

## Halogen bonds involving pentafluoriodobenzene: Answers from experimental electron density

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# Halogen Bonds

Halogen bonds recently experienced an increased interest in various fields of crystallography and biochemistry.[1,2] They denote an attractive interaction between a nucleophile or nucleophilic region

(electron donor) and an electrophilic region located at a halogen atom.[3] The electrophilic regions originate from an anisotropic distribution of the electron density at the halogen atom in the presence of a sufficient nucleophile. It forms a region of depleted electron density (ED), the so-called sigma hole, at the elongation of the covalent bond.

For decades, experimental diffraction data could only be used to obtain information about geometrical structures. With the recent improvements of X-ray devices, high resolution data was becoming available and thus the possibility to receive information about electron density directly from the diffraction data.[4]



Schematic presentation of halogen bond.  
R: molecular rest covalent bound to X,  
X: covalent bonding partner, D: electron donor

[1] P. Metrangolo, G. Resnati, *Cryst Growth Des.* **2012**, *12*, 5835–5838

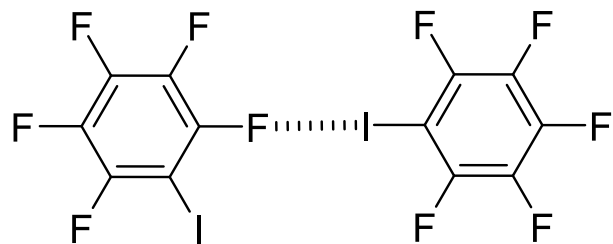
[2] R. Wilcken, M.O. Zimmermann, *J Med Chem.* **2013**, *56*, 1363–1388

[3] G. Cavallo, P. Metrangolo, *Chem. Rev.* **2016**, *116*, 2478–2601

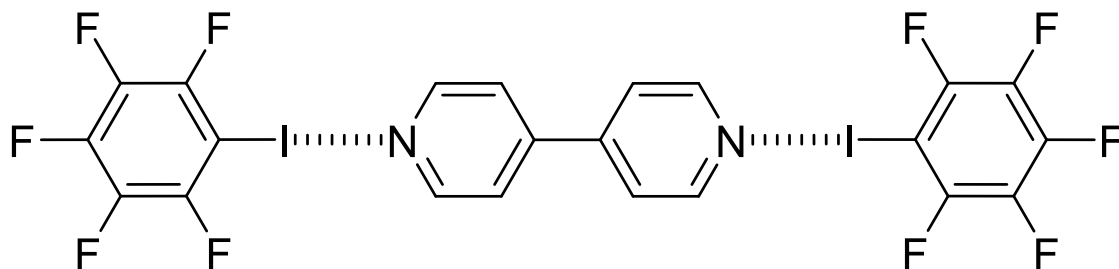
[4] R. Wang, T. S. Dols, *Anorg. All. Chem.* **2013**, *639 (11)*, 1933–1939

# Structures

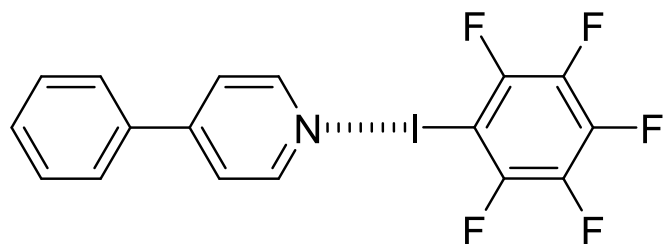
The presented structures are composed of an pentafluoroiodobenzene either solely (structure 1) or in combination with pyridine derivatives (2-4).



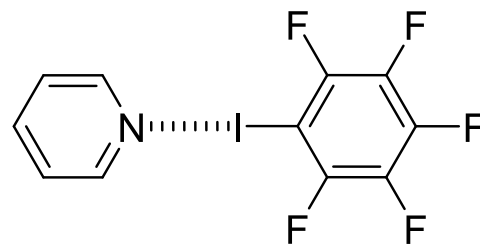
Structure 1:  
pentafluoroiodobenzene



Structure 4:  
pentafluoroiodobenzene, 4,4'-Bipyridine



Structure 2:  
pentafluoroiodobenzene, 4-Phenylpyridine



Structure 3:  
pentafluoroiodobenzene, Pyridine

# Geometrical Analysis

The high resolved diffraction data was analyzed *via* the Multipole Model of Hansen-Coppens.[5] The table shows the halogen and additional short contacts and the corresponding bond critical points (3, -1).

