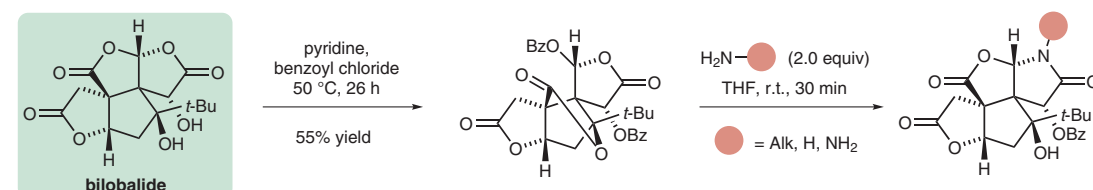


X. JIANG, X. HE, J. WONG, S. SCHEEF, S. C.-K. HAU, T. H. WONG, Y. QIN, C. H. FAN, B. MA, N. L. CHUG, J. HUANG, J. ZHAO, Y. YAN, M. XIAO, X. SONG, T. K. C. HUI, Z. ZUO, W. K.-K. WU, H. KO, K. H.-M. CHOW, B. W.-L. NG* (THE CHINESE UNIVERSITY OF HONG KONG, P. R. OF CHINA)

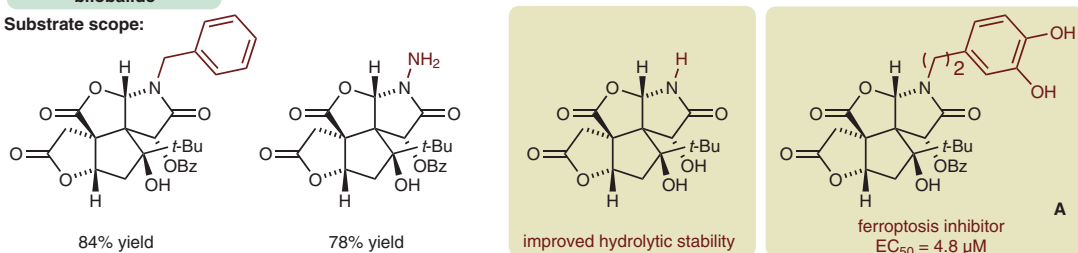
Lactone-to-Lactam Editing Alters the Pharmacology of Bilobalide

JACS Au 2024, DOI: 10.1021/jacsau.4c00416.

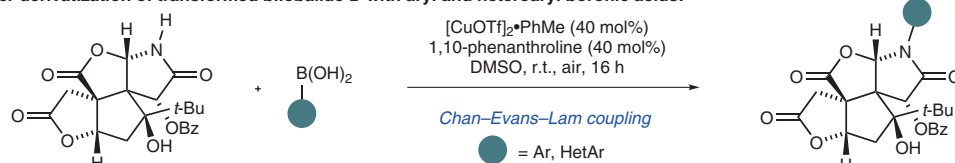
Late-Stage O-to-N Molecular Editing of Bilobalide Alters Pharmacology



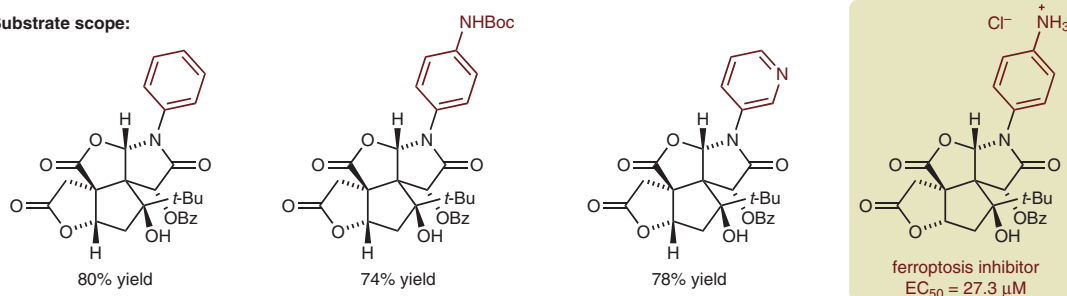
Substrate scope:



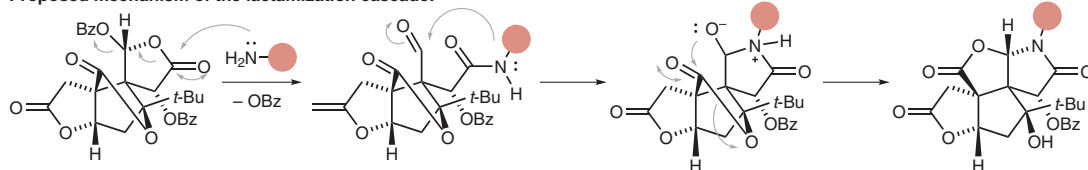
Further derivatization of transformed bilobalide D with aryl and heteroaryl boronic acids:



Substrate scope:



Proposed mechanism of the lactamization cascade:



Significance: Exploiting known skeletal rearrangements of GABA antagonist **bilobalide**, the authors developed an unprecedented N-to-O transformation to readily access lactam-type derivatives.

Comment: Bilobalide was reacted with amine nucleophiles to access lactam-type derivatives; these derivatives were modified further with copper-promoted coupling. Interestingly, the modified **A** demonstrated no GABA antagonism and atypically potent ferroptosis inhibition.

SYNFACTS Contributors: Dirk Trauner, Joseph A. Flores
Synfacts 2024, 20(10), 1091 Published online: 13.09.2024
DOI: 10.1055/s-0043-1775326; Reg-No.: T09724SF

© 2024, Thieme. All rights reserved.
Georg Thieme Verlag KG, Rüdigerstraße 14, 70469 Stuttgart, Germany

Category

Innovative Drug
Discovery and
Development

Key words

bilobalide
molecular editing
O-to-N
lactone-to-lactam
ferropoiesis
GPX4

Synfact
of the
Month

This document was downloaded for personal use only. Unauthorized distribution is strictly prohibited.