5, located in *para*-position

1
2
3 relative to -COOH, should withdraw some electron density from the
4
5 I2 bound to it. An opposite effect should be observed for I1 and
6
7 I3 in *meta*-positions. As a result, I2 should become a better XB
8
9 donor, while I1 and I3 should become better XB acceptors. Such
10
11 phenomenon was indeed observed in the structures of **1** and **2**. Thus,
12
13 analysis of the crystal structure of **1** showed that *para*-iodines I2
14
15 and I2B are involved in a stronger halogen bonding with oxygen of
16
17 the carboxyl group ($C5-I2\cdots O1B = 171.5 (2)^\circ$ and $I2\cdots O1B = 3.031$
18
19 $(6) \text{ \AA}$, $C5B-I2B\cdots O1 = 178.8 (2)^\circ$ and $I2B\cdots O1 = 3.138 (5) \text{ \AA}$) as well
20
21 as interact with the π -system of the neighboring benzene ring.
22
23 Both these facts indicate an improved XB donor (i.e. an electron
24
25 acceptor) behavior of *para*-iodines. *Meta*-iodines I1 and I3B, in
26
27 turn, act both as XB donors and XB acceptors ($C4-I1\cdots I3B = 158.8$
28
29 $(2)^\circ$ and $I1\cdots I3B = 3.8791 (7) \text{ \AA}$, $C4-I1\cdots I3B = 99.4 (2)^\circ$ and $I1\cdots I3B$
30
31 $= 3.7323 (7) \text{ \AA}$, $C6B-I3B\cdots I1 = 169.2 (2)^\circ$ and $I3B\cdots I1 = 3.7323 (7)$
32
33 \AA , $C6B-I3B\cdots I1 = 88.9 (2)^\circ$ and $I3B\cdots I1 = 3.8791 (7) \text{ \AA}$).

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41 Analysis of the structure of **2**, which contains co-crystallized
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43 ethanol, showed even more clear distinction between *para*-iodines
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45 I1 and I3 and *meta*-iodines I2. Former ones act only as XB donors
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47 ($C5-I2\cdots I3 = 169.8 (2)^\circ$ and $I2\cdots I3 = 3.8165 (9) \text{ \AA}$), while the
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49 latter ones favor XB acceptor behavior ($C4-I1\cdots I3 = 120.0 (3)^\circ$ and
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51 $I1\cdots I3 = 3.7851 (8) \text{ \AA}$, $C6-I3\cdots I2 = 99.3 (3)^\circ$ and $I3\cdots I2 = 3.8165$
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53 $(9) \text{ \AA}$, $C6-I3\cdots I1 = 169.9 (3)^\circ$ and $I3\cdots I1 = 3.7851 (8) \text{ \AA}$).

In order to characterize a σ -hole on each halogen atom, the calculated electrostatic potentials can be used. The maximum electrostatic potential on the atom can be represented by a value of $V_{S,max}$, which is proportional to the size of a σ -hole. The bigger the σ -hole on the atom, the bigger is the $V_{S,max}$ value. In turn, a bigger size of a σ -hole (and bigger $V_{S,max}$ value) corresponds to a higher XB donor ability of halogen. Our calculations show that $V_{S,max}$ values for I1, I2 and I3 in compounds **1** and **2** vary from 0.039 to 0.042, being smallest for *meta*-iodines I1 and I3 and biggest for *para*-iodines I2 (see section 2.3). Therefore, iodine atoms in *para*-position should reveal better XB donor ability than iodines in *meta*-positions, which is which is consistent with the results of our structural analysis.

Table 2. Halogen bonding in **1** and **2**.

	Atoms	Distance, Å	Angles, °	Sum of vdW radii, Å	Equivalent positions of (i)- (iii)
1	I2···O1B	3.138 (5)	C5-I2-O1B = 178.8 (2), C2B-O1B-I2 = 143.8 (5)	3.5	

	I1...I3B ⁽ⁱ⁾	3.7323 (7)	C4-I1-I3B ⁽ⁱ⁾ = 99.4 (2), C6B ⁽ⁱ⁾ -I3B ⁽ⁱ⁾ - I1 = 169.2 (2)	3.96	x, -1+y, z
	I3B ⁽ⁱ⁾ ...I1	3.8791 (7)	C6B ⁽ⁱ⁾ -I3B ⁽ⁱ⁾ - I1 = 88.9 (2), C4-I1- I3B ⁽ⁱ⁾ = 158.8 (2)	3.96	x, -1+y, z
2	I1...I3 ⁽ⁱⁱ⁾	3.7851 (8)	C4-I1-I3 ⁽ⁱⁱ⁾ = 120.0 (3), C6 ⁽ⁱⁱ⁾ -I3 ⁽ⁱⁱ⁾ -I1 = 169.9 (3)	3.96	1/2+x, - 1/2+y, z
	I2...I3 ⁽ⁱⁱⁱ⁾	3.8165 (9)	C5-I2-I3 ⁽ⁱⁱⁱ⁾ = 169.8 (2), C6 ⁽ⁱⁱⁱ⁾ -I3 ⁽ⁱⁱⁱ⁾ - I2 = 99.3 (3)	3.96	1/2-x, 1/2+y, 1/2-z

In contrast, the removal of a -COOH substituent should equalize, to a large extent, the XB properties of all the I atoms. This is reflected in our calculations, according to which, $V_{S,max}$ values are

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3 0.036 and are same for all iodines. However, the structural
4 analysis of 1,2,3-triiodobenzene³¹ molecule **3** (Figure 10) shows,
5 that two outermost iodines, I3 and I4, act as XB donors (C3-I3...I6
6 = 170.4 (1) ° and I3...I6 = 3.800 (2) Å , C7-I4...I2 = 170.4 (1) ° and
7 I4...I2 = 3.802 (2) Å), while another outermost iodine atom, I6,
8 reveals XB acceptor ability (C9-I6...I3 = 104.4 (1) ° and I3...I6 =
9 3.800 (2) Å). The middle iodine atom, I2, also favors the XB
10 acceptor behavior (C2-I2...I4 = 124.4 (1) ° and I2...I4 = 3.802 (2)
11 Å). Such difference in the XB donor-acceptor behavior of iodide
12 substituents is due to the weak positive mesomeric effect of the
13 neighboring iodine atoms.
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30 It should be noted, that molecules in **3** do not form infinite chains
31 of halogen bonds, like in **1** and **2**, but make two sets of four
32 molecules (Figure S3). Only two iodines in one molecule form
33 halogen bonds, while third iodine is not involved, i.e. in one
34 molecule I2 and I3 form XBs and I1 does not. In the second molecule
35 I4 and I6 form XBs, while I5 does not.
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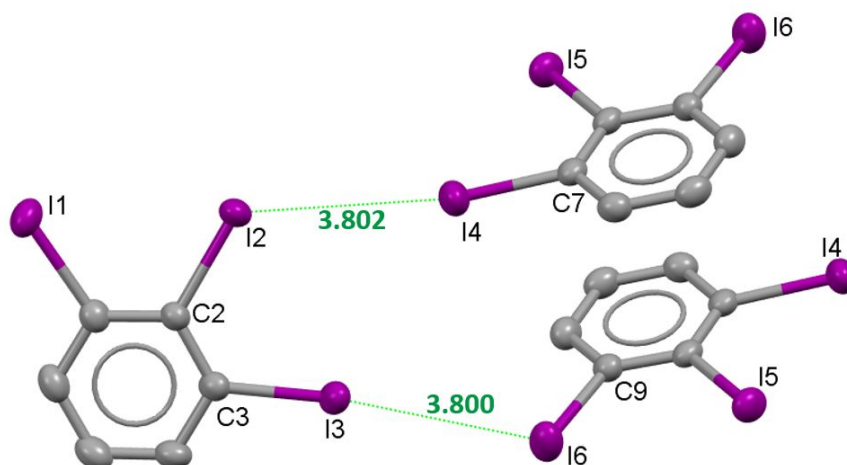


Figure 10. Structure of **3**. Hydrogens are omitted for clarity. Selected bond lengths (Å) and angles ($^{\circ}$): $I4^{(i)}-I2$ 3.802 (2), $I6^{(ii)}-I3$ 3.800 (2), $C2-I2-I4^{(i)}$ 124.4 (1), $C7^{(i)}-I4^{(i)}-I2$ 170.4 (1), $C3-I3-I6^{(ii)}$ 170.4 (1), $C9^{(ii)}-I6^{(ii)}-I3$ 104.4 (1). Equivalent positions: (i) $x, 1+y, z$; (ii) $2-x, 2-y, 1-z$.

Table 3. Halogen bonds in **3**.

	Atoms	Distance, Å	Angles, $^{\circ}$	Sum of vdW radii, Å	Equivalent positions of (i)-(ii)
3	$I2 \cdots I4^{(i)}$	3.802 (2)	$C2-I2-I4^{(i)} =$ 124.4 (1), $C7^{(i)}-I4^{(i)}-I2 =$ 170.4 (1)	3.96	$x, 1+y, z$

	I3...I6 ⁽ⁱⁱ⁾	3.800 (2)	C3-I3-I6 ⁽ⁱⁱ⁾ = 170.4 (1), C9 ⁽ⁱⁱ⁾ -I6 ⁽ⁱⁱ⁾ -I3 = 104.4 (1)	3.96	2-x, 2-y, 1-z
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Similar mesomeric effects can be observed in other iodobenzoic acids as well. For example, in 4-iodobenzoic acid (**4**)³² the iodine atom in a *para*-position should act as an XB donor because of the -M effect of a carboxyl group. According to our structural analysis, the iodine atom I1 interacts with other I1 iodine atoms from two adjacent molecules, acting both as an XB donor and as an XB acceptor (Figure 11). The corresponding I...I distance is 3.957 (1) Å, which is very close to the sum of vdW radii, so both I1...I1 interactions can, thus, be considered as extremely weak ones. The calculated $V_{S,max}$ value is 0.035.

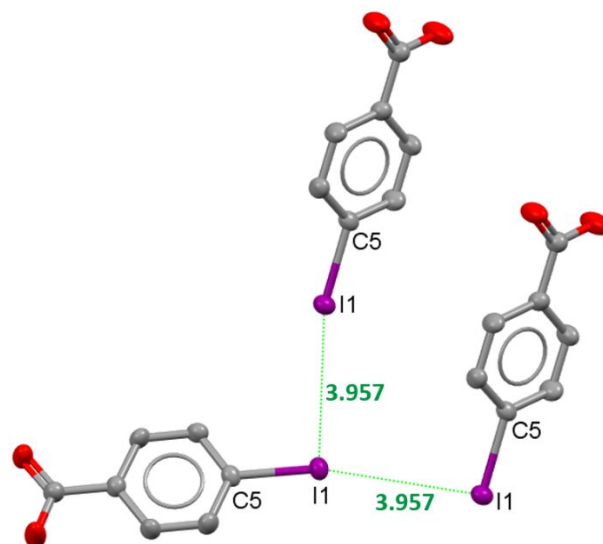
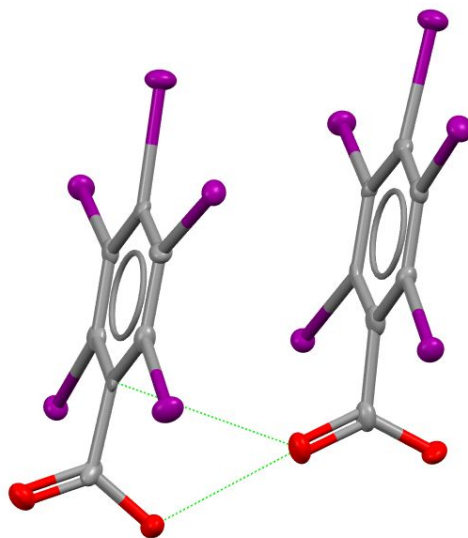


Figure 11. Structure of **4**. Hydrogens are omitted for clarity. Selected bond lengths (Å) and angles (°): I1-I1⁽ⁱ⁾ 3.957 (1), I1-I1⁽ⁱⁱ⁾ 3.957 (1), C5-I1-I1⁽ⁱ⁾ 165.9 (2), C5⁽ⁱ⁾-I1⁽ⁱ⁾-I1 96.1 (2), C5-I1-I1⁽ⁱⁱ⁾ 96.1 (2), C5⁽ⁱⁱ⁾-I1⁽ⁱⁱ⁾-I1 165.9 (2). Equivalent positions: (i) 1/2-x, 1/2+y, 1/2-z; (ii) 1/2-x, -1/2+y, 1/2-z.

