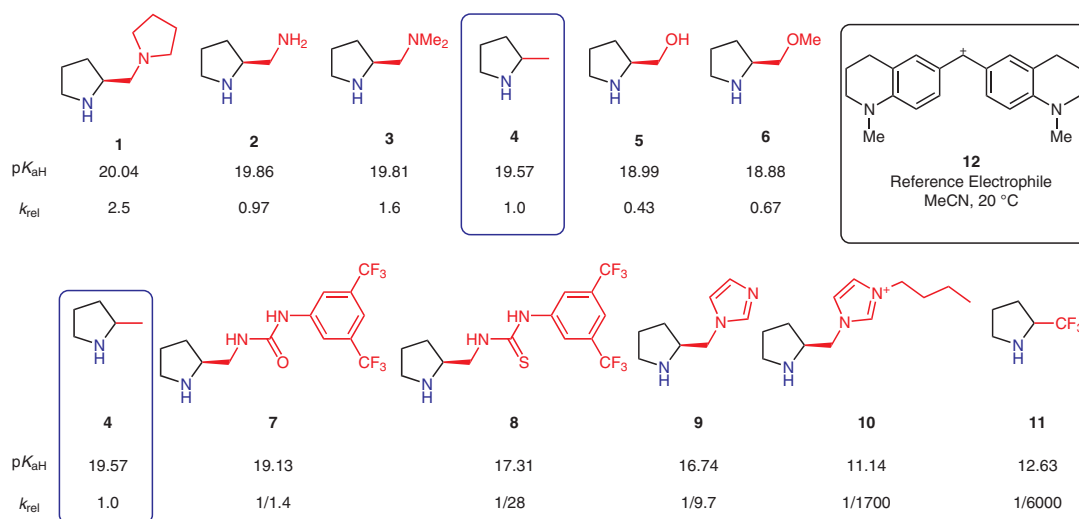


## Determination of Basicities and Nucleophilicities of a Series of Organocatalysts

Comparison of Brønsted basicities and relative rate constants for 2-substituted pyrrolidines



**Significance:** Given that organocatalytic sequences are typically initiated through nucleophilic attack of a secondary amine at a carbonyl group to generate an intermediate enamine or iminium ion, fundamental knowledge regarding the basicity and nucleophilicity of the catalysts is of value in optimizing these transformations. Whereas the Brønsted basicities of several pyrrolidines and imidazolidinones have previously been reported (see, for example: R. A. Evangelista, J. Hine *J. Org. Chem.* **1980**, *45*, 3890), these measurements were typically performed in aqueous solutions, and no systematic evaluation of the relative nucleophilicity of these species was disclosed. The current report provides Brønsted basicity data on a series of 32 pyrrolidines and imidazolidinones in acetonitrile and quantifies their nucleophilic reactivity in reactions with a range of common reference electrophiles.

**Comment:** The Brønsted basicities were determined photometrically by using a range of CH-acids as indicators. Most of the 2-substituted pyrrolidines evaluated had basicities in the range  $16 < pK_{aH} < 20$  with the 2-trifluoromethyl- (**11**) and the 2-imidazolium-substituted (**10**) derivatives being significantly less basic, like the imidazolidinones ( $10 < pK_{aH} < 12$ ). Most of the reactions followed second-order kinetics although, in some cases, a pyridine-derived additive was required to facilitate the deprotonation of the initially formed adduct. A wide reactivity range was observed across the substrates evaluated. Several trends regarding sterics and electronics are discussed. To conclude, the core learning is that Brønsted basicities are not a useful guide for estimating nucleophilic reactivities.