Sustainable Synthesis of Cannabinoids via Metal-Free Aromatic De-formylation

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Abstract:

Cannabinoids, the bioactive compounds of the Cannabis genus, have gained significant attention for their therapeutic potential in treating various disorders. Among them, cannabidiol (CBD) has been widely studied for its antioxidant, anticancer, anti-inflammatory, and neuroprotective effects. To enhance the accessibility and efficiency of cannabinoid synthesis, we developed a novel metal-free deformylation method for converting CBD-aldehyde into CBD. Our approach employs a methanol donor and a Brønsted acid catalyst, enabling high-yield conversion with minimal side reactions. This method was further applied to other cannabinoid aldehydes, successfully producing cannabinoids with varying alkyl chain lengths. Mechanistic studies suggest a nucleophilic substi-tution pathway that efficiently removes the aldehyde group, promoting selective and efficient syn-thesis. Compared to traditional catalytic methods, this strategy eliminates the need for metal cata-lysts, reducing potential contamination and improving sustainability. The developed methodology offers a scalable and cost-effective approach to synthesizing cannabinoids, expanding the synthetic toolkit for cannabinoid research and pharmaceutical applications. This advancement provides a valuable platform for producing bioactive cannabinoids with potential therapeutic benefits while addressing the growing demand for sustainable and efficient synthetic processes.