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Accelerated Microdroplet Synthesis of Benzimidazoles

An accelerated, metal-free, ambient-condition microdroplet method enables high-yield synthesis of benzimidazoles for drug development and pharmaceutical applications.

Purdue University researchers have developed an accelerated microdroplet synthesis of benzimidazoles. Benzimidazoles are an important class of heterocyclic compounds due to their wide application as active pharmaceutical moieties. Current methods to synthesize these compounds require lengthy reaction times, harsh conditions, and metal catalysts. Purdue University researchers have developed an accelerated metal free method of benzimidazole production that does not suffer from the drawbacks of contemporary benzimidazole synthesis. This synthetic method occurs under ambient conditions inside charged microdroplets produced from an electrospray ion source. The presence of intermediate arylamides provides evidence that the accelerated synthesis occurs through an acid catalyzed mechanism. The researchers utilized this benzimidazole synthetic method with a series of substituted diamine and carboxylic acid reactants and achieved yields of as high as 93%. These reactions can be scaled up to 1 gram and will prove useful in future analog design and drug development processes.

Technology Validation: Ten examples are shown as evidence of the scope of the chemistry. The accelerated synthesis has been scaled-up to establish the substituent-dependence and isolate products for NMR characterization. The researchers provide evidence for an acid catalyzed reaction mechanism based on the identification of the intermediate arylamides.

Advantages

-Metal Free Benzimidazole Synthesis

-Accelerated Synthesis of Benzimidazoles

-Ambient Condition Reaction

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Category
Chemicals & Advanced Materials/Green & Bio-Based Chemistry
Pharmaceuticals/Drug Discovery & Development
Pharmaceuticals/Biopharmaceuti

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Applications

-Drug Development

-Drug Synthesis

-Organic Synthesis

-Microdroplet Chemistry

Related Publications

Accelerated microdroplet synthesis of benzimidazoles by nucleophilic addition to protonated carboxylic acids.

Chemical Science, 2020

DOI: 10.1039/d0sc02467h

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Intellectual Property:

Provisional-Gov. Funding, 2020-05-19, United States | Utility Patent, 2021-05-18, United States | CON-Patent, 2023-09-12, United States

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