Tracing iodine

Pierangelo Metrangolo and **Giuseppe Resnati** celebrate the bicentenary of the discovery of iodine — a good time to also bring to its conclusion an international project that aims to define and categorize halogen bonding.

Two hundred years ago, the French chemist Bernard Courtois accidentally discovered iodine while investigating the corrosion of his copper vessels. Shortly after that, Humphrey Davy and Louis-Joseph Gay-Lussac independently identified it as a new element, and in 1813 Gay-Lussac named it after the Greek word *ιώδης* meaning violet. A year later, again in the Gay-Lussac laboratory, the first non-covalent adduct of iodine was prepared on reaction with ammonia — but it was only in 1863 that it was assigned the structure $I_2\cdots NH_3$ (ref. 1).

A number of adducts featuring similar attractive interactions with electron-donor species have marked the history of iodine. For example, the observation of $I_2\cdots$aromatic compound complexes made for a key contribution in the understanding of donor–acceptor adducts[2]. More recently, the development of dye-sensitized solar cells technology has relied on the I^-/I_3^- couple — the preferred redox mediator since these cells were first prepared, and still the one that yields the most stable and efficient devices[3].

Such non-covalent attractive interactions between the electropositive region of a covalently bonded halogen atom (including I_2) and the electronegative region of an atom or group of atoms (such as ammonia, aromatics, or I^- ions) are now interpreted in terms of halogen bonding. Iodine and its derivatives are the most prone to forming such bonds, and it is thus an interesting twist of fate that an IUPAC project aimed at delivering the first general definition of the halogen bond[4,5] should come to an end in the year of the bicentenary of the discovery of iodine.

The structural diversity of iodine-containing species is particularly noteworthy, and those are involved in a wide variety of fields ranging from materials science to biomedicine. Iodo aromatic compounds, for example, serve

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as radiocontrast agents in X-ray-imaging techniques; tincture of iodine, a common disinfectant, is a 2–7% solution of iodine along with iodide salts — the iodides form the halogen-bonded ion I_3^-, which is more soluble than elemental iodine in this ethanol–water mixture.

Iodine is essential to living organisms as a trace element. The human body typically contains 10–20 milligrams of iodine, more than 90% of which is stored in the thyroid gland. It is used for the biosynthesis of the thyroid hormone T3 (a tri-iodo-thyrosine) and pro-hormone T4 (its tetra-iodo- analogue) — both iodo-organic biomolecules relying on halogen bonding[6]. A very complex enzymatic system protects tissues from an excess of thyroid hormones through a series of iodination/de-iodination reactions — the O···I halogen bonds occurring makes these reactions extremely substrate-selective. For the metabolic functions controlled by T3 and T4 to be carried out, it is particularly important that iodine is ingested — a lack of dietary iodine can cause mental diseases or goitre.

The thyroid hormones are far from being the only iodinated biomolecules. At present, approximately 120 have been isolated from living organisms — including microorganisms, algae, marine invertebrates and higher animals. Their origin, possible biological activity and significance have been discussed in more than 80,000 original articles published in the past 60 years, according to the US National Library of Medicine.

The reactivity of iodine and its derivatives has also impacted synthetic and structural chemistry. In the past 10 years, the number of studies on polyvalent iodine compounds has increased dramatically. This surge in interest is mainly due to the combination of their very useful oxidizing properties with a benign environmental character and their commercial availability. For example, chiral hypervalent iodine compounds have recently proved effective for enantioselective oxidative coupling in asymmetric catalysis[7]. Crystal structures reported in the Cambridge Structure Database that involve iodo-carbons have also more than tripled in the past decade, including widely used species such as antimicrobial agents and the antifungal drug haloprogin.

Despite its 200 years of history, iodine is still very much part of recent developments in diverse areas of chemistry, and there is little doubt that it will continue to attract attention in the forthcoming decades. On this anniversary, we wish iodine many more years of success. ❐

References

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