Adonin *et al.* have reported³³ the synthesis of another iodobenzoic acid, i.e. pentaiodobenzoic acid (PIBA). In PIBA the electron density distribution is affected by the negative mesomeric effect of a -COOH group, which withdraws the electron density from the benzene ring. Thus, *ortho*- and *para*-iodines should act as XB donors, while iodines in *meta*-positions should accumulate excessive electron density favoring corresponding iodines to act as XB acceptors. Analysis of the crystal structure of pentaiodobenzoic acid (**5**) revealed that the carboxyl group is not coplanar with the benzene ring because of the steric hindrance as

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3 well as due to the strong hydrogen bonding between two carboxyl
4 groups in adjacent molecules (Figure 12). Therefore, conjugation
5 groups in adjacent molecules (Figure 12). Therefore, conjugation
6 breaks down, and -COOH group does not influence the XB donor-
7 acceptor properties of iodines. This is also confirmed by our
8 acceptor properties of iodines. This is also confirmed by our
9 computations, showing a small deviation of a σ -hole for all
10 iodines. The calculated $V_{S,max}$ is 0.050 for *ortho*-iodines and 0.047
11 for *meta*- and *para*-iodines (see section 2.3). The difference in
12 $V_{S,max}$ values is due to the +M effect of the iodines.
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41 **Figure 12.** Structure of **5**. Hydrogens and solvent molecules were
42 omitted for clarity.
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46 In a PIBA structure (Table 4), *meta*-iodines I2 and I4 form XBs
47 with adjacent molecules with I2 acting as an XB donor (C6-I2...I4 =
48 177.0 (1) ° and I2...I4 = 3.8592 (5) Å) and I4 acting as an XB
49 acceptor (C8-I4...I2 = 96.9 (1) ° and I4...I2 = 3.8592 (5) Å). *Ortho*-
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iodines I5 and I6 form even stronger XBs with oxygens from the carboxyl group O6 and O2, correspondingly, thus, acting as XB donors ($C9-I5\cdots O6 = 177.8 (1)^\circ$ and $I5\cdots O6 = 2.945 (3) \text{ \AA}$, $C14-I6\cdots O2 = 170.6 (1)^\circ$ and $I6\cdots O2 = 3.092 (3) \text{ \AA}$). This can be explained by a small positive mesomeric effect of the substituted iodines, that favors *meta*-positions to act as XB donors and *ortho*-positions as XB acceptors. Finally, *para*-iodines I3 and I8 form type I contacts with *ortho*- and *para*-iodines from the adjacent molecule ($C7-I3\cdots I9 = 126.9 (1)^\circ$ and $I3\cdots I9 = 3.9537 (6) \text{ \AA}$, $C7-I3\cdots I8 = 126.0 (1)^\circ$ and $I3\cdots I8 = 3.8730 (5) \text{ \AA}$, $C16-I8\cdots I3 = 129.8 (1)^\circ$ and $I8\cdots I3 = 3.8730 (5) \text{ \AA}$).

Table 4. Halogen bonds in **5**.

	Atoms	Distance, Å	Angles, °	Sum of vdW radii, Å	Equivalent positions of (i)-(iv)
	$I2 \cdots I4^{(i)}$	3.8592 (5)	$C6-I2-I4^{(i)} = 177.0 (1),$ $C8^{(i)}-I4^{(i)}-I2 = 96.9 (1)$	3.96	$x, 1/2-y,$ $1/2+z$

5	I3...I8 ⁽ⁱⁱ⁾	3.8730 (5)	C7-I3-I8 ⁽ⁱⁱ⁾ = 126.0 (1), C16 ⁽ⁱⁱ⁾ - I8 ⁽ⁱⁱ⁾ -I3 = 129.8 (1)	3.96	-x, -1/2+y, 1.5-z
	I3...I9 ⁽ⁱⁱⁱ⁾	3.9537 (6)	C7-I3-I9 ⁽ⁱⁱⁱ⁾ = 126.9 (1), C17 ⁽ⁱⁱⁱ⁾ - I9 ⁽ⁱⁱⁱ⁾ -I3 = 128.9 (1)	3.96	-x, 1-y, 1- z
	I5...O6 ^(iv)	2.945 (3)	C9-I5-O6 ^(iv) = 177.8 (1), C12 ^(iv) - O6 ^(iv) -I5 = 129.3 (3)	3.5	x, 1.5-y, - 1/2+z
	I6...O2 ⁽ⁱ⁾	3.092 (3)	C14-I6-O2 ⁽ⁱ⁾ = 170.6 (1), C3 ⁽ⁱ⁾ -O2 ⁽ⁱ⁾ -I6 = 120.8 (3)	3.5	x, 1/2-y, 1/2+z

Upon removal of a -COOH group from PIBA, all iodines should become equal and reveal similar properties in terms of their XB donor

ability. Our calculations of hexaiodobenzene (polymorphs **6a** - **6c**)^{34,35} indeed confirmed that $V_{S,max}$ (= 0.043) value is equal for all iodines I1-I3, I1B-I3B. According to the crystal structure analysis of hexaiodobenzene (polymorphs **6a** - **6c**), iodines in two polymorphs **6a** and **6b** demonstrate similar XB behavior. Thus, in **6a** two iodines I1 and I1B act as XB donors ($C-I\cdots I = 174.65^\circ$ and $I\cdots I = 3.766 \text{ \AA}$), two other iodines I3 and I3B act as XB acceptors ($C-I\cdots I2 = 124.28^\circ$ and $I\cdots I = 3.777 \text{ \AA}$) and the last two iodines I2 and I2B act both as XB donors and XB acceptors at the same time ($C-I\cdots I = 114.74^\circ$ and 176.94° , $I\cdots I = 3.766 \text{ \AA}$ and 3.777 \AA). In **6b** iodines I3 and I3B act as XB donors ($C-I\cdots I = 173.47^\circ$ and $I\cdots I = 3.742 \text{ \AA}$), iodines I1 and I1B act as XB acceptors ($C-I\cdots I = 125.37^\circ$ and $I\cdots I = 3.75 \text{ \AA}$) and iodines I2 and I2B act both as XB donors and XB acceptors at the same time ($C-I\cdots I = 176.41^\circ$ and 116.29° , $I\cdots I = 3.747 \text{ \AA}$ and 3.742 \AA). Finally, in the third polymorph **6c** all iodine atoms act as XB donors and XB acceptors (see Table 5). Interestingly, in **6c** polymorph I1, I2 and I3 form an XB triangle with sides $I1\cdots I2 = 3.7044 (5) \text{ \AA}$, $I2\cdots I3 = 3.9485 (6) \text{ \AA}$ and $I1\cdots I3 = 3.7125 (6) \text{ \AA}$ (Figure 13). In all three polymorphs XB angles are close to 90° and 180° , but not exactly because of the steric hindrances. Still all the XB interactions can be considered as type II contacts with $I\cdots I$ distances being less than the sum of vdW radii (3.96 \AA).

Table 5. Halogen bonds in **6a-6c**.

	Atoms	Distance, Å	Angles, °	Sum of vdW radii, Å	Equivalent positions of (i)-(vii)
6a	I1 ··· I2 ⁽ⁱ⁾	3.766	C1-I1-I2 ⁽ⁱ⁾ = 174.65, C2 ⁽ⁱ⁾ -I2 ⁽ⁱ⁾ -I1 = 114.74	3.96	1/2-x, - 1/2+y, 1/2-z
	I3 ··· I2B ⁽ⁱⁱ⁾	3.777	C3-I3-I2B ⁽ⁱⁱ⁾ = 124.28, C2B ⁽ⁱⁱ⁾ -I2B ⁽ⁱⁱ⁾ -I3 = 176.94	3.96	-1/2+x, 1/2-y, 1/2+z
6b	I2 ··· I1 ⁽ⁱⁱⁱ⁾	3.75	C2-I2-I1 ⁽ⁱⁱⁱ⁾ = 176.41, C1 ⁽ⁱⁱⁱ⁾ -	3.96	1-x, - 1/2+y, 1/2-z

			$I1^{(iii)} - I2 =$ 125.37		
	$I2 \cdots I3B^{(iv)}$	3.742	$C2 - I2 -$ $I3B^{(iv)} =$ 116.29, $C3B^{(iv)} -$ $I3B^{(iv)} - I2 =$ 173.47	3.96	$x, 1/2 - y,$ $1/2 + z$
6c	$I2 \cdots I1^{(v)}$	3.7044 (5)	$C1 - I2 - I1^{(v)}$ $= 174.2$ (1), $C3^{(v)} -$ $I1^{(v)} - I2 =$ 114.9 (1)	3.96	$1.5 - x,$ $1/2 + y,$ $1.5 - z$
	$I1 \cdots I3^{(vi)}$	3.7125 (6)	$C3 - I1 - I3^{(vi)}$ $= 178.3$ (1), $C2^{(vi)} -$ $I3^{(vi)} - I1 =$ 124.6 (1)	3.96	$2.5 - x,$ $1/2 + y,$ $1.5 - z$
	$I2 \cdots I3^{(vii)}$	3.9485 (6)	$C1 - I2 -$ $I3^{(vii)} =$ 123.5 (1), $C2^{(vii)} -$	3.96	$-1 + x, 1 + y,$ z

			$I3^{(vii)}-I2 =$		
			173.6 (1)		

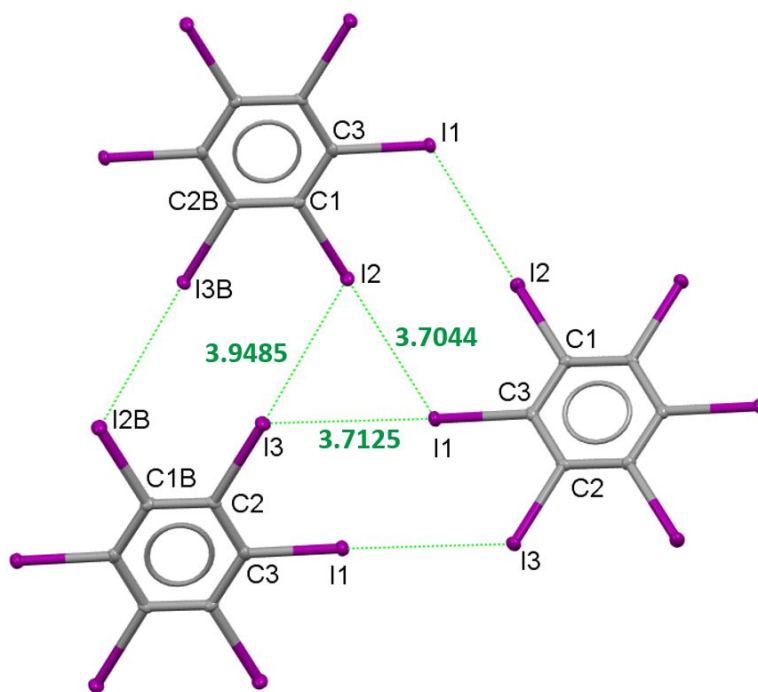


Figure 13. Halogen bond triangle in the structure of **6c**. Selected bond lengths (Å) and angles (°): $I1-I2^{(i)}$ 3.7044 (5), $I1-I3^{(ii)}$ 3.7125 (6), $I2^{(i)}-I3^{(ii)}$ 3.9485 (6), $C1^{(i)}-I2^{(i)}-I1$ 174.2 (1), $C3-I1-I2^{(i)}$ 114.9 (1), $C3-I1-I3^{(ii)}$ 178.3 (1), $C2^{(ii)}-I3^{(ii)}-I1$ 124.6 (1), $C1^{(i)}-I2^{(i)}-I3^{(ii)}$ 123.5 (1), $C2^{(ii)}-I3^{(ii)}-I2^{(i)}$ 114.9 (1). Equivalent positions: (i) $1.5-x, -1/2+y, 1.5-z$; (ii) $2.5-x, 1/2+y, 1.5-z$.

When comparing hexaiodobenzene (HIB) and PIBA we can conclude, that the difference in the XB behavior of iodines arises not from the electron-withdrawing properties of a carboxyl group, but is

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3 due to the steric factors as well as strong hydrogen bonding
4 between a -COOH group and ethanol. The revealed difference in the
5 calculated electrostatic potentials of iodine atoms ($V_{S,\max(\text{PIBA})} =$
6 $0.047/0.050$, $V_{S,\max(\text{HIB})} = 0.043$) is due to the extensive hydrogen
7 bonding between the carboxyl group and ethanol in the structure of
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14 **5**.

