SEPTEMBER 23-27 2024
19BMOS
BRAZILIAN MEETING ON ORGANIC SYNTHESIS
BENTO GONÇALVES, RS - BRAZIL

Batch and Continuous Flow Total Synthesis of Cannabidiol

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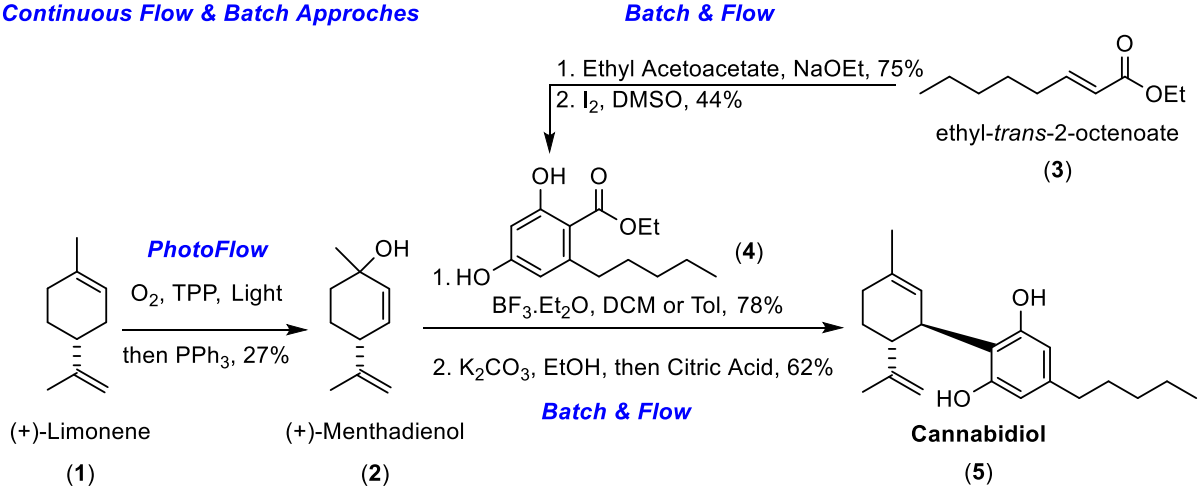
Keywords: *Cannabidiol, Continuous flow, Total Synthesis*

ABSTRACT

We present a comprehensive total synthesis of cannabidiol (**5**)[1,2] that integrates both batch and continuous flow conditions.[3,4] Our approach aims to streamline the synthesis of olivetolic acid derivatives and utilize an enantiomerically pure monoterpene moiety (*p*-mentha-2,8-dien-1-ol (**2**)), obtained from naturally occurring (*R*)-(+)-limonene (**1**) by photocatalysis. Key reactions include the synthesis of olivetolic ester (**4**) from ethyl-*trans*-2-octenoate (**3**) reacting with the enolate of ethyl acetoacetate followed by aromatization, and a Friedel-Crafts alkylation with **2** and decarboxylation. These reactions are successfully adapted to continuous flow, thus resulting in improved yields and selectivities. This study[5] not only offers a scalable and efficient route for cannabidiol synthesis but also contributes to the synthetic approaches to access cannabinoids with potential applications in medicinal and industrial contexts.



ACKNOWLEDGEMENTS

The authors thank the São Paulo Research Foundation FAPESP (grant 2013/07276-1, 2020/06874-6, 2023/04020-8 and F.C.B. fellowship 2021/06110-9), CNPq (K.T.O. research fellowship 303333/2022-7), FUNDECT (grant 204/2022), FAPERJ and CAPES Financial Code 001.

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