Archimica

TECHNOLOGY STRENGTHS

Iodine Chemistry

An efficient, versatile commercial resource

As part of its world leading expertise in the use of halogens, Archimica offers the pharmaceutical industry a broad range of technologies, products and expertise based on iodine chemistry for the manufacture of intermediates and APIs.

The keys to Archimica's offering in this area are the highly flexible manufacturing capability and the experience of the organization in harnessing the potential of iodine in almost limitless applications where the special nature of this compound can offer substantial benefits.

Iodine is of interest for pharmaceutical synthesis for a variety of reasons. It can easily be converted to various oxidation states. Iodine is used selectively as a substituent in pharmaceuticals. It also has the potential to activate carbon atoms in a mild way for nucleophilic substitutions or organometallic reactions such as metallations or couplings.

Archimica's expertise with iodine chemistry can be the starting point for innovative applications in areas which may not be readily apparent with traditional approaches to synthesis.

A full spectrum of capability

Iodine chemistry is a core competency of Archimica offering a stable, secure source of supply for pharmaceutical projects. Starting from elemental iodine, Archimica has the capability of producing inorganic iodine compounds such as sodium iodide and sodium iodate through oxidative and reductive approaches. We also have expertise in developing iodinating compounds that can be used to produce a broad range of both aliphatic and aromatic iodine-containing molecules. Beyond this manufacturing capability, Archimica has a great deal of expertise in the use of iodine chemistry in the downstream manufacture of more complex molecules.

- Methyl iodide (CH_3I)
- Diiodomethane (CH_2I_2)
- Chloroiodomethane (CH_2ClI)
- Special long chain alkyl iodides ($R\text{-}(CH_2)_n\text{-}I$ / $R\text{-}(CHR')\text{-}I$)

Aliphatic iodides

Archimica manufactures a broad range of one-carbon aliphatic iodine derivatives utilizing a variety of approaches.

We are a world leader in the manufacture of methyl iodide and can supply different grades of this material to satisfy the requirements of a wide range of applications. The product range includes low-moisture grades suitable for use in Grignard or other organometallic reactions.

Another important aliphatic iodide derivative – particularly for alkylations or cyclizations – is diiodomethane. The use of this material in the Simmons-Smith synthesis of cyclopropane derivatives and enantioselective cyclopropanation is well-known.

Other important uses of diiodomethane include ring expansion of cyclic ketones, the methylenation of carbonyl compounds, the ortho methylation of phenols and as an iodine source in the conversion of aminopurine derivatives to the corresponding iodo derivatives.

Archimica has developed a proprietary process for the production of chloroiodomethane that increases the availability of this compound for use in the preparation of chloromethyl derivatives. It is also useful for converting esters to chloromethylketones and enabling reactions with electrophiles to its carbon atom. Chloroiodomethane is also a useful reagent for cyclopropanation of alkenes according to Simmons-Smith and for the methylenation of allylic alcohols.

We also have expertise in the development of longer-chain alkyl iodides starting from a number of convenient raw materials.

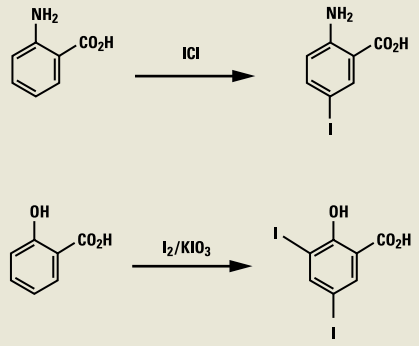
Aromatic iodides

Archimica has developed a comprehensive and flexible toolbox to introduce iodine to aromatic rings allowing the selection of the most efficient, cost effective method for any particular application.

We conduct direct iodination of aromatics using a variety of compounds.

Archimica has the flexibility to reduce costs associated with iodination of aromatics through the use of oxidizing agents that increase the atom utilization of iodine. One method employs chlorine gas to convert iodine to iodine monochloride (ICl). A number of other in situ methods have been developed which use iodide in the presence of oxidizing agents instead of elemental iodine. These are used, for example, in the manufacture of diiodosalicylic acid (Figure 1).

Figure 1



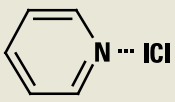
For inactivated aromatic substrates, the Sandmeyer reaction is the method of choice. Both the diazotization step and the decomposition of the intermediate diazonium salt can be carried out under very mild conditions, with no need for catalysts. This means that excellent yields of very pure products can be achieved.

Versatile reagents

Over the years of our work on custom synthesis projects, Archimica has developed a number of reagents that offer the development of specific, highly efficient functionalizations.

As an example, Iodine monochloride pyridine complex (Figure 2) is a very mild and efficient electrophilic iodinating agent for a wide range of aromatic, heterocyclic and aliphatic compounds. More powerful than iodine itself, the pyridine complex makes iodine monochloride safe to handle and to transport.

Figure 2



Excellence at the commercial scale

Archimica's expertise in the development of routes using iodine chemistry is supported by infrastructure and experience that allow the development of solutions using iodine at the commercial scale for pharmaceutical projects. Iodine and iodides are relatively expensive compounds with a high atom mass. As a result, atom efficiency at the large scale is critical for economics as well as high selectivity and yields. As reactive substances, iodine-based compounds require specially designed facilities and procedures to maintain optimum performance in their wide ranging applications. Archimica's iodine chemistry is integrated within our larger chemical toolbox – under cGMP conditions when required – including our work with organometallics, diazo chemistry and basic organic chemistries, such as nitrations, aminations, reductions and more.