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17 It should also be noted that both PIBA and HIB reveal
18 intramolecular I...I contacts similar to TIBA. The corresponding
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Table 6. The intramolecular I...I distances in compounds **5** and **6**.

Compound	Atoms	Distance, Å
5	I1...I2	3.548
	I2...I3	3.546
	I3...I4	3.524
	I4...I5	3.551
	I6...I7	3.564
	I7...I8	3.512
	I8...I9	3.508

	I9···I10	3.536
6a	I3···I2B = I3B···I2	3.501
	I1···I3 = I1B···I3B	3.500
	I3···I2B = I2···I3B	3.521
6b	I1···I2 = I1B···I2B	3.500
	I1···I3 = I1B···I3B	3.49
	I3···I2B = I3B···I2	3.49
6c	I1···I2 = I1B···I2B	3.4974 (6)
	I1···I3 = I1B···I3B	3.5182 (5)
	I3···I2B = I3B···I2	3.5096 (6)

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3 In order to explore the influence of the strength of a stronger
4 electron-withdrawing group on the XB donor-acceptor behavior of
5 iodine atoms, the 4-iodobenzonitrile³⁶ (**7**) and 3-iodobenzonitrile³⁷
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7 (**8**) were taken into consideration (Figure 14, Table 7).
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9 Accordingly, in the structure of **7** the iodine atom I1 in *para*-
10 position should act as an XB donor due to the strong negative
11 mesomeric effect of a nitrile group -CN. On the contrary, in a
12 compound **8** iodine I1 in *meta*-position relative to a -CN group
13 should act as an XB acceptor. The structural analysis on these two
14 iodobenzonitriles show the formation of a strong I1...N1 bonding in
15 the structure of **7**, in which *para*-iodine I1 acts as an XB donor.
16 The I1-N1 distance is equal to 3.123 Å (the sum of vdW radii is
17 3.53 Å) and the C1-I1-N1 angle is equal to 180.0 °. In the structure
18 of **8** the iodine atom I1 acts as an XB donor and an XB acceptor
19 upon interaction with iodines from two adjacent 3-iodobenzonitrile
20 molecules (Figure 14, Table 7). The I1-I1 distance is 3.806 (1) Å
21 vs. the sum of van der Waals radii being 3.96 Å. In contrast to **7**,
22 nitrogen atoms in **8** are involved in a hydrogen bonding and do not
23 form XBs with iodine atoms.
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47 Our calculations of the maximum of the electrostatic potential
48 surface revealed, that the $V_{S,max}$ values for I1 atoms of **7** and **8** are
49 almost equal, being 0.042 for **7** and 0.041 for **8**. However, the
50 demonstrated difference in the XB donor-acceptor behavior of these
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3 iodine atoms support our hypothesis, that a substituent other than
4 halogen does have an impact on the XB donor-acceptor behavior of
5 the halogens in a benzene ring. Specifically, *para*-iodine in **7**
6 acts a strong XB donor, while in the structure of **8**, the XB donor
7 ability of *meta*-iodine is less pronounced, and it acts both as an
8 XB donor and as an XB acceptor.
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10 Furthermore, there is a clear difference between the behavior of
11 *para*-iodines in compounds **4** and **7**. While *para*-iodine in the
12 structure of **7** demonstrates strong XB donor properties (calculated
13 $V_{S,max} = 0.042$), *para*-iodine in the structure of **4** reveals both XB
14 donor and XB acceptor properties (calculated $V_{S,max} = 0.035$). This
15 fact, supported by our calculations, shows that not only the
16 position of the halogen atom in a benzene ring, but also the
17 ability of the electron-withdrawing substituent to withdraw
18 electron density from a benzene ring affects the XB donor-acceptor
19 behavior of halogens.
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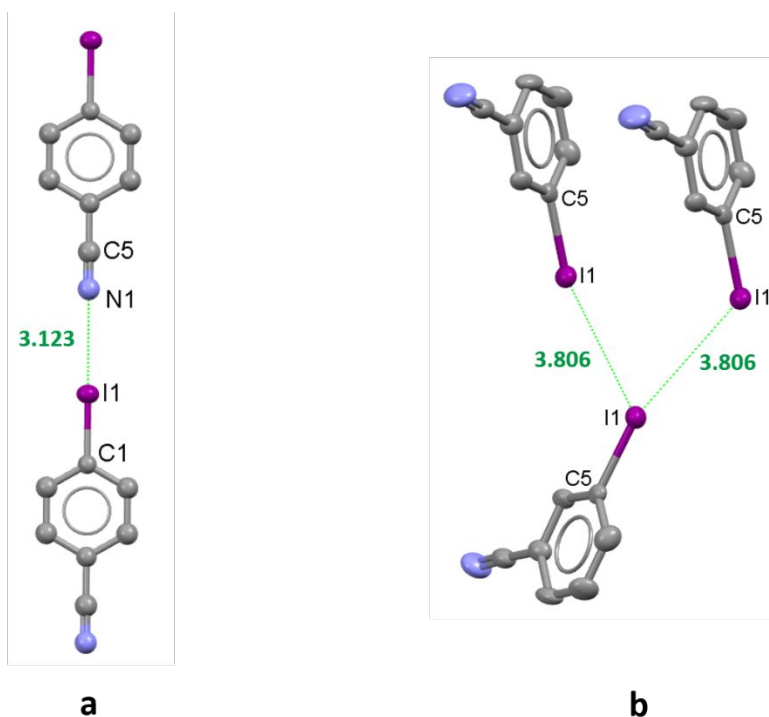


Figure 14. Halogen bonding in the structures of **7** (a) and **8** (b). Hydrogens are omitted for clarity. Selected bond lengths (Å) and angles (°): (a) I1-N1⁽ⁱ⁾ 3.123, C1-I1-N1⁽ⁱ⁾ 180.0, C5⁽ⁱ⁾-N1⁽ⁱ⁾-I1 180.0; (b) I1-I1⁽ⁱⁱ⁾ 3.806 (1), I1-I1⁽ⁱⁱⁱ⁾ 3.806 (1), C5-I1-I1⁽ⁱⁱ⁾ 165.4 (2), C5⁽ⁱⁱ⁾-I1⁽ⁱⁱ⁾-I1 128.3 (2), C5-I1-I1⁽ⁱⁱⁱ⁾ 128.3 (2), C5⁽ⁱⁱⁱ⁾-I1⁽ⁱⁱⁱ⁾-I1 165.4 (2). Equivalent positions: (i) $x, -1+y, z$; (ii) $1/2-x, -1/2+y, 1/2-z$; (iii) $1/2-x, 1/2+y, 1/2-z$.

Table 7. Halogen bonds in **7** and **8**.

	Atoms	Distance, Å	Angles, °	Sum of vdW radii, Å	Equivalent positions

					of (i) - (iii)
7	$I1 \cdots N1^{(i)}$	3.123	$C1-I1-N1^{(i)}$ $= 180.0,$ $C5^{(i)}-N1^{(i)}-$ $I1 = 180.0$	3.53	$x, -1+y, z$
8	$I1 \cdots I1^{(ii)}$	3.806 (1)	$C5-I1-I1^{(ii)}$ $= 165.4$ $(2), C5^{(ii)}-$ $I1^{(ii)}-I1 =$ $128.3 (2)$	3.96	$1/2-x, -$ $1/2+y,$ $1/2-z$
	$I1 \cdots I1^{(iii)}$	3.806 (1)	$C5-I1-$ $I1^{(iii)} =$ $128.3 (2),$ $C5^{(iii)}-$ $I1^{(iii)}-I1 =$ $165.4 (2)$	3.96	$1/2-x,$ $1/2+y,$ $1/2-z$

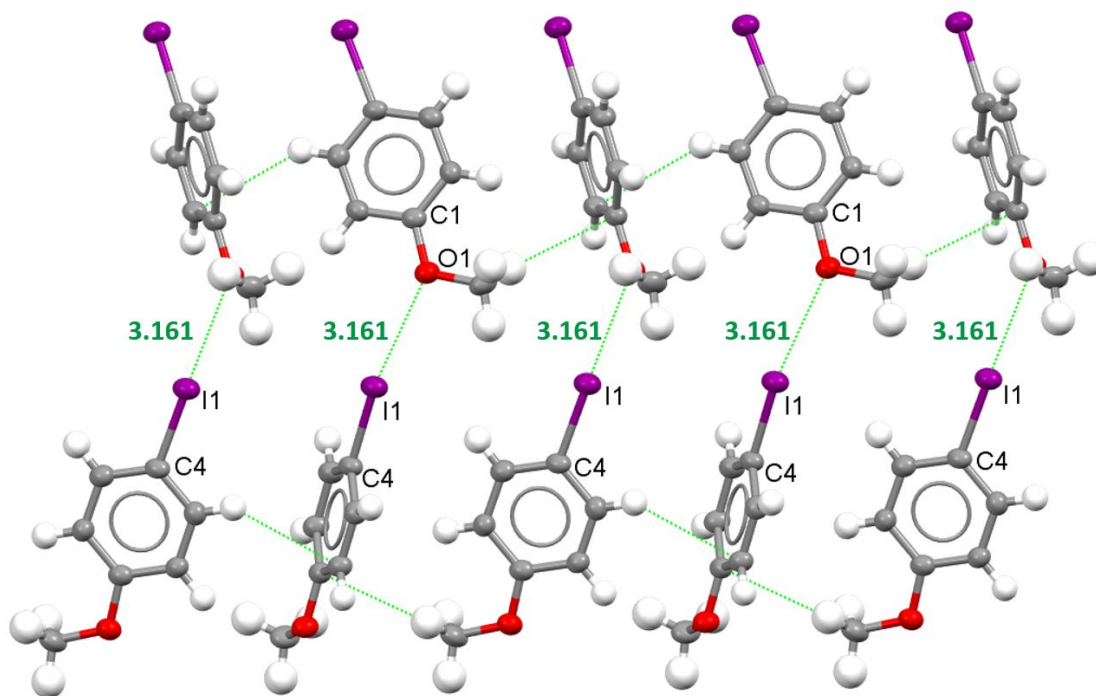
According to the above consideration, the replacement of the -M substituent to +M substituent should change the distribution of an electron density in a benzene ring as well as make an impact on the XB donor-acceptor behavior of iodide substituents. To verify

