Categorizing Halogen Bonding and Other Noncovalent Interactions Involving Halogen Atoms

The purpose of this two-year project is to take a comprehensive look at intermolecular interactions involving halogens as electrophilic species, and to classify them. The electron density around the halogen nucleus is highly anisotropic so that halogens can serve both as electron-acceptors and donors.[1]

While the task group acknowledges that the terminology used to name noncovalent interactions given by halogen atoms has to be as unifying as possible, it is the group's opinion it has always to be in keeping with the electrophile/nucleophile role the halogen atom plays.

First descriptions of systems involving halogen atoms as electrophilic "sticky" sites in self-organisation processes can be traced back to the mid-nineteenth century, when NH_3•I_2 and pyridine•alkyl iodides adducts were isolated.[2] About 60 years ago, Benesi and Hildebrand published their seminal work describing the distinct spectral (UV-Vis) changes that accompany the spontaneous complexation of various aromatic hydrocarbons with I_2 in nonpolar solvents such as CCl_4, C_6H_{14}, etc.[3] Shortly thereafter, these studies were extended to include Br_2, Cl_2, and interhalogens,[4,5] and provided experimental basis for the development of Mulliken's theory of charge-transfer complexes.[6] About the same time, X-ray crystallographic measurements of Br_2 complexes with dioxane and benzene reported by Hassel and co-workers provided evidence that these intermolecular complexes involve close contacts between electron-donor and acceptor molecules (with interatomic separation significantly shorter than the sum of their van der Waals radii).[7] In his 1970 Nobel lecture, Hassel unequivocally stressed the importance of intermolecular interactions involving halogen atoms as electrophilic species for directing molecular self-assembly phenomena.[8]

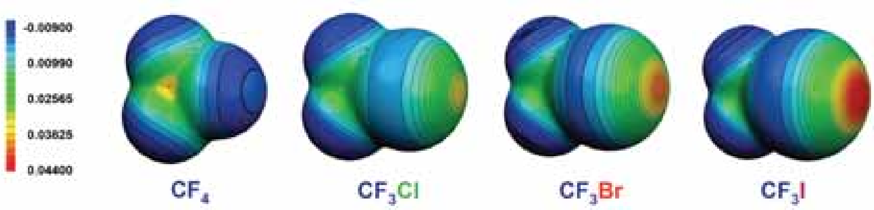
The term *halogen bonding* has been introduced for describing any noncovalent interaction involving halogens as acceptors of electron density.[9] The general scheme D•••X-Y thus applies to halogen bonding (XB), wherein X is the halogen (Lewis acid, XB-donor), D is any electron-donor (Lewis base, XB-acceptor), and Y is carbon, halogen, nitrogen, etc.[10] The term *halogen bonding* itself sheds light on the nature of XB, which possesses numerous similarities with hydrogen bonding (HB), wherein hydrogen functions as the acceptor of electron density.

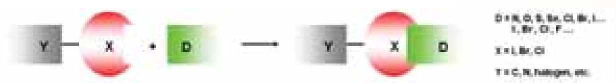
In our opinion, the use of the term *halogen bonding* has to be limited to those interactions wherein halogens function as acceptors of electron density. Use of this term to address interactions in which halogen atoms function as electron-donors is conceptually misleading and contrasts with the clear tendency, well-documented in the literature, to differently name interactions such as -H•••X-Y (typically named hydrogen bonds).

This project will attempt to give a modern definition of *halogen bonding* that is as inclusive as possible, and takes into account all current experimental and theoretical pieces of information on both gaseous and condensed halogen-bonded systems in chemical and biological systems. After a reviewing process, the definition will eventually be submitted as Recommendations for *Pure and Applied Chemistry*, and will hopefully be included in the *IUPAC Gold Book*.

The whole community of researchers dealing with the study and use of intermolecular interactions will be called to be involved in this project. A dedicated website <www.halogenbonding.eu> will be set up as a public discussion forum for consideration of public comments. The project will be advertised in major meetings relevant to related fields (e.g. the 26th European Crystallography Meeting in Darmstadt, 29 August–2 September 2010 and the XXII General Assembly and Congress of the International Union of Crystallography (IUCr) to be held in Madrid, Spain, 22–29 August 2011). In the second year of the project, an international symposium open to the public will be organized for consideration of public comments, presentation, and dissemination of results.

The kick-off meeting of the project will be organized in Milan next 7 May 2010, where the Politecnico di Milano will host the 2nd International Workshop on Halogen Bonding.





