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OVERVIEW

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1.1 INTRODUCTION

To the best of our knowledge, there was no book that focused on iodine chemistry and application.[1] This book will cover all of the areas related to iodine in their entirety. Therefore, it is expected to be a useful guide for both academic and industrial chemists who want to synthesize complex compounds or develop new materials by using iodine reagents or intermediates. The book consists of the following parts.

Part 1: Characteristics, elemental of iodine
Part 2: Production of iodine
Part 3: Synthesis of iodine compounds
Part 4: Biological application of iodine
Part 5: Industrial application of iodine
Part 6: Bioinorganic chemistry and environmental chemistry of iodine
Part 7: Radioisotope of iodine

[1] The books dealing with the biological activity of iodine [1] and the development of new reactions using variously hypervalent iodine as catalysts [2, 3] partially involve iodine chemistry and applications, while none of them cover the whole area of iodine chemistry.

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1.2 DISCOVERY AND NAMING

In 1811, French chemist Barnard Courtois found that violet vapor with a strong smell was generated while producing niter from seaweed ashes and that when the vapor was cooled down it turned into a purplish black flake-like crystalline material having a metallic luster. His friend, who was entrusted with the research of this unknown material, announced his results in the journal *Annales de Chimie* on December 9, 1813. In the following year, 1814, based on the results of Joseph Louis Gay-Lussac's research, it was clarified that this material was a chemical element similar to chlorine. Iodine was named after "iodes," which means violet or purple in Greek. Industrial production began in the same year, and in 1816 iodine was used as a medical sterilizing agent.

1.3 PHYSICOCHEMICAL PROPERTIES

Iodine is a nonmetallic element of the halogen family (fluorine, chlorine, bromine, iodine, and astatine) and appears in group 17 of the periodic table. Iodine under standard conditions is a purplish-black solid and has a glittering crystalline appearance. It has a moderate vapor pressure at room temperature and in an open vessel slowly sublimes to a deep violet vapor. If heated under the proper conditions, iodine can be made to melt at 113.7°C and to boil at 184°C. The density of iodine is 4.98 g/cm^3. Because of its high electronegativity, it forms iodides with almost all elements, with iodine possessing the formal oxidation state −1. Iodine is known in compounds with formal oxidation states ranging from −1, +1, +3, +5, and +7. Iodine also reacts with other halogens, fluorine, chlorine, and bromine, and forms interhalogens such as IF_5, ICl, and IBr. These compounds are used for halogenation reactions. Iodine dissolves easily in most organic solvents such as hexane, benzene, carbon tetrachloride, and chloroform owing to its lack of polarity, but is only slightly soluble in water. However, the solubility of elemental iodine in water can be increased by the addition of sodium or potassium iodide.

1.4 PRODUCTION

The concentration of iodine in brown seaweeds is so high that these marine algae have been used as the raw material for iodine production since the first half of the nineteenth century. Today, iodine production is conducted in areas where brines from natural gas (Japan) and oil fields (United States) contain high iodine concentrations, as well as from Chilean caliche deposits. About 2/3 of the total iodine production in the world originates from Chile and 1/3 from Japan, together accounting for nearly 90% of the iodine globally. Two methods are employed for the production of iodine in Japan: (1) the "blowing out" method, which takes advantage of the high vapor pressure of molecular iodine and is ideal for large-scale production, including the processing of brine at high temperature; and (2) the "ion-exchange resin" method, which uses a resin that adsorbs iodide and is suitable for both small and large production plants. In contrast, iodine production in Chile is based on the mining and leaching of nitrate ores (caliches). Caliches contain lautarite ($Ca(IO_3)_2$) and dietzeit ($Ca(IO_3)_2 \cdot 8CaCrO_4$). The solutions from the leaching of caliches carry iodine in the iodate form. Part of the iodate in solution is subsequently reduced to iodide by using sulfur dioxide obtained by the combustion of sulfur. The resulting iodide is combined with the remainder of the untreated iodate solution to generate elemental iodine.

1.5 SYNTHESIS

Generally, organic iodides can be divided into two classes of alkyl iodides and aryl iodides. Since alkyl iodides show the highest reactivity among alkyl halides, typical reactions of alkyl iodides include nucleophilic substitution, elimination, reduction, and the formation of organometallics. On the other hand, aryl halides do not undergo direct displacement by nucleophiles as observed in the case of alkyl halides, because of their low reactivity toward nucleophilic substitution. Therefore, aryl iodides undergo nucleophilic substitutions, iodine–metal exchange for organometallic compounds, and coupling reactions. The development of new reactions for the synthesis of aromatic compounds is one of the hot research fields in organic chemistry. As such, the hypervalent iodine-mediated cross-coupling reactions have been studied extensively. The new concept of halogen bonding has recently been introduced in the life sciences to develop novel drugs and in the material sciences to develop liquid crystals and organic conductors.