Table 1: Geometrical Results

Structure	Bond	dist.(Å)	$R_{ij}$ (Å)	$d_1$ (Å)	$d_2$ (Å)
<b>1</b>	I2...F1	3.0718(5)	3.0724	1.7478	1.3245
	F3...F7 <sup>a</sup>	2.7759(8)	2.7761	1.3726	1.4035
	F4...F6 <sup>c</sup>	2.8627(8)	2.8636	1.4434	1.4203
<b>2</b>	I1...N1	2.8010(4)	2.8017	1.5152	1.2864
	H14...F4 <sup>d</sup>	2.50	2.5334	1.0962	1.4371
	H20...F3 <sup>d</sup>	2.46	2.6713	1.4541	1.2172
	H18...I1 <sup>a</sup>	3.12	3.1602	2.0040	1.1563
<b>3</b>	I1...N1	2.7374(5)	2.7374	1.4741	1.2633
	F2...H12 <sup>c</sup>	2.66	2.7108	1.5440	1.1669
	F3...H15 <sup>b</sup>	2.67	2.7138	1.5516	1.1622
	F4...H12 <sup>a</sup>	2.62	2.6821	1.5108	1.1713
<b>4</b>	I1...N1	2.7866(8)	2.7869	1.5103	1.2766

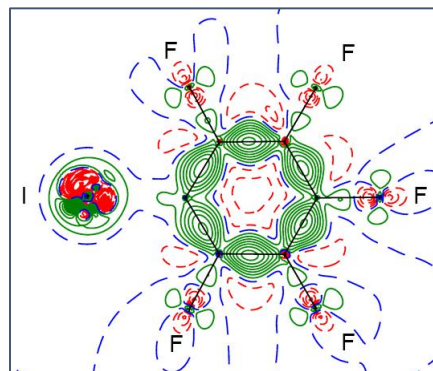
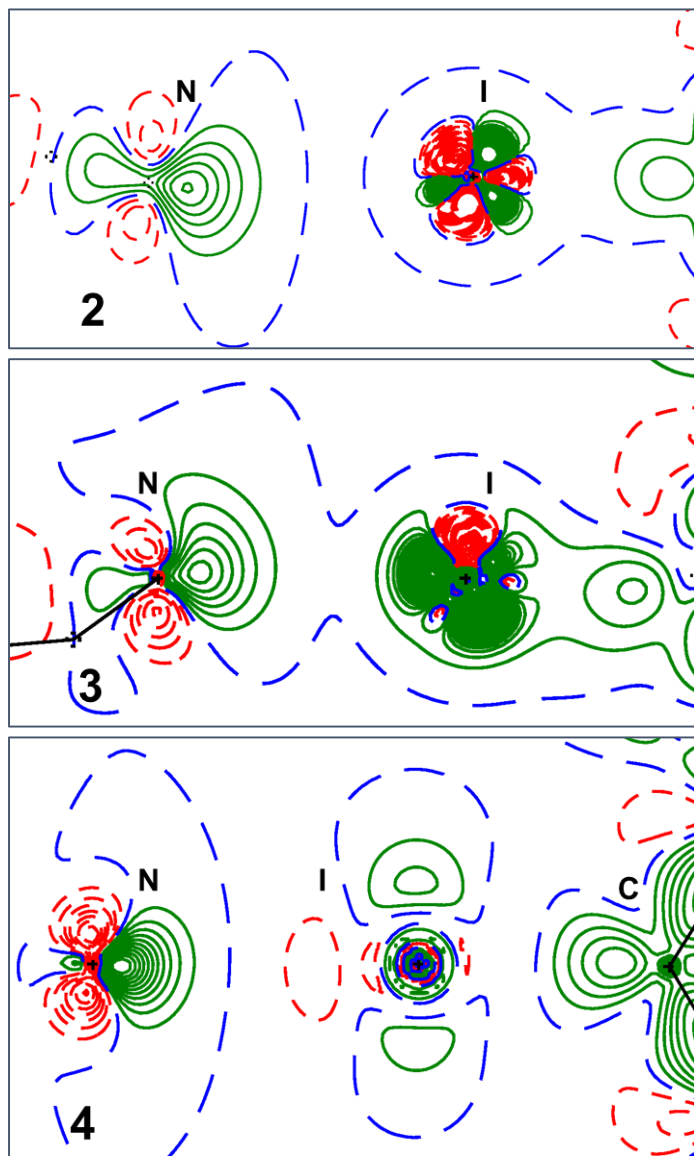
$a = +x, +y, +z$ ;  $b = -x, -y, -z$ ;  $c = 1/2 - x, 1/2 + y, 1/2 - z$ ;

