SJU Saint Joseph's University

Benzoxaborole Protecting Groups

Lead Inventor

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Unmet Need

Two newly FDA-approved drugs, tavaborole and crisaborole, contain a benzoxaborole functionality and as a result, the benzoxaborole pharmacophore is increasingly being investigated across the pharmaceutical industry.

Due to their sensitivity to certain reactions, chemically synthesizing benzoxaboroles can be challenging. The versatile protecting groups discovered at St. Joseph's University (formerly the University of the Sciences in Philadelphia) and described here can mask this undesired reactivity.

This invention can serve as a useful tool to any medicinal chemist pursuing a benzoxaborole in their drug design studies and for more efficient syntheses of benzoxaborole-containing drug candidates.

Opportunity

The Tomsho Lab has synthesized zwitterionic benzoxaborole complexes that can be used in mild oxidation reactions, substitution conditions, and mild reductive conditions in good yields compared to the literature. Solubility in organic solvents also improved, which facilitated reactions where the unprotected substrate was not soluble.

Due to synthetic struggles while pursuing benzoxaborole-containing analogs of a natural product, Dr. Tomsho and his colleagues searched the literature to seek potential protecting groups of the benzoxaborole functionality. One 2013 report described benzoxaborole protection, however the stability of this group was very limited.

The team has reported the design, synthesis and evaluation of two families of compounds that form divalent, zwitterionic complexes with benzoxaboroles. These compounds efficiently and reversibly protect the benzoxaborole functionality through one or more chemical steps that are incompatible with the unprotected benzoxaborole. The chemical robustness of these protecting groups has been characterized, and it was determined that these protecting groups offered improved reaction scope diversity when compared with the previous state of the art.

Unique Attributes

After initial investigation, the Tomsho team created a rigidified and semi-conjugated system that exhibits enhanced stability to reaction conditions and to common synthetic manipulations (i.e., extractions, flash chromatography).

- Rigidified and semi-conjugated system that exhibits enhanced stability to reaction conditions and to common synthetic manipulations, i.e., extractions, flash chromatography.
- Protected benzoxaboroles have significantly enhanced stability under both oxidative and reductive conditions.
- Protecting groups shield boron from nucleophilic attack.
- Ability to introduce boron earlier in the chemical synthesis process, enabling access to a greater range of benzoxaborole compounds.
- Enhanced synthesis efficiency of any product containing benzoxaborole.

Clinical Applications

This invention can be a useful synthetic tool for any company / laboratory that is pursuing the synthesis of benzoxaborole-containing targets. Reagents can be commercialized through a chemical supply company making them available for purchase by academic labs and / or companies.

Stage of Development

In laboratory use.

Intellectual Property

US Patent No. 11,427,603 B2, issued August, 2022.

US Patent No. 11,773,114 B2, issued October, 2023.

Collaboration or Licensing Opportunity

Actively seeking licensee for commercialization.

References and Publications

Gamrat, J. M.; Mancini, G.; Burke, S. J.; Colandrea, R. C.; Sadowski, N. R.; Figula, B. C.; Tomsho, J. W. Protection of the Benzoxaborole Functionality: Synthesis and Functionalization of Zwitterionic Benzoxaborole Complexes. Submitted March 16, 2018.

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