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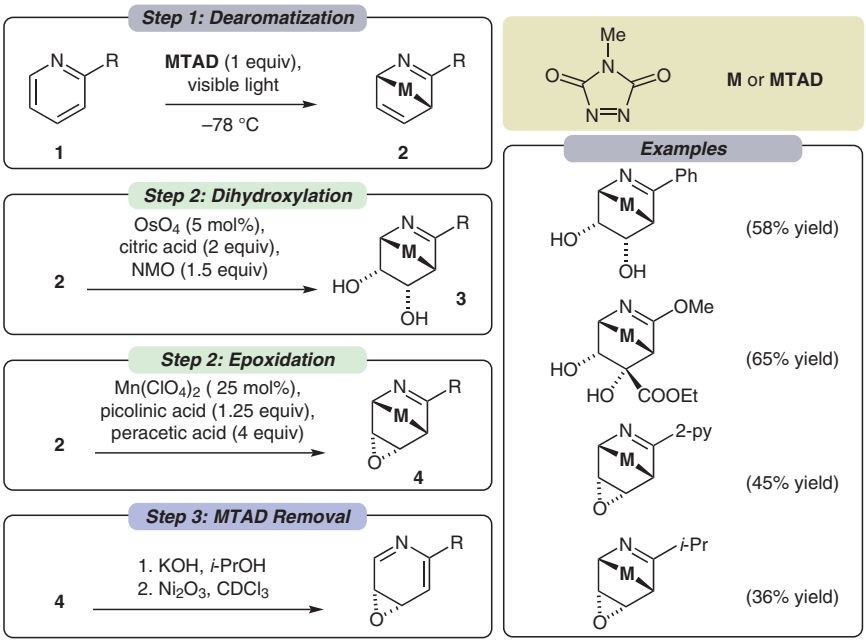
Oxidative Dearomatization of Pyridines
J. Am. Chem. Soc. **2024**, *146*, 2358–2363, DOI: 10.1021/jacs.3c13603.

Arenophile Cycloaddition-Mediated Dearomative Pyridine Oxidation



Significance: Nitrogen heterocycles commonly appear in bioactive natural products and pharmaceuticals, with pyridines and piperidines being among the most abundant. The transformation of pyridines into piperidines is challenging due to the loss of aromaticity. So far, major advances have been made in the functionalization of pyridines via hydrogenation or C–C formation, but oxygenated piperidines remain challenging to access via dearomatization strategies. The authors demonstrate that dearomatization via an arenophile cycloaddition strategy facilitates subsequent oxidation reactions – dihydroxylation or epoxidation – and streamlines access to oxidized dihydropyridines.

Comment: The authors employ MTAD (*N*-methyl-1,2,4-triazoline-3,5-dione; **M**), a potent arenophile, to elicit a reversible cycloaddition reaction that dearomatizes pyridines **1**. The dearomatized products **2** then readily undergo canonical olefin oxidations to afford diols **3** or epoxides **4**. Notably, 2-substitution was required for cycloaddition with MTAD. Alkyl, aryl, and alkoxy substituents were demonstrated to be compatible, as were subsequent derivatization reactions. MTAD can be removed in a two-step sequence by treatment with hydroxide and Ni_2O_3.

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Synfacts 2024, 20(04), 0415 Published online: 13.03.2024
DOI: 10.1055/s-0043-1773209; **Reg-No.:** T03724SF

Category
Innovative Drug Discovery and Development

Key words
oxidation
pyridine functionalization
arenophile

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