The members of the task group are all leaders in their respective fields: Gautam R. Desiraju, Bangalore, India (supramolecular chemistry); Pui Shing Ho, Colorado, US (biophysical chemistry); Lars Kloo, Stockholm, Sweden (inorganic chemistry); Anthony C. Legon, Bristol, UK (physical chemistry); Roberto Marquardt, Strasbourg, France (quantum chemistry); Pierangelo Metrangolo, Milan, Italy (materials chemistry); Peter Politzer, Ohio, US (theoretical chemistry); Giuseppe Resnati, Milan, Italy (organic chemistry); and Kari Rissanen, Jyväskylä, Finland (structural chemistry).

References

1. T. Clark, M. Hennemann, J. S. Murray, P. Politzer. *J. Mol. Model*. **13**, 291 (2007).
2. F. Guthrie. *Chem. Soc.* **16,** 239 (1863); A. B. Prescott. Pyridine alkyl iodides. *J. Am. Chem. Soc.* **18**, 91 (1896).
3. H. A. Benesi, J. H. Hildebrand. A spectrophotometric investigation of the interaction of iodine with aromatic hydrocarbons. *J. Am. Chem. Soc*. **71**, 2703 (1949).
4. R. M. Keefer, L. J. Andrews. The interaction of bromine with benzene and certain of its derivatives. *J. Am. Chem. Soc.* **72**, 4677 (1950).
5. L. J. Andrews, R. M. Keefer. *Molecular complexes in organic chemistry.* Holden-Day San-Francisco Holden-Day, 1964.
6. (a) R. S. Mulliken. Molecular compounds and their spectra. *J. Am. Chem. Soc.* **74**, 811 (1952). (b) R. S. Mulliken, W. B. Person. *Molecular Complexes. A Lecture and Reprint Volume.* New York: Wiley, 1969.
7. (a) O. Hassel, K. O. Stromme. Halogen-molecule bridges in solid addition compounds. *Nature* **182**, 1155 (1958). (b) ibid. Structure of the crystalline compound benzene-bromine (1:1). *Acta Chem. Scand*. **12**, 1146 (1958).
8. O. Hassel. Structural aspects of interatomic charge-transfer bonding. *Science* **170**, 497 (1970).
9. P. Metrangolo, G. Resnati. Halogen versus Hydrogen. *Science* **321**, 918 (2008).
10. P. Metrangolo, F. Meyer, T. Pilati, G. Resnati, G. Terranno. Halogen bonding in supramolecular chemistry. *Angew. Chem. Int. Ed*, **47**, 6114 (2008).

For more information and comments, contact Task Group Chairs Pierangelo Metrangolo <pierangelo.metrangolo@polimi.it> and Giuseppe Resnati <giuseppe.resnati@polimi.it>.

www.iupac.org/web/ins/2009-032-1-100

Risk Assessment of Effects of Cadmium on Human Health

Cadmium is a metal that occurs generally in low concentrations of various chemical species in the ecosystem, with high concentrations in some areas. Dispersion into the environment occurs from multiple sources including inadequate disposal of electronic waste. Sources in industrialized countries have been better controlled recently, but in many areas exposures exceed those that occurred before industrialization.

Cadmium accumulates in humans because of its very long biological half time in human tissues, particularly in the kidneys (10–30 years). In high exposure areas in Japan a clinical disease—Itai-itai disease—occurs. This disease is characterized by multiple fractures of bones, and damaged kidneys. Recent epidemiological studies have reported less severe cadmium-related effects on kidneys and bones among humans exposed to cadmium species in the environment of countries such as China, Belgium, Sweden, UK, and USA, sometimes in areas without obvious excessive exposure. Subgroups such as diabetics may be particularly affected. Cadmium is classified as carcinogenic to humans by the International Agency for Research on Cancer, based on studies of occupational exposures. A few recent publications have reported such effects following environmental exposures.

It is important to consider all published information in a risk assessment of the effects on human health from cadmium species. This is the task of the present project. The European Food Safety Authority (EFSA) has recently reviewed cadmium. Their report will prove valuable, but only considers exposure through food. Likewise, a report from the Joint Expert Committee on Food Additives (JECFA) is due in June 2010, and will be available to the task group by the time of its second working meeting.

Task group members will compile and evaluate all relevant literature, and write a manuscript for publication in *PAC*. Focus will be on health risks related to cadmium exposure at low level exposures. References will be made to existing risk assessment documents from WHO/IPCS, WHO/FAO/JECFA, ATSDR, USEPA, EU-RAR, EFSA, and others. The Chemistry and Human Health Division can provide guidance on risk assessment methodology and, as appropriate, provide assessments of risks to human health from chemicals of exceptional toxicity. This project should provide a model for such activities conforming to current best practice.

For more information and comments, contact Task Group Chair Gunnar F. Nordberg <gunnar.nordberg@envmed.umu.se>.

www.iupac.org/web/ins/2009-034-2-700