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3 this hypothesis, we have studied 2,4-diiodoaniline (**9**), 4-
4 iodoaniline (**10**), 2-iodoaniline (**11**), 2-iodophenol (**12**), 4-
5 iodoaniline (**10**), 2-iodoaniline (**11**), 2-iodophenol (**12**), 4-
6 iodoaniline (**10**), 2-iodoaniline (**11**), 2-iodophenol (**12**), 4-
7 iodophenol (**13**), 3-iodophenol (**14**), 2,4,6-triiodophenol (**15**), 4-
8 iodophenol (**13**), 3-iodophenol (**14**), 2,4,6-triiodophenol (**15**), 4-
9 iodoanisole (**16**) and 3,4,5-triiodoanisole (**17**). Thus, when
10 carboxyl group is changed to an electron-donating group with a
11 positive mesomeric effect (like $-\text{NH}_2$, $-\text{OH}$ and $-\text{OCH}_3$), the electron
12 density redistributes in the opposite direction (Figure 3), making
13 *ortho*- and *para*- positions favorable XB acceptors and *meta*-
14 positions favorable XB donors.
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24 Among the hitherto known structures, in 2,4-diiodoaniline (**9**)³⁸
25 *para*-iodine I2 interacts only with the π -system of a benzene ring
26 and in 4-iodoaniline (**10**)³⁹ there are no halogen or hydrogen bonds.
27 But in 2-iodoaniline (**11**)⁴⁰ iodines I1 form $\text{I}\cdots\text{I}$ contacts acting
28 both as XB donor and XB acceptor ($\text{C2}-\text{I1}\cdots\text{I1}^{(i)} = 172.7 (2)^\circ$ and
29 $\text{I1}\cdots\text{I1}^{(i)} = 3.799 (2) \text{ \AA}$, $\text{C2}^{(i)}-\text{I1}^{(i)}\cdots\text{I1} = 107.2 (2)^\circ$ and $\text{I1}^{(i)}\cdots\text{I1} =$
30 $3.799 (2) \text{ \AA}$; equivalent position of (i) is $-x+y, -x, 1/3+z$). When
31 moving from iodoanilines to iodophenols, in 2-iodophenol (**12**)⁴¹
32 iodine atoms I1 form only type I contacts and in 4-iodophenol
33 (**13**)³⁷ iodines I1 interact with a benzene ring. Iodine atoms I1 and
34 I3 show the XB donor and the XB acceptor behavior in 3-iodophenol
35 (**14**)³⁷ ($\text{C1}-\text{I1}\cdots\text{O1} = 157.92^\circ$ and $\text{I1}\cdots\text{O1} = 3.332 \text{ \AA}$) and 2,4,6-
36 triiodophenol (**15**)⁴² ($\text{C4}-\text{I3}\cdots\text{O1} = 75.64^\circ$ and $\text{I3}\cdots\text{O1} = 3.446 \text{ \AA}$),
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55 correspondingly.
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3 In order to demonstrate the effect of +M substituent, a methoxy -
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5 OCH₃ substituent was selected. Thus, in 4-iodoanisole (**16**)⁴³
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7 (Figure 15, Table 8) a positive mesomeric effect of the methoxy
8
9 group should favor iodine in *para*-position to act as a halogen
10
11 bond acceptor. However, according to the structural analysis, an
12
13 iodine atom I1 participates in a weak interaction with an oxygen
14
15 atom O1 from the ether group of an adjacent molecule and acts as
16
17 an XB donor. The I1...O1 distance is 3.161 (5) Å vs. the sum of vdW
18
19 radii of 3.50 Å, the C-I...O angle is 172.1 (2) °. The calculated
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21 $V_{S,max}$ value for I1 is 0.025. If we compare three structures, 4-
22
23 iodoaniline (**10**), 4-iodophenol (**13**) and 4-iodoanisole (**16**), we can
24
25 see, that although for all these structures the $V_{S,max}$ value for
26
27 *para*-iodine is very similar (0.021 for **10**, 0.026 for **13** and 0.025
28
29 for **16**), the XB donor-acceptor behavior differs significantly.
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31 Thus, in a case of stronger electron-donating substituents -NH₂
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33 (**10**) and -OH (**13**) the iodine atoms do not participate in a halogen
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35 bonding. It can be explained by the fact, that in both structures
36
37 **10** and **13** electrons on the nitrogen and oxygen atoms are hindered
38
39 by the broad region of a positive electrostatic potential (Figure
40
41 **17**), which is reflected in the $V_{S,max}$ values being 0.050-0.068 for
42
43 the amino group and 0.061-0.075 for the hydroxy group (Table S4).
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45 This makes impossible the I...N and I...O interactions to happen.
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3 In a case of the methoxy $-OCH_3$ substituent, which reveals a much
4 weaker positive mesomeric effect, the *para*-iodine atom I1 acts as
5 an XB donor upon interaction with oxygen from a neighboring
6 molecule (**16**). According to our computational analysis, a region
7 with a positive electrostatic potential from CH_3 is shifted to the
8 side, thus, opening a negative region on oxygen and giving space
9 for iodine to approach (Figure 17). This is also confirmed by a
10 very small $V_{S,max}$ value on oxygen O1 (0.009).
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47 **Figure 15.** Weak interactions in the structure of **16**. Selected bond
48 lengths (Å) and angles (°): I1-O1⁽ⁱ⁾ 3.161 (5), C4-I1-O1⁽ⁱ⁾ 172.1
49 (2), C1⁽ⁱ⁾-O1⁽ⁱ⁾-I1 129.4 (4). Equivalent positions: (i) 1.5-x, y,
50 1/2+z.
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Table 8. Halogen bonds in **11** and **14-17**.

	Atoms	Distance, Å	Angles, °	Sum of vdW radii, Å	Equivalent positions of (i-vii)
11	I1 ··· I1 ⁽ⁱ⁾	3.799 (2)	C2-I1-I1 ⁽ⁱ⁾ = 107.2 (2), C2 ⁽ⁱ⁾ - I1 ⁽ⁱ⁾ -I1 = 172.7 (2)	3.96	-x+y, -x, 1/3+z
14	I1 ··· O1 ⁽ⁱⁱ⁾	3.332 (3)	C1-I1-O1 ⁽ⁱⁱ⁾ = 157.9 (1), C4 ⁽ⁱⁱ⁾ - O1 ⁽ⁱⁱ⁾ -I1 = 102.8 (3)	3.5	1/2-x, 1-y, -1/2+z
15	I3 ··· O1 ⁽ⁱⁱⁱ⁾	3.446 (8)	C4-I3- O1 ⁽ⁱⁱⁱ⁾ = 75.6 (3),	3.5	1/2+x, 1/2- y, -z

			$C3^{(iii)} -$ $O1^{(iii)} - I3 =$ 154.1 (6)		
16	$I1 \cdots O1^{(iv)}$	3.161 (5)	$C4 - I1 - O1^{(iv)}$ $= 172.1$ (2), $C1^{(iv)} -$ $O1^{(iv)} - I1 =$ 129.4 (4)	3.5	$1.5 - x, y,$ $1/2 + z$
17	$I1 \cdots I3^{(v)}$	3.9294 (5)	$C3 - I1 - I3^{(v)}$ $= 160.8$ (1), $C5^{(v)} - I3^{(v)} -$ $I1 = 82.7$ (1)	3.96	$-x, 1/2 + y,$ $1/2 - z$
	$I2 \cdots O1^{(vi)}$	3.270 (3)	$C4 - I2 - O1^{(vi)}$ $= 177.2$ (1), $C1^{(vi)} -$ $O1^{(vi)} - I2 =$ 126.6 (3)	3.50	$-1 + x, 1/2 -$ $y, -1/2 + z$

	I3...I3 ^(vii)	3.9350	C5-I3-	3.96	1-x, -y, -z
		(5)	I3 ^(vii) =		
			C5 ^(vii) -		
			I3 ^(vii) -I3 =		
			141.8 (1)		

In the structure of 3,4,5-triiodoanisole (**17**)⁴⁴ an iodine atom in *para*-position should favor XB acceptor behavior and two iodines in *meta*-positions should favor XB donor behavior because of the +M effect of a methoxy group -OCH₃. According to the crystal structure analysis, all three iodine atoms reveal different XB activity (Figure 16, Table 8). Thus, *meta*-iodine I1 acts as an XB donor with the I3 atom from an adjacent molecule. The corresponding I1...I3 distance is 3.9294 (5) Å vs. the sum of vdW radii of 3.96 Å, the C3-I1...I3 angle is 160.8 (1) °. Another *meta*-iodine I3 acts as an XB acceptor with the I1 atom from an adjacent molecule (I3-I1 = 3.9294 (5) Å, C5-I3-I1 = 82.7 (1) °) and also forms type I contacts with an another I3 atom. Finally, *para*-iodine I2 acts as an XB donor and interacts with the oxygen atom O1 from adjacent molecule with I2-O1 = 3.270 (3) Å, C4-I2-O1 = 177.2 (1) °.

The calculated $V_{s,max}$ values for the iodine atoms of **17** are 0.034, 0.033 and 0.036 for I1, I2 and I3, respectively. These values together with the XB donor-acceptor behavior of iodines in **17** let

us assume that the weak positive mesomeric effect of an ether group $-OCH_3$ does not affect the iodine atoms to a large extent. Furthermore, upon a comparison of compounds **16** and **17**, it can be clearly seen that the $V_{S,max}$ numbers on *para*-iodines differ significantly (0.025 for **16** and 0.033 for **17**), thus, resulting in an assumption, that *meta*-iodines in **17** have a higher impact on the chemical properties of *para*-iodine than the methoxy group.

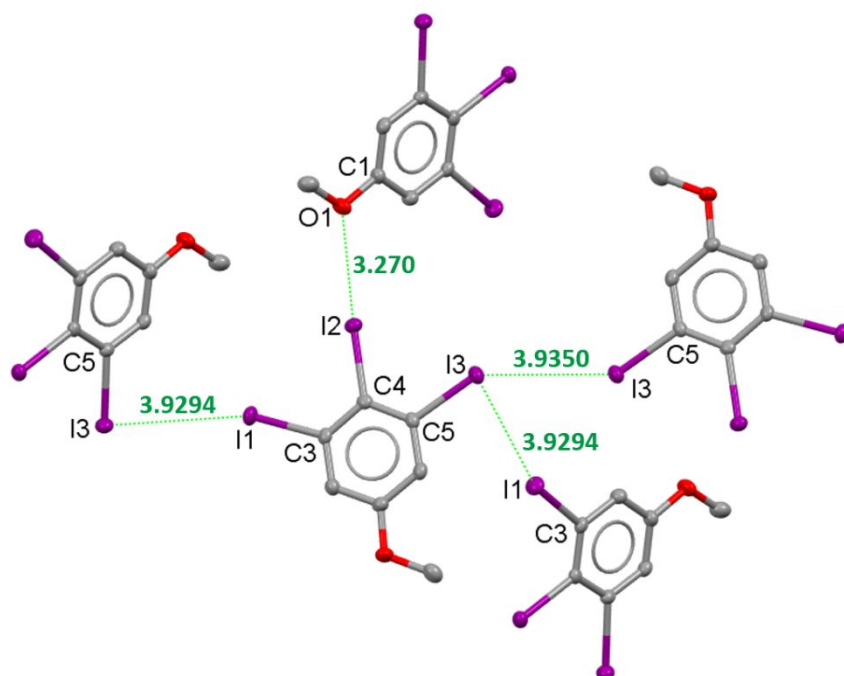


Figure 16. Halogen bonding in the structure of **17**. Hydrogens are omitted for clarity. Selected bond lengths (Å) and angles ($^{\circ}$): I1-I2⁽ⁱ⁾ 3.7044 (5), I1-I3⁽ⁱⁱ⁾ 3.7125 (6), I2⁽ⁱ⁾-I3⁽ⁱⁱ⁾ 3.9485 (6), C1⁽ⁱ⁾-I2⁽ⁱ⁾-I1 174.2 (1), C3-I1-I2⁽ⁱ⁾ 114.9 (1), C3-I1-I3⁽ⁱⁱ⁾ 178.3 (1), C2⁽ⁱⁱ⁾-I3⁽ⁱⁱ⁾-I1 124.6 (1), C1⁽ⁱ⁾-I2⁽ⁱ⁾-I3⁽ⁱⁱ⁾ 123.5 (1), C2⁽ⁱⁱ⁾-I3⁽ⁱⁱ⁾-

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3 I2⁽ⁱ⁾ 114.9 (1). Equivalent positions: (i) 1.5-x, -1/2+y, 1.5-z;
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5 (ii) 2.5-x, 1/2+y, 1.5-z.
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8 9 2.3. Computational analysis

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11 Analysis of the map of electrostatic potential (further MEP) helps
12 to predict and estimate non-covalent interactions.^{74,75} It was shown
13
14 that the magnitude of the sigma-hole (further $V_{S,max}$) correlates
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16 with the strength of a non-covalent interaction.^{74,76} Moreover,
17
18 groups of substituents with electron-donating (EDG) or electron-
19
20 withdrawing (EWG) effects can influence $V_{S,max}$ and, correspondingly,
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22 the interaction strength. EWG can increase $V_{S,max}$ by depleting the
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24 electron density, while in case of EDG the $V_{S,max}$ may decrease due
25
26 to the additional electron density in the system.^{7,76-78}
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33 The influence of the substituent on the $V_{S,max}$ value of the halide
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35 in structures **1-17** can be clearly seen (Figure 17, Table 9, Table
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37 S4). Our computational results indeed show, that in the case of
38
39 the electron-withdrawing groups the $V_{S,max}$ value of the iodine atom
40
41 is always bigger, than in the case of the electron-donating groups.
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45 An increase in the $V_{S,max}$ values on the iodine atoms can be seen
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47 upon introduction of a carboxyl group in the structures of **1-2**
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49 (0.039-0.042) and **5** (0.047-0.050) vs. the structures of **3** (0.036)
50
51 and **6** (0.043). Thus, the difference in the $V_{S,max}$ values of the
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53 iodines in TIBA (**1, 2**) and 1,2,3-triiodobenzene (**3**) is due to
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3 electron-withdrawing effect of a carboxyl group. There is also a
4
5 small deviation in the $V_{S,max}$ values between *meta*- and *para*-
6
7 positions in TIBA, with a higher value for *para*-iodine and smaller
8
9 values for *meta*-iodines. In the case of PIBA (**5**) and HIB (**6**),
10
11 although the -COOH group is not located within the same plane with
12
13 the benzene ring in **5**, the increase of $V_{S,max}$ on the iodine atom can
14
15 be still seen comparing to **6**. The highest $V_{S,max}$ values are found
16
17 for *ortho*-iodines (**5**), reflecting higher ability of these iodines
18
19 to act as XB donors, which correlates with the conducted structural
20
21 analysis.
22
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24
25