$d = 1/2 + x, 1/2 - y, 1/2 + z$ ;

$d_1$  ( $d_2$ ): distance from the 1. (2.) atom to the (3, -1) critical point,

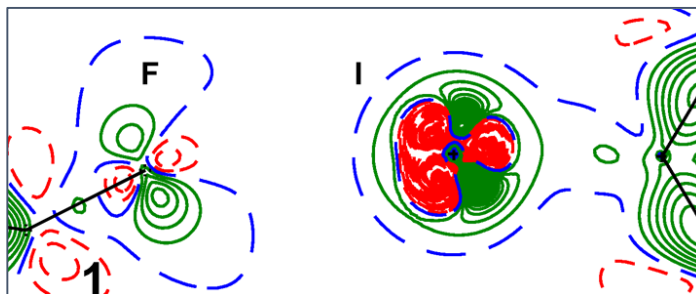
$R_{ij} = d_1 + d_2$

# Deformation Density



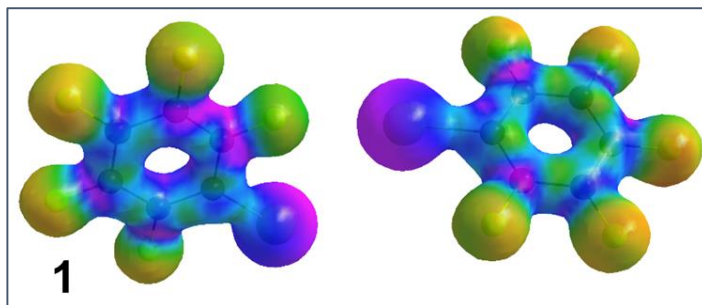
Deformation densities (contour lines drawn at  $\rho = 0.5 \text{ e}\text{\AA}^{-3}$ ; (MoleCoolQt; Huebschle & Dittrich, 2011) of the halogen bonds of 2-4 (left) and 1 (bottom) and of the pentafluoriodobenzene (top). The colors denote negative (red) and positive (green) electron densities relative to the Independent Atom Modell (IAM).

The deformation densities of structures 2 and 3 show a rather atypical shape for a halogen bond, where the ED relative to the IAM is symmetrically distributed around the halogen atom. Solely structure 4 expresses the typical deformation of the ED and a single zero line between the iodine and the nitrogen atom. Structure 1 shows a halogen bond between fluorine and iodine, where the fluorine expresses the typical ED distribution with less density pointing toward the bond direction.

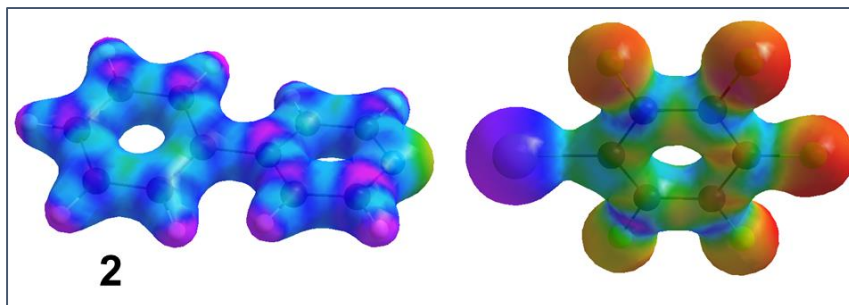




# Electrostatic potential

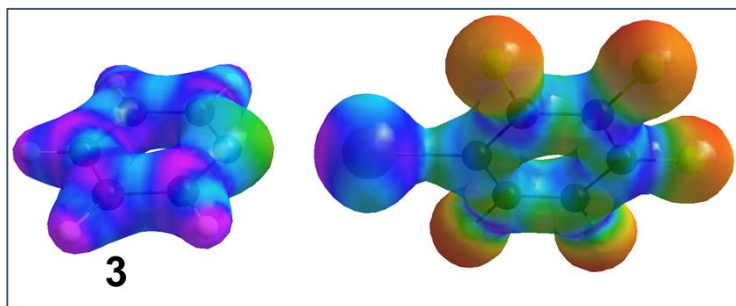


The electrostatic potential (ESP) of structures 2-4 show a pronounced negative polarization of the nitrogen atom towards the iodine.

