

ORGANOMETALLIC CHEMISTRY

Boronic Acids

- (Hetero)aromatic Boronic Acids
- Alkyl and Vinyl Boronic Acids
- Boronic Acid Esters
- Highly Functionalized Boronic Acids

Tailor-made Boronic Acids – From Development Phase to Large Scale Manufacturing

At Euticals, we have a long history in manufacturing of boronic acids. Our chemists have developed technologies to target virtually any type of boronic acid from kilograms to commercial scale. This includes boronic acids that are typically difficult to handle and our boronic acids are of very high purity and contain none of the typical impurities such as isomers or borinic acids.

In particular heterocyclic and highly functionalized derivatives have become a major area within Euticals custom synthesis operations, and are a substantial part of our product portfolio. In addition, we can provide alkyl and vinyl boronic acids via safe and convenient routes that have been designed and scaled at Euticals.

To meet customers needs, we apply a tailor-made synthesis for each product from this area taking advantage of our experience based on more than 150 different types of boronic acids that have been developed and manufactured at Euticals. Such production has been operated at scales up to multi 100 mtons per year in one of the worlds largest cryogenic equipment (> 60m³, all FDA-inspected cGMP) situated in Europe and the United States.

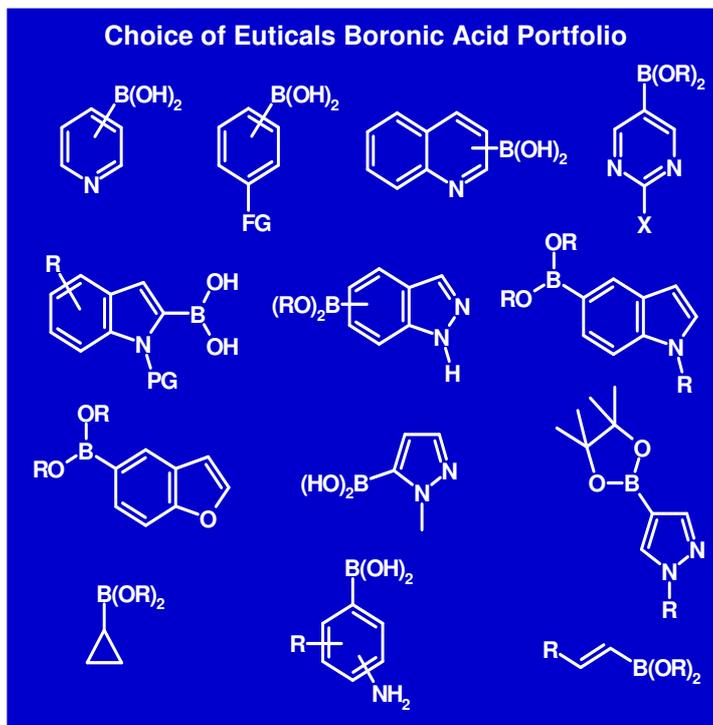
Versatile Building Blocks – Carbocyclic-, Heterocyclic- and other Boronic Acids

Boronic acid derivatives from Pyridine, Pyrimidine, Quinoline, Indole, Indazole as well as a broad range of other N-, S- and O-heterocyclic boronic acids have been produced in multi 100 kg scale. In all cases, the use of costly transition metals and borane starting materials could be avoided, resulting in higher value for the customer and beneficially in a product free of heavy metals. Typical yields are above 80 % and typical product purities are > 99.0 %. Inorganic impurities, e.g. lithium and boric acid salts and organic impurities can be removed easily yielding high quality products.

In some cases, the boronic acid itself is unstable or the downstream chemistry requires exclusion of the free acid.

Euticals has already produced a variety of different esters, usually generated *in situ* without the need for additional steps, therefore saving time and money.

A striking example for this is the synthesis of 1-Methylpyrazole boronic acid pinacol ester.



In the pharmaceutical industry, there is oftent a demand for highly functionalized biphenyls carrying substituents which are unstable towards various reaction conditions applied in the synthesis of boronic acids. The Euticals solution for this challenge consists of two practical processes: The boronic acid is introduced at first, and in a second step the desired functionality is created without affecting the boronic acid function. 4-Formylphenylboronic acid, one of our largest-scale products in the field of boronic acids, serves as an excellent example for this technology: The formyl-group enables a broad range of chemistry building up more complex structures, for instance by reduction, oxidation, amination or aldol-condensation reactions.

Our portfolio also includes a large number of aliphatic and vinyl boronic acids prepared in high yields (up to 86%) via a unique Euticals “one-pot” procedure starting from readily available and inexpensive raw materials. The materials produced offer heretofore unknown levels of purity due to the high regioselectivity of our technology even in examples where the formation of isomers is possible.

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