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27 In iodobenzonitriles **7-8** the difference in the $V_{S,max}$ values of the
28
29 iodine between *meta*- and *para*-positions is neglectable. However,
30
31 in iodophenols **12-15** the $V_{S,max}$ values are increasing in the row of
32
33 *para*- < *meta*- < *ortho*-, with the highest values in 2,4,6-
34
35 triiodophenol (**15**) being 0.035 and 0.048 for *ortho*- and 0.037 for
36
37 *para*-position.
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41
42 In the case of iodoanilines **9-11** the $V_{S,max}$ values for *para*-position
43
44 are lower, than for *ortho*-positions (0.021 and 0.027 vs. 0.027 and
45
46 0.034) with the highest values found for 2,4-diiodoaniline **9**.
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50 The presence of several iodine atoms in one molecule affects the
51
52 $V_{S,max}$ value of iodide substituents due to the +M effect of the
53
54 iodine. For example, the $V_{S,max}$ value for *p*-iodine in 4-iodoanisole
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56 (**16**) is smaller, than that in 3,4,5-triiodoanisole (**17**). The
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3 corresponding values are 0.025 for **16** and 0.033 for **17**. Another
4
5 example of the same trend can be observed upon comparison of the
6
7 2,4-diiodoaniline (**9**) and 2-iodoaniline (**11**) structures: the $V_{S,max}$
8
9 value for *o*-iodine is higher in the case of diiodoaniline (0.034
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11 for **9** vs. 0.027 for **11**).

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15 In order to trace the influence of the nature of the substituent
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17 other than halogen on the XB donor-acceptor properties of the
18
19 iodide substituents, several groups of compounds were considered.
20
21 Thus, first group is represented by the compounds with three iodide
22
23 substituents, i.e. 3,4,5-triiodobenzoic acid (**1**, **2**), 1,2,3-
24
25 triiodobenzene (**3**) and 3,4,5-triiodoanisole (**17**). The $V_{S,max}$ values
26
27 increase in a row of **17** < **3** < **1**, **2**. Another group is represented
28
29 by compounds 4-iodobenzoic acid (**4**), 4-iodobenzonitrile (**7**), 4-
30
31 iodoaniline (**10**), 4-iodophenol (**13**) and 4-iodoanisole (**16**). All
32
33 these structures have the iodine atom in *para*-position. The $V_{S,max}$
34
35 values increase in a row of **10** < **16** < **13** < **4** < **7**. Finally, third
36
37 group is represented by compounds, having iodine in *meta*-position,
38
39 namely, 3-iodobenzonitrile (**8**) and 3-iodophenol (**14**). The $V_{S,max}$
40
41 value for iodine in the structure of **8** is much higher, than that
42
43 in the structure of **14**. All these correlations confirm our
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45 hypothesis, that electron-withdrawing groups withdraw electron
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47 density from benzene ring and, therefore, increase the size of a
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49 σ -hole. On the contrary, electron-donating groups donate electron
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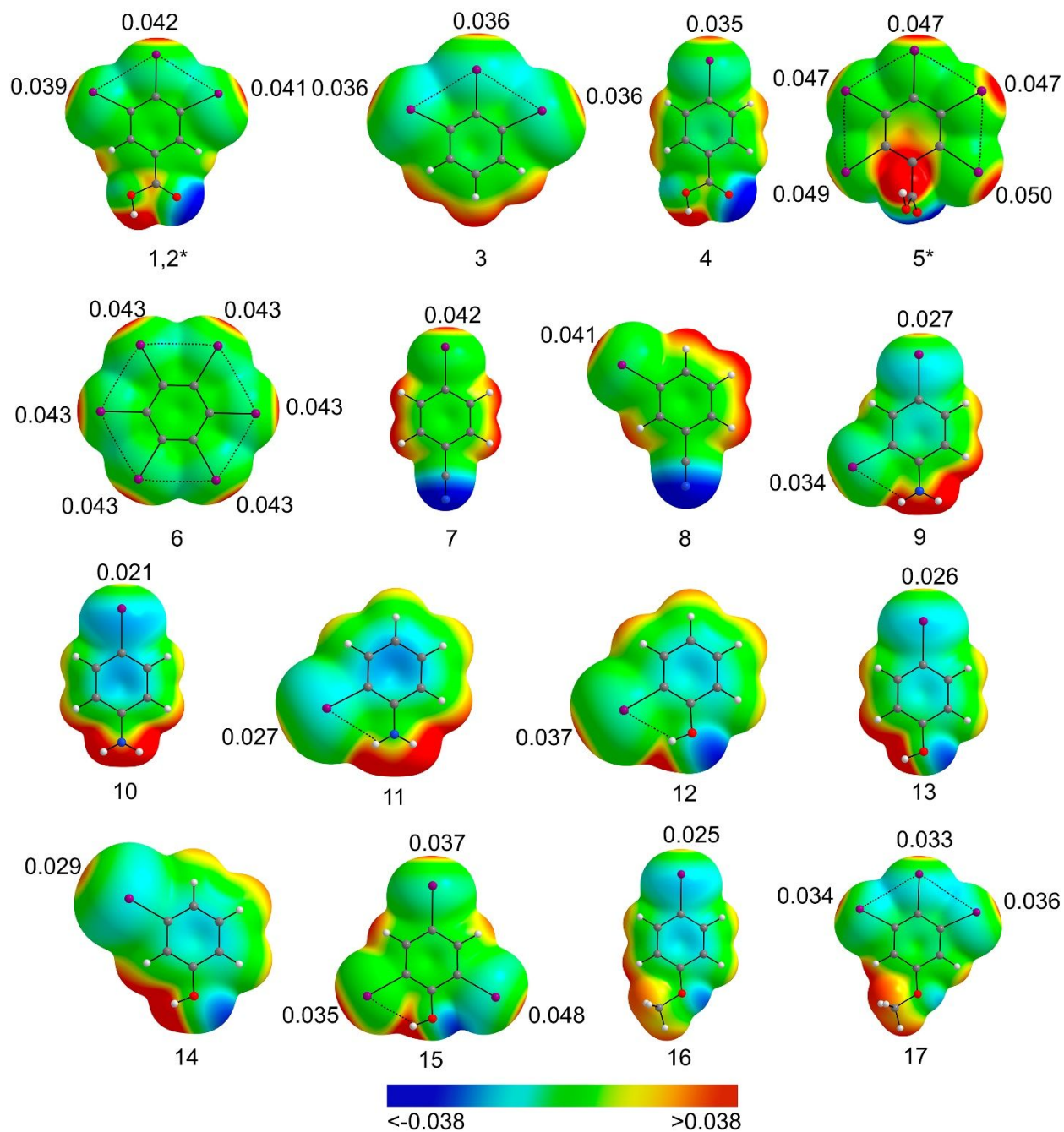
density to the benzene ring, thus, decreasing the size of a σ -hole. Therefore, iodide substituents reveal better XB donor ability in the case of electron-withdrawing substituents (**1-2**, **4**, **7-8**) and are less likely to act as XB donors in the case of electron-donating substituents (**9-17**).

Table 9. Maximum ESP ($V_{S,max}$) of the selected halogenated molecules (calculated at the PBE0-D3/def2-TZVP level).

Molecule	Atom	$V_{S,max}$, a.u.
1, 2*	I1	0.039
	I2	0.042
	I3	0.041
3	I1	0.036
	I2	0.036
	I3	0.036
4	I1	0.035
5*	I1	0.049
	I2	0.047
	I3	0.047
	I4	0.047
	I5	0.050
6	I1	0.043
	I2	0.043
	I3	0.043
	I1B	0.043
	I2B	0.043
	I3B	0.043
7	I1	0.042
8	I1	0.041
9	I1	0.034
	I2	0.027
10	I1	0.021
11	I1	0.027
12	I1	0.037
13	I1	0.026
14	I1	0.029
15	I1	0.037
	I2	0.048

	I3	0.035
16	I1	0.025
17	I1	0.034
	I2	0.033
	I3	0.036

*calculations performed for structure omitting the solvent molecule



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2
3 **Figure 17.** Electrostatic potential calculated at the PBE0-D3/def2-
4 TZVP computational level on the 0.001 au molecular surface with
5 the $V_{S,max}$ values at iodide atoms; same ESP color scale from -0.038
6 to 0.038 eÅ⁻¹ was applied for all of the molecules with a blue
7 color for negative, green for neutral and red for positive values;
8 a color scheme for atoms: H - white, C - gray, O - red, I - purple.
9
10 *calculations performed for structure omitting the solvent
11 molecule.
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22 3. CONCLUSIONS

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25 The conducted structural analysis complemented with the MEP
26 computational analysis show, that the nature of the substituent
27 other than halogen in a benzene ring has an impact on the XB donor
28 and acceptor properties of the iodinated benzenes. The electron-
29 withdrawing substituents, such as -COOH and -CN, increase the
30 ability of iodines in *ortho*- or *para*-positions to act as halogen
31 bond donors. On the other hand, the electron-donating
32 substituents, such as -OH, -NH₂ and -OCH₃, enhance the XB donor
33 properties of iodines in *meta*-position. It is reflected in the
34 size of the σ -hole on the iodine atoms, which can be expressed by
35 the value of maximum electrostatic potential ($V_{S,max}$). The stronger
36 the mesomeric effect of the EWG or EDG, the higher impact it makes
37 on the XB donor-acceptor properties of the iodide substituents.
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39 Such structural correlations can potentially be exploited in the
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3 crystal engineering for the design of crystal structures with pre-
4 defined contacts.
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7 8 9 4. EXPERIMENTAL

10 11 12 4.1. Experimental details

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15 3,4,5-triiodobenzoic acid (TIBA) crystals **1** and **2** were obtained by
16 a slow evaporation of an ethanol solvent with an evaporation vessel
17 covered with a parafilm under ambient conditions. TIBA was
18 purchased from Fluka AG, Chemische Fabrik. The isolated yields are
19 95 % for **1** and 87 % for **2**. Elemental analysis of **1**: found C 16.93
20 %, H 0.83 %, N 0.1 %; calculated C 16.8 %, H 0.6 %, N 0 %. Elemental
21 analysis of **2**: found C 19.57 %, H 1.554 %, N 0.253%; calculated C
22 19.79 %, H 1.65 %, N 0 %. ¹H NMR of **1** (MeOD, δ): 8.425 (s, 2H, Ar).
23
24 ¹H NMR of **2** (MeOD, δ): 1.178 (t, 3H, CH₃ from ethanol), 3.739 (q,
25 2H, CH₂ from ethanol), 8.425 (s, 2H, Ar). Signal of -COOH proton
26 is too broad to be observable. The obtained crystals of **1** were
27 analyzed with SuperNova Dual X-ray diffractometer using Cu source.
28 Crystals of **2** were analyzed with Bruker KAPPA APEX II CCD X-ray
29 diffractometer. Details on the XRD experiments can be found in
30 ESI.
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50 4.2. Computational details

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53 All of the molecules were subjected to full energy minimization
54 and ESP calculation at DFT level using PBE0⁷⁹-D3⁸⁰ dispersion
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3 corrected functional with a 6-31G* basis set for all atoms except
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5 for iodine, for which a def2-TZVP⁸¹ basis with a pseudopotential
6
7 for the inner-core electrons was used. Wavefunction files were
8
9 obtained in Gaussian 09 (revision D.01) program package.⁸²
10
11 Electrostatic potential of **1-17** was calculated with the QTAIM
12
13 (Quantum Theory of Atoms in Molecules)⁸³ method and visualized in
14
15 the AIMALL⁸⁴ software by plotting a map of an electrostatic
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17 potential (further MEP) at the 0.001 au contour of its electronic
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19 density as suggested by Bader *et al.*⁸⁵
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28 5. ASSOCIATED CONTENT