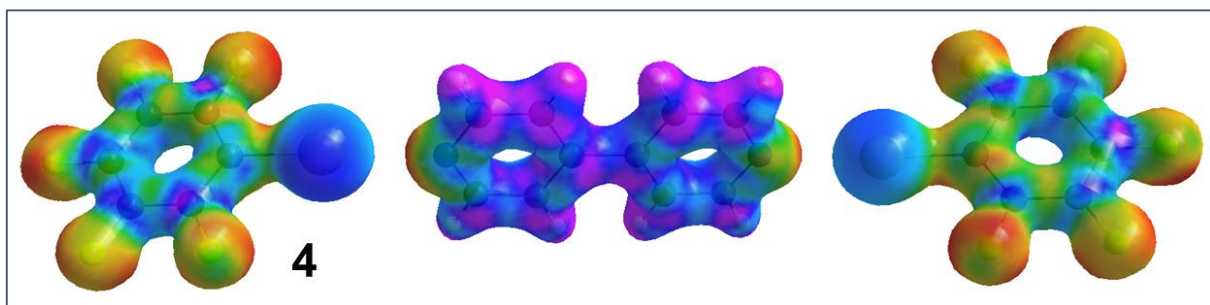


The halogen on the other hand expresses an overall homogenous and spherical ESP. Only structure 4 shows the typical aspherical shape and the positive polarization of the ESP in bonding direction, the sigma hole.

Electrostatic potential mapped on an isosurface of electron density  $\rho = 0.5 \text{ e}\text{\AA}^{-3}$  (*MoleCoolQt*; Huebschle & Dittrich, 2011).



The ESP of structure 1 does also not show the typical properties of a halogen bond, which could be due to the reduced strength compared to the nitrogen donor.



# Topological Analysis

The table shows the topological properties of halogen bond and other interactions on their bond critical point (3, -1).

Table 2: Topological Results

Structure	Bond	$\rho(e\cdot\text{\AA}^{-3})$	$\nabla^2\rho(e\cdot\text{\AA}^{-5})$	$G(a.u.)$	$\frac{G}{\rho}(a.u.)$	$V(a.u.)$	$E(a.u.)$
<b>1</b>	I2...F1	0.081(2)	1.063(2)	0.0092	0.76	-0.0073	0.0019
	F3...F7 <sup>a</sup>	0.059(2)	0.958(2)	0.0077	0.88	-0.0054	0.0022
	F4...F6 <sup>c</sup>	0.046(2)	0.846(2)	0.0066	0.96	-0.0043	0.0022
<b>2</b>	I1...N1	0.213(3)	1.998(2)	0.0229	0.72	-0.0250	-0.0021
	H14...F4 <sup>d</sup>	0.046(2)	0.677(2)	0.0054	0.79	-0.0037	0.0016
	H20...F3 <sup>d</sup>	0.044(2)	0.613(2)	0.0049	0.75	-0.0034	0.0015
	H18...I1 <sup>a</sup>	0.040(2)	0.407(2)	0.0034	0.57	-0.0025	0.0009
<b>3</b>	I1...N1	0.208(5)	1.845(6)	0.0214	0.70	-0.0238	-0.0023
	F2...H12 <sup>c</sup>	0.027(2)	0.416(2)	0.0032	0.79	-0.0020	0.0011
	F3...H15 <sup>b</sup>	0.027(2)	0.411(2)	0.0031	0.78	-0.0020	0.0011
	F4...H12 <sup>a</sup>	0.033(2)	0.480(2)	0.0037	0.76	-0.0025	0.0013
<b>4</b>	I1...N1	0.229(8)	2.245(7)	0.0257	0.76	-0.0282	-0.0024

$a = +x, +y, +z$ ;  $b = -x, -y, -z$ ;  $c = 1/2 - x, 1/2 + y, 1/2 - z$ ;

$d = 1/2 + x, 1/2 - y, 1/2 + z$ ;

$\rho$ : Electron density,

$\nabla^2\rho$ : Laplacian of the electron density.

