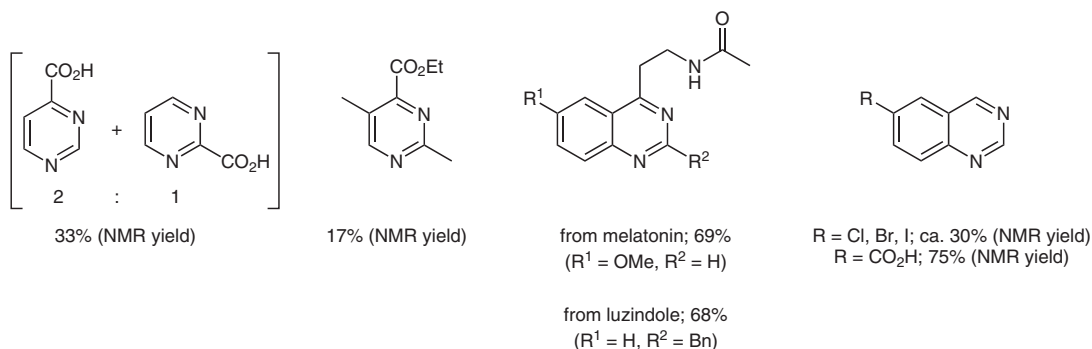
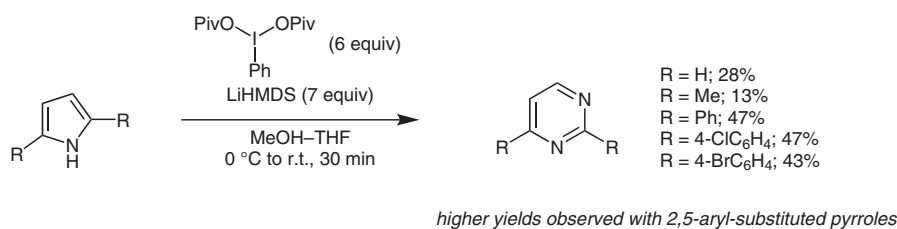
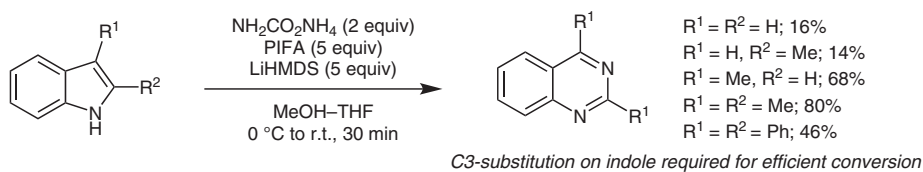


Skeletal Editing of Indoles and Pyrroles by LiHMDS Nitrogen Insertion Reaction



Significance: Skeletal editing is attractive for late-stage diversification of bioactive molecules to modulate physicochemical and/or pharmacokinetic properties. Indoles are abundant and pharmaceutically relevant heterocycles; carbon atom and nitrogen atom insertion methods are known. Nitrogen atom insertion to pyrroles, generating pyrimidines, is challenging (carbon atom insertions are known). Reported here is a new method for nitrogen atom insertion reactions of 1*H*-indoles and 1*H*-pyrroles. This transformation is made possible by the discovery of lithium bis(trimethylsilyl)amide (LiHMDS) as a competent nitrogen atom source.

Comment: The present method is applicable to unprotected substrates, which is convenient for high-throughput and late-stage structural diversification of indole and pyrrole libraries. However, yields for 1*H*-indoles are lower than for TBS-protected indoles (complementary protocol from the same group; *Science* **2022**, 377, 1104–1109). The ability to access pyrroles using the current approach with LiHMDS is a considerable achievement; pyrroles are not viable substrates using the complementary protocol. The identification of LiHMDS as an atom transfer reagent for nitrogen insertion reactions is noteworthy and should be explored.