31 **Supporting Information.**

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34 Details on the XRD experiments and structure determination of **1**
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36 and **2**, CSD refcodes of **3-17**, structural image of **3**, hydrogen
37
38 contacts in **1** and **2**, halogen contacts in **1**, **2**, **11**, **12**, **14** and **15**,
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40 structures **1-17** with the labels of the atoms, maximum ESP ($V_{S,max}$)
41
42 of the selected halogenated molecules.
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46 **Accession Codes**

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50 CCDC 2011890 and 20111891 contain the supplementary
51
52 crystallographic data for this paper. These data can be obtained
53
54 free of charge via www.ccdc.cam.ac.uk/data_request/cif, or by
55
56
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1
2
3 emailing data_request@ccdc.cam.ac.uk, or by contacting The
4 Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge
5
6 CB2 1EZ, UK; fax: +44 1223 336033.
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20 7. REFERENCES

- 21
22
23 (1) Hassel, O.; Hvoslef, J. The Structure of Bromine 1,4-
24 Dioxanate. *Acta Chem. Scand.* **1954**, *5*, 873.
25
26 (2) Hassel, O. Structural Aspects of Interatomic Charge-Transfer
27 Bonding. *Science (80-.)*. **1970**, *170*, 497-502.
28
29 (3) Dumas, J.-M.; Peurichard, H.; Gomel, M. CX4...base
30 Interactions as Models of Weak Charge-Transfer Interactions:
31 Comparison with Strong Charge-Transfer and Hydrogen-Bond
32 Interactions. *J. Chem. Res.* **1978**, No. 2, 54-57.
33
34 (4) Bruckmann, A.; Pena, M. A.; Bolm, C. Organocatalysis through
35 Halogen-Bond Activation. *Synlett* **2008**, No. 6, 900-902.
36
37 <https://doi.org/10.1055/s-2008-1042935>.
38
39 (5) Sutar, R. L.; Huber, S. M. Catalysis of Organic Reactions
40 through Halogen Bonding. *ACS Catal.* **2019**, *9*, 9622-9639.
41
42 <https://doi.org/10.1021/acscatal.9b02894>.
43
44 (6) Bulfield, D.; Huber, S. M. Halogen Bonding in Organic
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

- 1
2
3 Synthesis and Organocatalysis. *Chem. - A Eur. J.* **2016**, *22*,
4 14434-14450. <https://doi.org/10.1002/chem.201601844>.
5
6
7
8 (7) Aakeröy, C. B.; Wijethunga, T. K.; Desper, J. Practical
9
10 Crystal Engineering Using Halogen Bonding: A Hierarchy Based
11
12 on Calculated Molecular Electrostatic Potential Surfaces. *J.*
13
14 *Mol. Struct.* **2014**, *1072*, 20-27.
15
16
17 <https://doi.org/10.1016/j.molstruc.2014.02.022>.
18
19 (8) Ciancaleoni, G. Cooperativity between Hydrogen- and Halogen
20
21 Bonds: The Case of Selenourea. *Phys. Chem. Chem. Phys.* **2018**,
22
23 *20*, 8506-8514. <https://doi.org/10.1039/c8cp00353j>.
24
25
26 (9) Arman, H. D.; Rafferty, E. R.; Bayse, C. A.; Pennington, W.
27
28 T. Complementary Selenium•••iodine Halogen Bonding and
29
30 Phenyl Embraces: Cocrystals of Triphenylphosphine Selenide
31
32 with Organoiodides. *Cryst. Growth Des.* **2012**, *12*, 4315-4323.
33
34
35 <https://doi.org/10.1021/cg201348u>.
36
37 (10) Rissanen, K. Halogen Bonded Supramolecular Complexes
38
39 and Networks. *CrystEngComm* **2008**, *10*, 1107-1113.
40
41
42 <https://doi.org/10.1039/b803329n>.
43
44 (11) Metrangolo, P.; Neukirch, H.; Pilati, T.; Resnati, G.
45
46 Halogen Bonding Based Recognition Processes: A World
47
48 Parallel to Hydrogen Bonding. *Acc. Chem. Res.* **2005**, *38*, 386-
49
50 395. <https://doi.org/10.1021/ar0400995>.
51
52
53 (12) Metrangolo, P.; Meyer, F.; Pilati, T.; Resnati, G.;
54
55 Terraneo, G. Halogen Bonding in Supramolecular Chemistry.
56
57
58
59
60

- 1
2
3 *Angew. Chemie - Int. Ed.* **2008**, *47*, 6114–6127.
4
5 <https://doi.org/10.1002/anie.200800128>.
6
7
8 (13) Scholfield, M. R.; Vander Zanden, C. M.; Carter, M.;
9
10 Ho, P. S. Halogen Bonding (X-Bonding): A Biological
11
12 Perspective. *Protein Sci.* **2013**, *22*, 139–152.
13
14 <https://doi.org/10.1002/pro.2201>.
15
16
17 (14) Erdélyi, M. Application of the Halogen Bond in Protein
18
19 Systems. *Biochemistry* **2017**, *56*, 2759–2761.
20
21 <https://doi.org/10.1021/acs.biochem.7b00371>.
22
23
24 (15) Auffinger, P.; Hays, F. A.; Westhof, E.; Ho, P. S.
25
26 Halogen Bonds in Biological Molecules. *Proc. Natl. Acad.*
27
28 *Sci. U. S. A.* **2004**, *101*, 16789–16794.
29
30 <https://doi.org/10.1073/pnas.0407607101>.
31
32
33 (16) Berger, G.; Soubhye, J.; Meyer, F. Halogen Bonding in
34
35 Polymer Science: From Crystal Engineering to Functional
36
37 Supramolecular Polymers and Materials. *Polym. Chem.* **2015**, *6*,
38
39 3559–3580. <https://doi.org/10.1039/c5py00354g>.
40
41
42 (17) Fourmigué, M.; Batail, P. Activation of Hydrogen- and
43
44 Halogen-Bonding Interactions in Tetrathiafulvalene-Based
45
46 Crystalline Molecular Conductors. *Chem. Rev.* **2004**, *104*,
47
48 5379–5418. <https://doi.org/10.1021/cr030645s>.
49
50
51 (18) Yamamoto, H. M.; Yamaura, J. I.; Kato, R.
52
53 Multicomponent Molecular Conductors with Supramolecular
54
55 Assembly: Iodine-Containing Neutral Molecules as Building
56
57
58
59
60

- 1
2
3 Blocks. *J. Am. Chem. Soc.* **1998**, *120*, 5905–5913.
4
5 <https://doi.org/10.1021/ja980024u>.
6
7
8 (19) Metrangolo, P.; Präsang, C.; Resnati, G.; Liantonio,
9
10 R.; Whitwood, A. C.; Bruce, D. W. Fluorinated Liquid
11
12 Crystals Formed by Halogen Bonding. *Chem. Commun.* **2006**, No.
13
14 31, 3290–3292. <https://doi.org/10.1039/b605101d>.
15
16
17 (20) Xu, J.; Liu, X.; Ng, J. K. P.; Lin, T.; He, C.
18
19 Trimeric Supramolecular Liquid Crystals Induced by Halogen
20
21 Bonds. *J. Mater. Chem.* **2006**, *16*, 3540–3545.
22
23 <https://doi.org/10.1039/b606617h>.
24
25
26 (21) Nguyen, H. L.; Horton, P. N.; Hursthouse, M. B.;
27
28 Legon, A. C.; Bruce, D. W. Halogen Bonding: A New
29
30 Interaction for Liquid Crystal Formation. *J. Am. Chem. Soc.*
31
32 **2004**, *126*, 16–17. <https://doi.org/10.1021/ja0369941>.
33
34
35 (22) Metrangolo, P.; Pilati, T.; Resnati, G. Halogen
36
37 Bonding and Other Noncovalent Interactions Involving
38
39 Halogens: A Terminology Issue. *CrystEngComm* **2006**, *8*, 946–
40
41 947. <https://doi.org/10.1039/b610454a>.
42
43
44 (23) Wilcken, R.; Zimmermann, M. O.; Lange, A.; Joerger, A.
45
46 C.; Boeckler, F. M. Principles and Applications of Halogen
47
48 Bonding in Medicinal Chemistry and Chemical Biology. *J. Med.*
49
50 *Chem.* **2013**, *56*, 1363–1388.
51
52 <https://doi.org/10.1021/jm3012068>.
53
54
55 (24) Cavallo, G.; Metrangolo, P.; Milani, R.; Pilati, T.;

- 1
2
3 Priimagi, A.; Resnati, G.; Terraneo, G. The Halogen Bond.
4
5 *Chem. Rev.* **2016**, *116*, 2478–2601.
6
7 <https://doi.org/10.1021/acs.chemrev.5b00484>.
8
9
10 (25) Clark, T.; Hennemann, M.; Murray, J. S.; Politzer, P.
11
12 Halogen Bonding: The σ -Hole. *J. Mol. Model.* **2007**, *13*, 291–
13
14 296. <https://doi.org/10.1007/s00894-006-0130-2>.
15
16
17 (26) Metrangolo, P.; Resnati, G. Type II Halogen···halogen
18
19 Contacts Are Halogen Bonds. *IUCrJ* **2014**, *1*, 5–7.
20
21 <https://doi.org/10.1107/S205225251303491X>.
22
23
24 (27) Desiraju, G. R.; Shing Ho, P.; Kloo, L.; Legon, A. C.;
25
26 Marquardt, R.; Metrangolo, P.; Politzer, P.; Resnati, G.;
27
28 Rissanen, K. Definition of the Halogen Bond (IUPAC
29
30 Recommendations 2013). *Pure Appl. Chem.* **2013**, *85*, 1711–1713.
31
32 <https://doi.org/10.1351/PAC-REC-12-05-10>.
33
34
35 (28) Ouellette, R. J.; Rawn, J. D. *Electrophilic Aromatic*
36
37 *Substitution*; 2018. [https://doi.org/10.1016/b978-0-12-](https://doi.org/10.1016/b978-0-12-812838-1.50013-x)
38
39 [812838-1.50013-x](https://doi.org/10.1016/b978-0-12-812838-1.50013-x).
40
41
42 (29) Pramanik, S.; Dey, T.; Mukherjee, A. K. Five Benzoic
43
44 Acid Derivatives: Crystallographic Study Using X-Ray Powder
45
46 Diffraction, Electronic Structure and Molecular
47
48 Electrostatic Potential Calculation. *J. Mol. Struct.* **2019**,
49
50 *1175*, 185–194.
51
52 <https://doi.org/10.1016/j.molstruc.2018.07.090>.
53
54
55 (30) Allen, F. H.; Satish Goud, B.; Hoy, V. J.; Howard, J.
56
57
58
59
60

- 1
2
3 A. K.; Desiraju, G. R. Molecular Recognition via Iodo---
4 Nitro and Iodo---Cyano Interactions: Crystal Structures of
5 the 1:1 Complexes of 1,4-Diiodobenzene with 1,4-
6 Dinitrobenzene and 7,7,8,8-Tetracyanodimethane (TCNQ). *J.*
7 *Chem. Soc. Chem. Commun.* **1994**, 2729-2730.
8 [https://doi.org/10.1002/\(SICI\)1099-](https://doi.org/10.1002/(SICI)1099-1409(200006/07)4:4<393::AID-JPP227>3.3.CO;2-2)
9 1409(200006/07)4:4<393::AID-JPP227>3.3.CO;2-2.
- 10
11
12
13
14
15
16
17
18
19 (31) Novak, I.; Li, D. 1,2,3-Triiodobenzene. *Acta*
20 *Crystallogr. Sect. E Struct. Reports Online* **2007**, *63*, 2006-
21 2007. <https://doi.org/10.1107/S1600536806054535>.
22
23
24
25
26 (32) Nygren, C. L.; Wilson, C. C.; Turner, J. F. C. On the
27 Solid State Structure of 4-Iodobenzoic Acid. *J. Phys. Chem.*
28 *A* **2005**, *109*, 2586-2593. <https://doi.org/10.1021/jp047189b>.
29
30
31
32
33 (33) Adonin, S. A.; Bondarenko, M. A.; Novikov, A. S.;
34 Abramov, P. A.; Sokolov, M. N.; Fedin, V. P. Halogen Bonding
35 in the Structures of Pentaiodobenzoic Acid and Its Salts.
36 *CrystEngComm* **2019**, *21*, 6666-6670.
37 <https://doi.org/10.1039/c9ce01106d>.
38
39
40
41
42
43
44 (34) Steer, R. J.; Watkins, S. F.; Woodward, P. Crystal and
45 Molecular Structure of Hexaiodobenzene. *J. Chem. Soc.* **1970**,
46 403-408. <https://doi.org/10.1017/CBO9781107415324.004>.
47
48
49
50
51 (35) Ghosh, S.; Reddy, C. M.; Desiraju, G. R.
52 Hexaiodobenzene: A Redetermination at 100 K. *Acta*
53 *Crystallogr. Sect. E Struct. Reports Online* **2007**, *63*, 910-
54
55
56
57
58
59
60