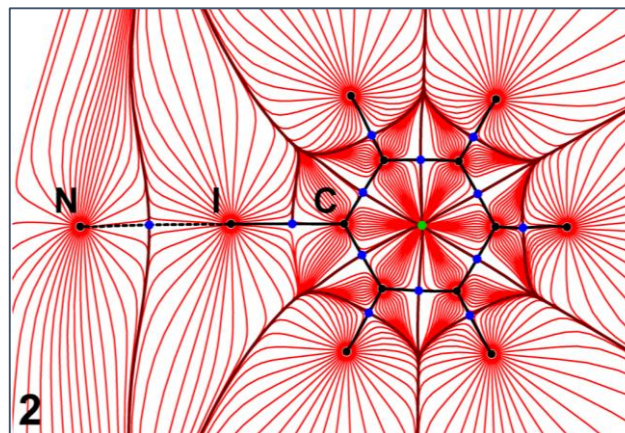
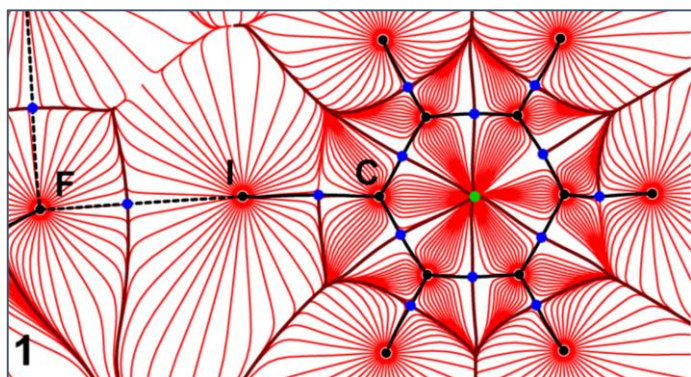
$G$ : Kinetic energy density,

$\frac{G}{\rho}$ : Ratio between kinetic energy density and electron density,

$V$ : Potential energy density

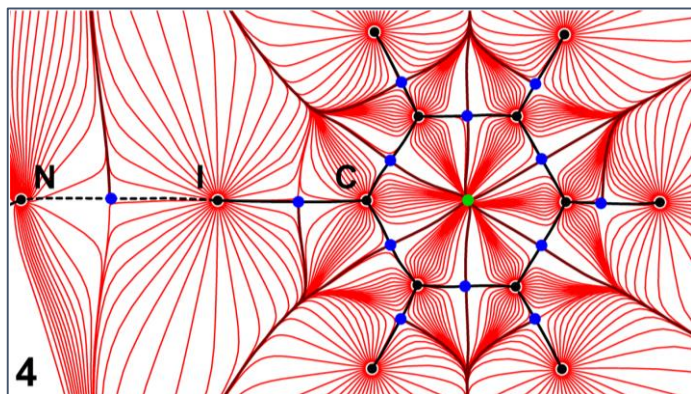
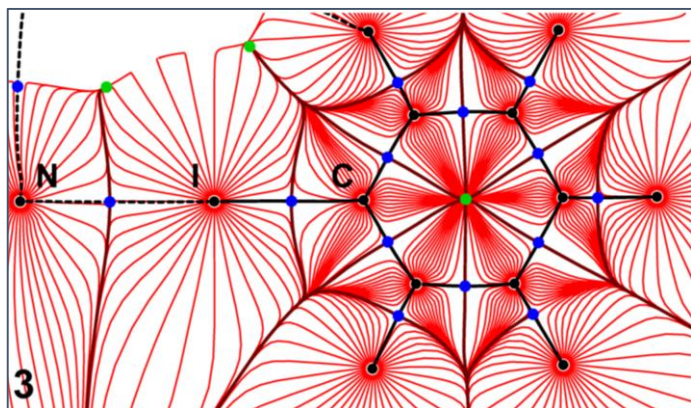
$E$ : Total energy density

# Topological Analysis



Gradient vector field of the electron density of the halogen bonds (2-4) and pentafluoroiodobenzene (1). The bond paths are displayed with black lines (solid: covalent, dashed: non-covalent interaction) and the BCP is marked with a blue dot.

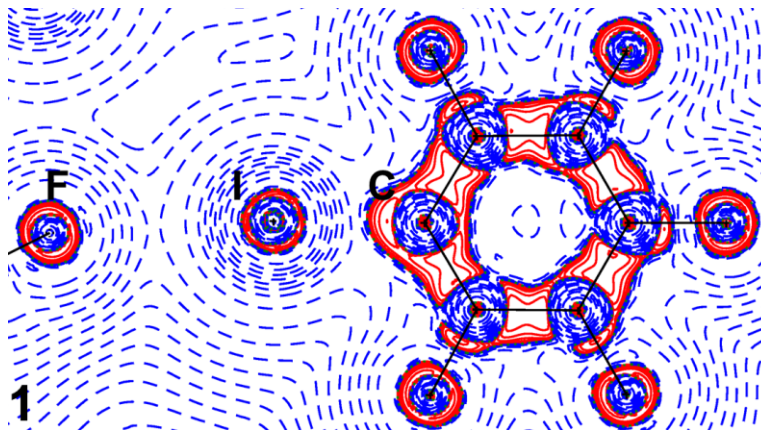
The gradient field of all pentafluoroiodobenzene structures is highly symmetrical. The bond critical point (BCP) lies closer to the nitrogen or fluorine atom. The bond path of all halogen bonds is approximately straight. Considering the electron densities in the bond critical points (Table 2), the halogen bonds between nitrogen and iodine show a significantly higher value implying a stronger bond character than fluorine. This statement is encouraged by the less straight bond path of structure 1.