1.6 INDUSTRIAL APPLICATION

The industrial process for the production of acetic acid is currently dominated by the carbonylation of methanol. The three-step process involves iodomethane as an intermediate and requires a catalyst, usually a metal complex, such as rhodium iodide (Monsanto process) or iridium iodide (Cativa process). Nylon is an industrially important and useful material with multiple applications, including as an engineering resin and fiber. Thermoplastic forms of nylon are stabilized with copper iodide. Nylon fiber producers use potassium iodide for tire and airbag cord nylon. The potassium iodide reacts in situ with cupric acetate to form cupric iodide, which acts as a heat stabilizer. A polarizer with the function of transmitting and blocking light is a basic component of liquid-crystal displays (LCDs), along with the liquid crystal that functions as a switch for light. LCDs are used in a wide range of instruments, including computer and TV screens, navigation systems for automobiles, and instrument displays. The most common materials used in polarizing films are stretched polyvinyl alcohol films treated with absorbing iodine.

1.7 RECYCLE

Recovery of expensive iodine from used iodine-containing materials or iodine compounds, and, further, the manufacturing step of iodine-containing materials such as X-ray contrast agents and liquid crystal films, is very beneficial from the viewpoint of economy, natural environmental conservation, and conservation of natural resources. Many iodine manufacturers have recently focused on collecting and recycling iodine from waste streams in view of their sustainability.

1.8 BIOLOGICAL ACTIVITY

Iodine is an essential component of hormones produced by the thyroid gland. Thyroid hormones, and therefore iodine, are essential for mammalian life. The optimal dietary iodine intake for healthy adults is 150–250 μg/day. In regions where iodine in soils and drinking water is low, humans and animals may become iodine-deficient. Iodine deficiency has multiple adverse effects on humans due to inadequate thyroid hormone production that are termed the iodine deficiency disorders. Iodine deficiency during pregnancy and infancy may impair growth and neurodevelopment of the offspring and increase infant mortality. Deficiency during childhood reduces somatic growth and cognitive and motor function. In most countries, the best strategy to control iodine deficiency in populations is iodization of salt, one of the most cost-effective ways to contribute to economic and social development.

1.9 PHARMACEUTICALS

Halogens have played an important role in the development of pharmaceuticals for several decades. The effectiveness of many complex molecules is significantly enhanced by the presence of halogen atoms. The majority of halogenated drugs contain fluorine, followed by chlorine, while those with bromine are rare. Only a few iodine-containing drugs are known, such as the thyroid hormone thyroxine, an anti-herpesvirus, the antiviral drug idoxuridine, and amiodaron, a class III antiarrhythmic agent. Since C–I bonds are highly polarizable, the iodinated compounds are relatively unstable.

On the other hand, iodinated contrast media for X-rays categorized as diagnostic drugs are very stable compared to the iodinated therapeutic agents. X-ray contrast media (XRCMs) are substances that enable the visualization of soft tissues in X-ray examination. The iodine atoms function as the X-ray absorbers, and their utility can be attributed to their high atomic weight. The nonionic XRCMs, developed in the 1980s, including iopamidol, iohexol, and iopromide, offer a significant margin of safety, have fewer side effects, and provide a high level of comfort to the patients, compared to ionic compounds.

The widely used iodine tincture is an alcohol solution of iodine and potassium iodide. Iodophores are iodine complexes with surfactants that act as iodine carriers.

These are water-soluble and less irritating to the skin and other tissues than the tincture. Iodine and iodophores have a wide range of antimicrobial action against Gram-positive and -negative bacteria, tubercle bacilli, fungi, and viruses. The most popular iodophore for surgical scrub and gargle is povidone iodine.

1.10 AGROCHEMICALS

In the past three decades a significant increase of halogenated active ingredients in the field of modern crop protection research and development was observed. Interestingly, there has been a remarkable rise in the number of commercial products containing "mixed" halogens, for example, one or more further halogen atoms. Generally, iodine-containing compounds are in the minority, and some of them are "mixed" with other halogens like bromine or chlorine. A selection of three modern iodine-containing agrochemicals is as follows: iodosulfuron–methyl–sodium (herbicide), proquinazid (fungicide), and flubendiamide (insecticide). The iodo-containing compounds can reflect (i) a moderate chemical and biological stability, (ii) a good hydrophobicity or lipophilicity, which increases biological membrane permeability, (iii) a high bulkiness, and (iv) halogen bonding interactions.

1.11 ISOTOPES

In the past, with major nuclear power plant accidents occurring in Three Mile Island in the United States in 1979, Chernobyl in Ukraine (the former Soviet Union) in 1986, and recently with the Fukushima disaster, the world is once again reminded of the real dangers of contamination with radioactive materials, including radioactive iodine. Radioactive iodine is associated with such risks but can also be of great benefit when used for medical purposes. Radioactive iodine has been used in the field of medicine (nuclear medicine), as diagnostic and therapeutic radiopharmaceuticals and therapeutic medical devices, throughout the world. The isotopes iodine-123 [^{123}I] and iodine-125 [^{125}I] are used as radiopharmaceuticals to diagnose a patient's condition based on abnormalities in the internal distribution of radioactivity. Therapeutic radiopharmaceuticals include compounds labeled with radioactive iodine isotopes such as iodine-125 [^{125}I] and iodine-131 [^{131}I]. Therapeutic radiopharmaceuticals are administered orally or intravenously to the body to treat lesions with internal radiation.

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