- 1
2
3 911. <https://doi.org/10.1107/S1600536807002279>.
4
5 (36) Giordano, N.; Afanasjevs, S.; Beavers, C. M.; Hobday,
6 C. L.; Kamenev, K. V.; O'Bannon, E. F.; Ruiz-Fuertes, J.;
7 Teat, S. J.; Valiente, R.; Parsons, S. The Effect of
8 Pressure on Halogen Bonding in 4-Iodobenzonitrile. *Molecules*
9 **2019**, *24*, 1-23. <https://doi.org/10.3390/molecules24102018>.
10
11 (37) Merz, K. Substitution Effect on Crystal Packings of
12 Iodobenzonitriles and Iodophenols. *Cryst. Growth Des.* **2006**,
13 *6*, 1615-1619.
14
15 (38) Smith, G.; Wermuth, U. D. 2,4-Diiodoaniline. *Acta*
16 *Crystallogr. Sect. E Struct. Reports Online* **2009**, *65*, 2018.
17 <https://doi.org/10.1107/S1600536809030438>.
18
19 (39) Dey, A.; Jetti, R. K. R.; Boese, R.; Desiraju, G. R.
20 Supramolecular Equivalence of Halogen, Ethynyl and Hydroxy
21 Groups. A Comparison of the Crystal Structures of Some 4-
22 Substituted Anilines. *CrystEngComm* **2003**, *5*, 248-252.
23 <https://doi.org/10.1039/b304785g>.
24
25 (40) Parkin, A.; Spanswick, C. K.; Pulham, C. R.; Wilson,
26 C. C. 2-Iodoaniline at 100 K. *Acta Crystallogr. Sect. E*
27 *Struct. Reports Online* **2005**, *61*, 1087-1089.
28 <https://doi.org/10.1107/S1600536805007038>.
29
30 (41) Prout, K.; Fail, J.; Jones, R. M.; Warner, R. E.;
31 Emmett, J. C. A Study of the Crystal and Molecular
32 Structures of Phenols with Only Intermolecular Hydrogen
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

- 1
2
3 Bonding. *J. Chem. Soc. Perkin Trans. 2* **1988**, No. 3, 265–284.
4
5 <https://doi.org/10.1039/P29880000265>.
6
7
8 (42) Nath, N. K.; Saha, B. K.; Nangia, A. Isostructural
9
10 Polymorphs of Triiodophloroglucinol and Triiodoresorcinol.
11
12 *New J. Chem.* **2008**, 32, 1693–1701.
13
14 <https://doi.org/10.1039/b804905j>.
15
16
17 (43) Goubitz, K.; Sonneveld, E. J.; Schenk, H. Crystal
18
19 Structure Determination of a Series of Small Organic
20
21 Compounds from Powder Data. *Zeitschrift fur Krist.* **2001**,
22
23 216, 176–181. <https://doi.org/10.1524/zkri.216.3.176.20326>.
24
25
26 (44) Al-Zoubi, R. M.; Al-Mughaid, H.; Al-Zoubi, M. A.;
27
28 Jaradat, K. T.; McDonald, R. Facile, One-Pot, and Gram-Scale
29
30 Synthesis of 3,4,5-Triiodoanisole through a C-H
31
32 Iodination/Ipso-Iododecarboxylation Strategy: Potential
33
34 Application towards 3,4,5-Trisubstituted Anisoles. *European*
35
36 *J. Org. Chem.* **2015**, 2015, 5501–5508.
37
38 <https://doi.org/10.1002/ejoc.201500887>.
39
40
41 (45) Elhiti, M.; Stasolla, C. Ectopic Expression of the
42
43 Brassica SHOOTMERISTEMLESS Attenuates the Deleterious
44
45 Effects of the Auxin Transport Inhibitor TIBA on Somatic
46
47 Embryo Number and Morphology. *Plant Sci.* **2011**, 180, 383–390.
48
49 <https://doi.org/10.1016/j.plantsci.2010.10.014>.
50
51
52
53 (46) Miyamoto, K.; Inui, A.; Uheda, E.; Oka, M.; Kamada,
54
55 M.; Yamazaki, C.; Shimazu, T.; Kasahara, H.; Sano, H.;

- 1
2
3 Suzuki, T.; Higashibata, A.; Ueda, J. Polar Auxin Transport
4 Is Essential to Maintain Growth and Development of Etiolated
5 Pea and Maize Seedlings Grown under 1g Conditions: Relevance
6 to the International Space Station Experiment. *Life Sci. Sp.*
7
8
9
10 to the International Space Station Experiment. *Life Sci. Sp.*
11
12 *Res.* **2019**, *20*, 1-11.
13
14 <https://doi.org/10.1016/j.lssr.2018.11.001>.
15
16
17 (47) Zhang, L.; Yan, P.; Shen, C.; Zhang, L.; Wei, J.; Xu,
18
19 H.; Li, X.; Han, W. Effects of Exogenous TIBA on Dwarfing,
20
21 Shoot Branching and Yield of Tea Plant (*Camellia Sinensis*
22
23 L.). *Sci. Hortic. (Amsterdam)*. **2017**, *225*, 676-680.
24
25 <https://doi.org/10.1016/j.scienta.2017.07.060>.
26
27
28 (48) Ice, R. D.; Christian, J. E.; Plumlee, M. P. Metabolic
29
30 Fate of Orally Administered 2,3,5-triiodobenzoic Acid in
31
32 Lactating Animals. *J. Pharm. Sci.* **1968**, *57*, 399-404.
33
34 <https://doi.org/10.1002/jps.2600570306>.
35
36
37 (49) McGee, C. E.; Born, G. S.; Christian, J. E.; Liska, B.
38
39 J. Metabolites of 2,3,5-Triiodobenzoic Acid in Cow's Milk.
40
41 *J. Dairy Sci.* **1969**, *52*, 1864-1866.
42
43 [https://doi.org/10.3168/jds.S0022-0302\(69\)86858-X](https://doi.org/10.3168/jds.S0022-0302(69)86858-X).
44
45
46 (50) Li, Y.; Zhang, Z.; Wu, Q. Isolation and Expression
47
48 Analysis of the Ethylene Receptor Gene MiETR1b in Mango
49
50 (*Mangifera Indica*). *Hortic. Plant J.* **2016**, *2*, 1-8.
51
52 <https://doi.org/10.1016/j.hpj.2016.02.008>.
53
54
55 (51) Gerritse, J.; Gottschal, J. C. Mineralization of the
56
57
58
59
60

- 1
2
3 Herbicide 2,3,6-trichlorobenzoic Acid by a Co-culture of
4
5 Anaerobic and Aerobic Bacteria. *FEMS Microbiol. Lett.* **1992**,
6
7 101, 89-98. [https://doi.org/10.1111/j.1574-](https://doi.org/10.1111/j.1574-6968.1992.tb05765.x)
8
9 6968.1992.tb05765.x.
10
11
12 (52) Gichner, T.; Lovecka, P.; Vrchotova, B. Genomic Damage
13
14 Induced in Tobacco Plants by Chlorobenzoic Acids-Metabolic
15
16 Products of Polychlorinated Biphenyls. *Mutat. Res. - Genet.*
17
18 *Toxicol. Environ. Mutagen.* **2008**, 657, 140-145.
19
20 <https://doi.org/10.1016/j.mrgentox.2008.08.021>.
21
22
23 (53) McDowell, R. W.; Landolt, R. R.; Kessler, W. V.; Shaw,
24
25 S. M. Placental Transfer of 2, 3, 5-triiodobenzoic Acid in
26
27 the Rat. *J. Pharm. Sci.* **1971**, 60, 695-699.
28
29 <https://doi.org/10.1002/jps.2600600507>.
30
31
32 (54) Ali, A. H. N.; Jarvis, B. C. Effects of 2,3,5-
33
34 Triiodobenzoic Acid on the Regeneration of Callus and
35
36 Adventitious Roots on Stem Cuttings of Mung Bean, *Phaseolus*
37
38 *Aureus* ROXB. *Biochem. und Physiol. der Pflanz.* **1988**, 183,
39
40 509-513. [https://doi.org/10.1016/s0015-3796\(88\)80013-1](https://doi.org/10.1016/s0015-3796(88)80013-1).
41
42
43 (55) Abdelgadir, H. A.; Jäger, A. K.; Johnson, S. D.; Van
44
45 Staden, J. Influence of Plant Growth Regulators on
46
47 Flowering, Fruiting, Seed Oil Content, and Oil Quality of
48
49 *Jatropha Curcas*. *South African J. Bot.* **2010**, 76, 440-446.
50
51 <https://doi.org/10.1016/j.sajb.2010.02.088>.
52
53
54 (56) Safa, A. R.; Tseng, M. T.; Ballou, R. J. Influence of
55
56
57
58
59
60

- 1
2
3 a Plant Growth Regulator (2,3,5-Triiodobenzoic Acid) on
4
5 Cultured Mammary Tumor Cells. 69621.
6
- 7
8 (57) Andrejauskas, E.; Hertel, R.; Marmé, D. 3,4,5-
9
10 Triiodobenzoic Acid Affects [3H]Verapamil Binding to Plant
11
12 and Animal Membrane Fractions and Smooth Muscle Contraction.
13
14 *Biochem. Biophys. Res. Commun.* **1986**, *138*, 1269-1275.
15
- 16
17 (58) Šebánek, J.; Jandáková, B. The Effect of Jasmonic and
18
19 2, 3, 5-Triiodobenzoic Acid on the Correlation between
20
21 Cotyledons and Their Axillary Buds in Flax *Linum*
22
23 *Usitatissimum* and Pea *Pisum Sativum* Seedlings. *Biochem. und*
24
25 *Physiol. der Pflanz.* **1984**, *179*, 351-357.
26
27 [https://doi.org/10.1016/s0015-3796\(84\)80011-6](https://doi.org/10.1016/s0015-3796(84)80011-6).
28
29
- 30
31 (59) Beck, C.; Jensen, S. B.; Reglinski, J. The Selenium
32
33 Mediated De-Iodination of Iodophenols: A Model for the
34
35 Mechanism of 5' Thyronine de-Iodinase. *Bioorganic Med. Chem.*
36
37 *Lett.* **1994**, *4*, 1353-1356. [https://doi.org/10.1016/S0960-](https://doi.org/10.1016/S0960-894X(01)80360-7)
38
39 [894X\(01\)80360-7](https://doi.org/10.1016/S0960-894X(01)80360-7).
40
- 41
42 (60) Kadar, M.; Nagy, Z.; Karancsi, T.; Farsang, G. The
43
44 Electrochemical Oxidation of 4-Bromoaniline, 2,4-
45
46 Dibromoaniline, 2,4,6-Tribromoaniline and 4-Iodoaniline in
47
48 Acetonitrile Solution. *Electrochim. Acta* **2001**, *46*, 3405-
49
50 3414.
51
- 52
53 (61) Bianco Prevot, A.; Pramauro, E. Analytical Monitoring
54
55 of Photocatalytic Treatments. Degradation of 2,3,6-
56
57
58
59
60

