Category

Innovative Drug Discovery and Development

Key words

atomic carbon equivalent

Cl-DADO

skeletal editing

late-stage diversification

Synfact of the Month

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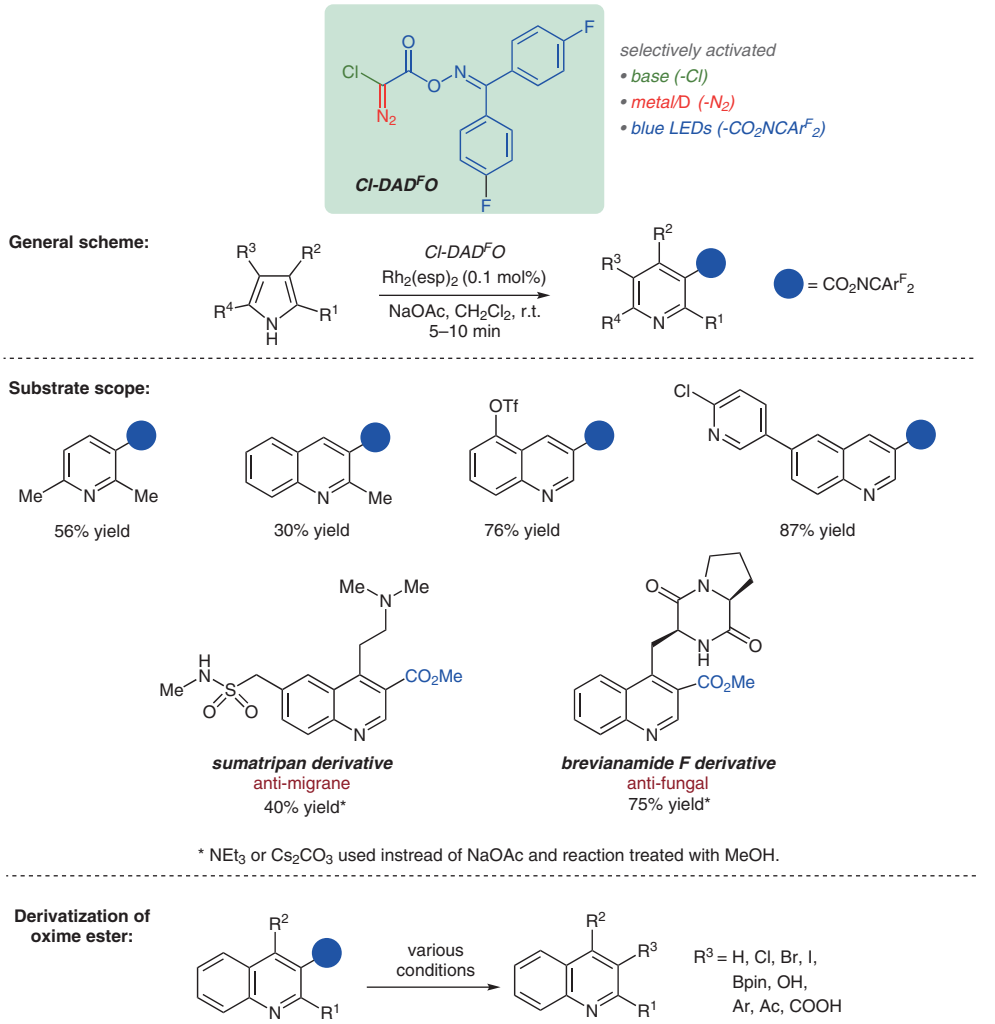
Atomic Carbon Equivalent: Design and Application to Diversity-Generating Skeletal Editing from Indoles to 3-Functionalized Quinolines
ACS Catal. **2024**, *14*, 13343–13351, DOI: 10.1021/acscatal.4c03868.

Skeletal Editing of Indoles and Pyrroles Enabled by a Novel, Atomic Carbon Equivalent



Significance: Indoles and pyrroles are common structural motifs in drug discovery. As such, any chemical tool that allows for the late-stage diversification of these heterocycles would be of high value to the medicinal chemistry community. The Glorius group has developed an atomic carbon equivalent called Cl-DAD^{F}O that allows for the skeletal editing of indoles and pyrroles to their corresponding ring-expanded quinoline and pyridine derivatives, respectively. The photosensitive oxime ester group provides a handle for subsequent structural diversification.

Comment: The ring expansion product was reliably generated for pyrroles and indoles with substituents at all positions, including C2. Following ring-expansion, radical reaction of the oxime ester allowed for further diversification. This skeletal editing sequence was applied to several drug molecules and natural products, including the anti-migrane medication sumatripan and the anti-fungal natural product brevianamide F.

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