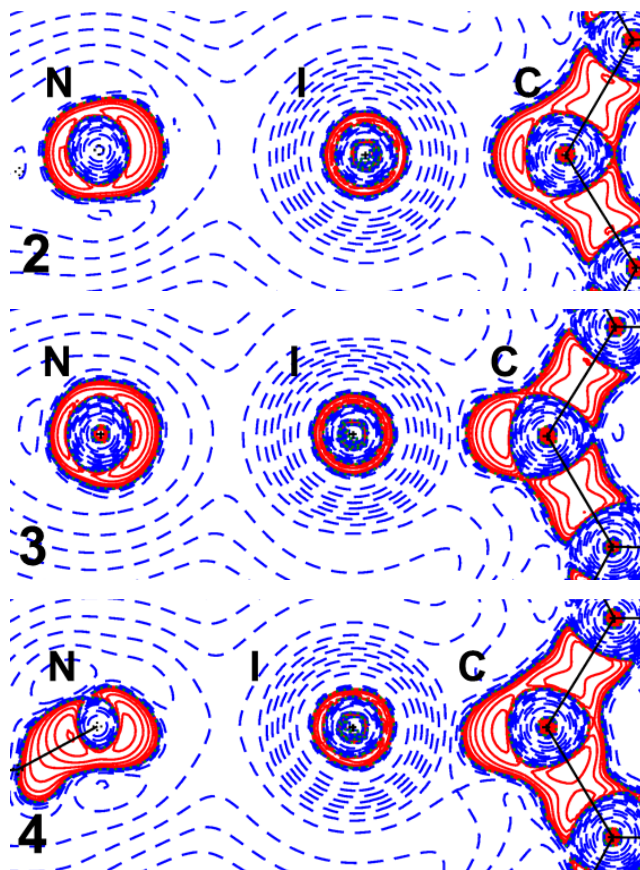


# Laplacian

Laplacian of the electron density at the halogen bond (2-4) and the pentafluoriodobenzene (1). Positive values are shown in blue, negative ones in red, contours at  $\pm 2^n \cdot 10^{-3} \text{ e}\text{\AA}^{-5}$ .



The Laplacian of the electron density displays regions of concentrated (negative Laplacian) or depleted (positive Laplacian) electron density.



Around the iodine atom of all structures the Laplacian has a symmetrical shape and therefore does not express the typical deformation of a halogen bond, that would show two small regions of concentrated ED perpendicular to the halogen bond. However, all structures show a region of depleted electron density in the bonding region, indicating a stronger non-covalent than covalent character, as is expected for the electrostatic character of a halogen bond.

$$L = -\nabla^2 \rho = - \left[ \frac{\partial^2 \rho}{\partial x^2} + \frac{\partial^2 \rho}{\partial y^2} + \frac{\partial^2 \rho}{\partial z^2} \right]$$

$L$ : Negative of the Laplacian  
 $\rho$ : Electron density  
 $x, y, z$ : Room coordinates

# Conclusion

Four crystal structures containing an iodine involved in a halogen bond were measured in high-resolution diffraction experiments, processed in a multipole refinement and analyzed *via* the Atom in Molecule (AIM) approach. The strongest bonds were found for the systems with nitrogen, but also a halogen bond between fluorine and iodine can be found in **1**. The topological analysis does not show the typical properties of a halogen bond, except for the asymmetrical distribution of the electrostatic potential in **4**. On the other hand, the straight alignment of the bonding partners, as well as the depleted electron density in the bonding area and the higher electrostatic potential of the nitrogen site facing the iodine are typical features of a halogen bond. In general, even though halogen bonds are known for several years, detailed properties were only analyzed recently as the experimental and computational conditions improved. Furthermore, halogen bonds involving iodine were only poorly researched experimentally up to now, so the actual properties of the systems are yet to be determined.