- 1
2
3 Trichlorobenzoic Acid in Aqueous TiO₂ Dispersions. *Talanta*
4
5 **1999**, *48*, 847-857. <https://doi.org/10.1016/S0039->
6
7 9140(98)00101-5.
8
9
10 (62) Balavoine, F.; Madec, D.; Mioskowski, C. Highly
11
12 Regioselective Palladium-Catalyzed Condensation of Terminal
13
14 Acetylenes with 2,5-Diodobenzoic Acid. *Tetrahedron Lett.*
15
16 **1999**, *40*, 8351-8354. <https://doi.org/10.1016/S0040->
17
18 4039(99)01697-4.
19
20
21 (63) Wang, R.; Ding, Y. L.; Liu, H.; Peng, S.; Ren, J.; Li,
22
23 L. Copper-Catalyzed Multicomponent Reactions of 2-
24
25 Iodoanilines, Benzylamines, and Elemental Sulfur toward 2-
26
27 Arylbenzothiazoles. *Tetrahedron Lett.* **2014**, *55*, 945-949.
28
29 <https://doi.org/10.1016/j.tetlet.2013.12.054>.
30
31
32 (64) Ács, P.; Müller, E.; Rangits, G.; Lóránd, T.; Kollár,
33
34 L. Palladium-Catalysed Carbonylation of 4-Substituted 2-
35
36 Iodoaniline Derivatives: Carbonylative Cyclisation and
37
38 Aminocarbonylation. *Tetrahedron* **2006**, *62*, 12051-12056.
39
40 <https://doi.org/10.1016/j.tet.2006.09.076>.
41
42
43 (65) Yao, F.; Hao, W.; Cai, M. Z. Copper(I)-Catalyzed
44
45 Tandem Reaction of 2-Iodophenols with Isothiocyanates in
46
47 Room Temperature Ionic Liquids. *J. Organomet. Chem.* **2013**,
48
49 *723*, 137-142.
50
51 <https://doi.org/10.1016/j.jorganchem.2012.09.010>.
52
53
54 (66) Rao, M. L. N.; Meka, S. Pd-Catalyzed Protecting-Group-

- 1
2
3 Free Cross-Couplings of Iodophenols with Atom-Economic
4
5 Triarylbismuth Reagents. *Tetrahedron Lett.* **2020**, *61*, 151512.
6
7 <https://doi.org/10.1016/j.tetlet.2019.151512>.
8
9
10 (67) Wang, Y.; Wang, M.; Han, L.; Zhao, Y.; Fan, A.
11
12 Enhancement Effect of P-Iodophenol on Gold Nanoparticle-
13
14 Catalyzed Chemiluminescence and Its Applications in
15
16 Detection of Thiols and Guanidine. *Talanta* **2018**, *182*, 523-
17
18 528. <https://doi.org/10.1016/j.talanta.2018.01.093>.
19
20
21 (68) Keshavarz, M. H.; Gharagheizi, F.; Shokrolahi, A.;
22
23 Zakinejad, S. Accurate Prediction of the Toxicity of Benzoic
24
25 Acid Compounds in Mice via Oral without Using Any Computer
26
27 Codes. *J. Hazard. Mater.* **2012**, *237-238*, 79-101.
28
29 <https://doi.org/10.1016/j.jhazmat.2012.07.048>.
30
31
32 (69) El-Athman, F.; Jekel, M.; Putschew, A. Reaction
33
34 Kinetics of Corrinoid-Mediated Deiodination of Iodinated X-
35
36 Ray Contrast Media and Other Iodinated Organic Compounds.
37
38 *Chemosphere* **2019**, *234*, 971-977.
39
40 <https://doi.org/10.1016/j.chemosphere.2019.06.135>.
41
42
43 (70) Xi, Y.; Yang, X.; Zhang, H.; Liu, H.; Watson, P.;
44
45 Yang, F. Binding Interactions of Halo-Benzoic Acids, Halo-
46
47 Benzenesulfonic Acids and Halo-Phenylboronic Acids with
48
49 Human Transthyretin. *Chemosphere* **2020**, *242*, 125135.
50
51 <https://doi.org/10.1016/j.chemosphere.2019.125135>.
52
53
54 (71) Muzikář, M.; Křesinová, Z.; Svobodová, K.; Filipová,
55
56
57
58
59
60

- 1
2
3 A.; Čvančarová, M.; Cajthamlová, K.; Cajthaml, T.
4
5 Biodegradation of Chlorobenzoic Acids by Ligninolytic Fungi.
6
7 *J. Hazard. Mater.* **2011**, *196*, 386–394.
8
9 <https://doi.org/10.1016/j.jhazmat.2011.09.041>.
10
11
12 (72) Zhang, Y.; Zheng, J. M. Three Ln(III)-2,3,5-
13
14 Trichlorobenzoate Coordination Polymers (Ln = Tb, Ho and
15
16 Er): Syntheses, Structures and Magnetic Properties. *Inorg.*
17
18 *Chem. Commun.* **2015**, *59*, 21–24.
19
20 <https://doi.org/10.1016/j.inoche.2015.06.018>.
21
22
23 (73) Mantina, M.; Chamberlin, A. C.; Valero, R.; Cramer, C.
24
25 J.; Truhlar, D. G. Consistent van Der Waals Radü for the
26
27 Whole Main Group. *J. Phys. Chem. A* **2009**, *113*, 5806–5812.
28
29 <https://doi.org/10.1021/jp8111556>.
30
31
32 (74) Politzer, P.; Murray, J. S.; Clark, T. Halogen Bonding
33
34 and Other σ -Hole Interactions: A Perspective. *Phys. Chem.*
35
36 *Chem. Phys.* **2013**, *15*, 11178–11189.
37
38 <https://doi.org/10.1039/c3cp00054k>.
39
40
41 (75) Perera, M. D.; Desper, J.; Sinha, A. S.; Aakeröy, C.
42
43 B. Impact and Importance of Electrostatic Potential
44
45 Calculations for Predicting Structural Patterns of Hydrogen
46
47 and Halogen Bonding. *CrystEngComm* **2016**, *18*, 8631–8636.
48
49 <https://doi.org/10.1039/c6ce02089e>.
50
51
52 (76) Kolář, M.; Hostaš, J.; Hobza, P. The Strength and
53
54 Directionality of a Halogen Bond Are Co-Determined by the
55
56
57
58
59
60

- Magnitude and Size of the σ -Hole. *Phys. Chem. Chem. Phys.* **2014**, *16*, 9987-9996. <https://doi.org/10.1039/c3cp55188a>.
- (77) Clark, T.; Hennemann, M.; Murray, J. S.; Politzer, P. Halogen Bonding: The σ -Hole. *J. Mol. Model.* **2007**, *13*, 291-296. <https://doi.org/10.1007/s00894-006-0130-2>.
- (78) Lim, J. Y. C.; Beer, P. D. Sigma-Hole Interactions in Anion Recognition. *Chem* **2018**, *4*, 731-783. <https://doi.org/https://doi.org/10.1016/j.chempr.2018.02.022>.
- (79) Adamo, C.; Barone, V. Toward Reliable Density Functional Methods without Adjustable Parameters: The PBE0 Model. *J. Chem. Phys.* **1999**, *110*, 6158-6170. <https://doi.org/10.1063/1.478522>.
- (80) Steinmetz, M.; Grimme, S. Benchmark Study of the Performance of Density Functional Theory for Bond Activations with (Ni,Pd)-Based Transition-Metal Catalysts. *ChemistryOpen* **2013**, *2*, 115-124. <https://doi.org/10.1002/open.201300012>.
- (81) Schäfer, A.; Huber, C.; Ahlrichs, R. Fully Optimized Contracted Gaussian Basis Sets of Triple Zeta Valence Quality for Atoms Li to Kr. *J. Chem. Phys.* **1994**, *100*, 5829-5835. <https://doi.org/10.1063/1.467146>.
- (82) Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Scalmani,

1
2
3 G.; Barone, V.; Mennucci, B.; Petersson, G. A.; Nakatsuji,
4
5 H.; Caricato, M.; Li, X.; Hratchian, H. P.; Izmaylov, A. F.;
6
7 Bloino, J.; Zheng, G.; Sonnenb, J.; Fox, D. J. *Gaussian 09*,
8
9 *Revision C.01*; Gaussian, Inc., Wallingford CT, 2009.

10
11
12 (83) Bader, R. F. W. *Atoms in Molecules: A Quantum Theory*;
13
14 Clarendon Press: Oxford, 1990.

15
16
17 (84) Keith, T. A. *AIMAll (Version 12.06.03)*; TK Gristmill
18
19 Software, Overland Park KS, USA, 2012 (aim.tkgristmill.com).

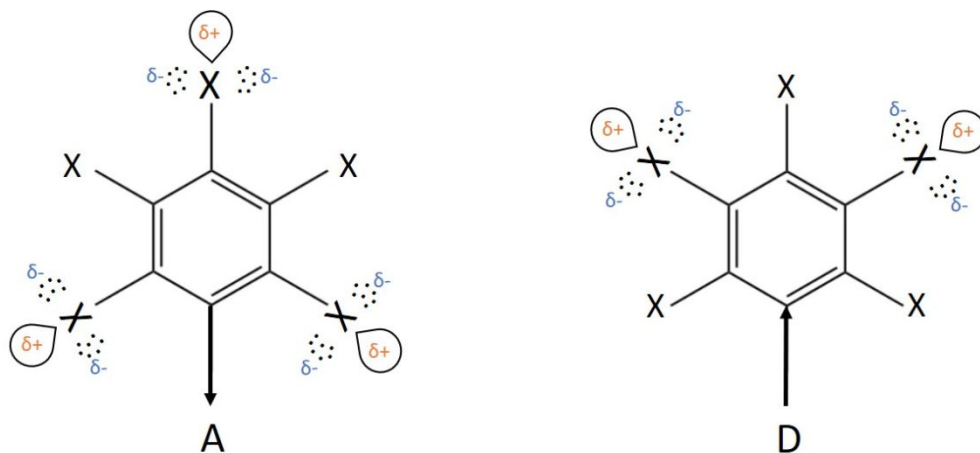
20
21 (85) Bader, R. F. W.; Carroll, M. T.; Cheeseman, J. R.;
22
23 Chang, C. Properties of Atoms in Molecules: Atomic Volumes.
24
25 *J. Am. Chem. Soc.* **1987**, *109*, 7968–7979.
26
27 <https://doi.org/10.1021/ja00260a006>.
28
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48 **Manuscript title:** Influence of substituents in aromatic ring on
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50 the strength of halogen bonding in iodobenzene derivatives
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5 Matti Haukka*

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10 **TOC graphic:**



27 where X = I or H, A = electron acceptor (-COOH, -CN), D = electron donor (-OH, -NH₂, -OCH₃)

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47 **Synopsis:**

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50 Structural and computational MEP analyses of 3,4,5-triiodobenzoic
51 acid (**1**, **2**), 1,2,3-triiodobenzene (**3**), 4-iodobenzoic acid (**4**),
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53 pentaiodobenzoic acid ethanol solvate (**5**), hexaiodobenzene (**6a**,
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3 **6b, 6c**), 4-iodobenzonitrile (**7**), 3-iodobenzonitrile (**8**), 2,4-
4 diiodoaniline (**9**), 4-iodoaniline (**10**), 2-iodoaniline (**11**), 2-
5 iodophenol (**12**), 4-iodophenol (**13**), 3-iodophenol (**14**), 2,4,6-
6 triiodophenol (**15**), 4-iodoanisole (**16**), 3,4,5-triiodoanisole (**17**)
7
8 have been conducted. The results show that the mesomeric effect of
9
10 the substituents other than halogen in the benzene ring has an
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12 impact on the XB donor-acceptor properties of the iodide
13
14 substituents in *ortho*-, *meta*- and *para*-positions. Thus, electron-
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16 withdrawing (EWG) substituents with negative mesomeric effect,
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18 e.g. carboxyl -COOH and nitrile -CN, favor iodines in *ortho*- and
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20 *para*-positions to act as halogen bond donors. On the other hand,
21
22 electron-donating (EDG) substituents, like amino -NH₂, hydroxy -
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24 OH and methoxy -OCH₃ groups, which reveal positive mesomeric
25
26 effect, increase the ability of *meta*-iodines to act as halogen
27
28 bond donors. Furthermore, EWG and EDG substituents with stronger
29
30 mesomeric effect make a higher impact on the XB donor ability of
31
32 the iodide substituents. Such correlation is reflected in the size
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34 of the σ -hole on the iodine atoms. Thus, the sigma-holes on *o*- and
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36 *p*-iodine atoms are bigger than on *m*-iodine atoms in the presence
37
38 of EWG, making *o*- and *p*-iodines favorable XB donors. Similarly,
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40 the size of the sigma-hole on *m*-iodines is being larger than the
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42 ones on the *o*- and *p*-iodines in the presence of EDG, making *m*-
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44 iodines to favor XB donor behavior. This is confirmed by our MEP
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46 calculations, in which the size of the σ -hole is expressed by the
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3 value of maximum electrostatic potential ($V_{s,max}$), being maximum in
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5 the case of strong EWG substituents and minimum in the case of
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7 strong EDG substituents.
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