Title: **Selected examples of halogen bonding in catalysis.**

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This research work aims to provide a general vision about the use of halogen bonding (XB) in catalysis, with selected examples of the use of this supramolecular interaction found in the literature having been summarized. This non-conventional weak interaction has been attracting increasing attention since its discovery and description, due to a gradual better understanding of its nature, and it represents an innovative and promising tool to incorporate to the existing toolbox in supramolecular catalysis.

Since its serendipitous discovery in 1814 by Jean-Jacques Colin when mixing ammonia with iodine, halogen bonding has attracted lots of attention, mainly from the mid-90s, in the areas of crystal engineering, polymer science and medicinal chemistry. As referred to its chemistry in solution, halogen bonding has been mainly studied in molecular recognition and self-assembly processes, although in the last years applications of halogen bonding in catalysis have been reported.

Halogen bonding involves the interaction of the σ-hole, or lower electron density area in the electrostatic potential surface of a halogen atom (due to the anisotropically distributed electron density on the halogen surface) with the nucleophilic region of another atom (see Figure 1A). In the halogen bonding process, the halogen compound involved is referred to as the halogen bond donor (electron acceptor), and the compound with an electron rich motif (Y) is referred to as halogen bond acceptor (electron donor). Halogen bonding is not a purely electrostatic process, but also involves orbitalic interactions between the lone pair of the halogen bond acceptor and a σ antibonding molecular orbital of the halogen bond donor (see Figure 1C). The relative contributions of electrostatic and covalent factors to halogen bonding depend on the nature of the halogen bond donor and acceptor groups.

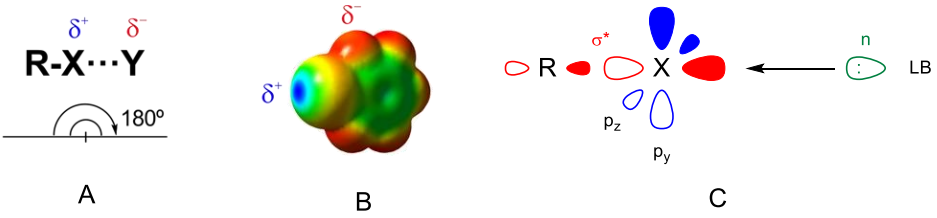

Figure 1. A) Halogen bonding representation between a halogen (X) and another atom (Y). B) Electrostatic model (with the σ-hole in blue) of the surface of 1,2,3,4,5-pentafluoro-6-iodobenzene. C) Orbitalic representation of the halogen bonding.

The strength of the halogen bonds increases as the electron-withdrawing nature of the atom, or moiety, bound to a given halogen increases. The strength of halogen bonding involving the same halogen bond acceptor follows the following trend C(sp)-X > C(sp^2)-X > C(sp^3)-X, with haloalkynes being particularly good halogen bond donors.

The acceptable strength of halogen bonding, its high directionality, the possibility to create diverse 1D-, 2D- and 3D-architectures, its non-pronounced dependence with the character of the solvent and its sensitivity to the steric effects produced by the environment has prompted chemists to use halogen bonding in a number of ways in supramolecular catalysis.

The following roles of halogen bonding in catalysis have been found in the literature, and selected examples for each of them are discussed in this document:

1. Activation of reactants containing halogen bond-motifs by catalysts containing complementary halogen bond motifs.
2. Substrate preorganization or orientation induced by halogen bonding.
3. Handling or separation of reagents or catalysts.
4. Construction of the skeleton of the transition-metal based catalyst.

Keywords: Halogen bond, σ-hole, acceptor, donor, supramolecular catalysis, organocatalysis, catalysis, activation, preorganization, handling, separation, construction.