

Benzothiazoyl sulfonamides as new tunable chiral H-bond donors and Brønsted acids in organic organocatalysis

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Over the past two decades, organic synthesis underwent to a significant transformation. Indeed, attempts to find an alternative transformation to well established enantioselective transition metal catalyzed reactions led to generation of new field in organic synthesis – organocatalysis. In this field, organic transformations are catalyzed with small chiral organic molecules. This type of catalysis underwent tremendous development over the past 20 years and has become an integral part of the organic catalytic transformations that are now commonly performed in the laboratories of synthetic and medicinal chemists. Many of these reactions are catalyzed by Brønsted acids. In terms of the pKa, acids generally employed in organocatalytic reactions can be divided into two main groups: weakly acidic (pKa => 10), also called hydrogen bonding catalysts, and stronger Brønsted acids (typically pKa = <3). Surprisingly, the acid catalyzed transformations using acids with pKa ranging from 3 to 10 were till recently completely ignored. Interestingly, such pKa window covers all carboxylic acids. In the past 5 years, however, the use of chiral carboxylic acids to catalyze organic transformation started to flourish. However, with results far beyond expectation. We believe that the reason for disappointing results is due to somewhat more difficult spatial control (and the associated enantioselectivity of the reactions) connected with the carboxylic acid hydrogen. The goal of this project is to develop novel chiral Brønsted acids that bear hydrogen atom with pKa like carboxylic acid, but do not have carboxylic group. The second goal is to develop organocatalytic reactions that would be catalyzed by such acids.^{1–4}

Litterature

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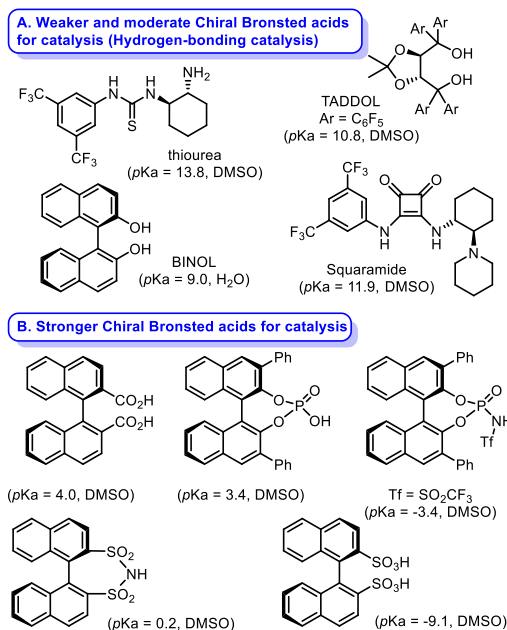


Figure 1. Examples of most commonly used weaker (A) and stronger (B) Chiral Brønsted Acids in organocatalytic reactions. pKa values in brackets

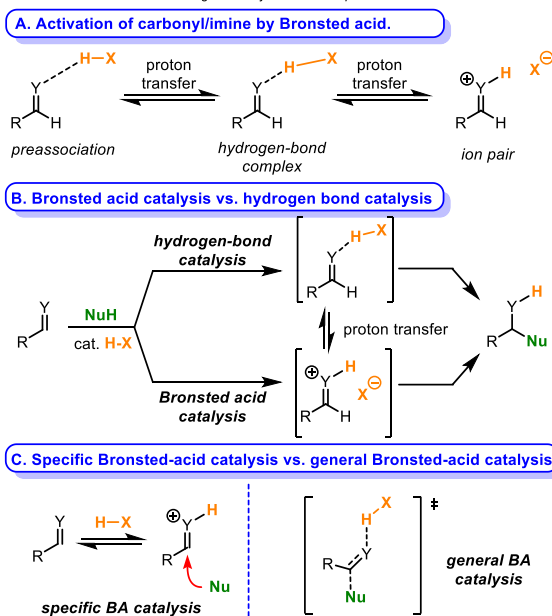


Figure 2. Brønsted acid catalysis. (A) Three key interactions of carbonyl/imine group with Brønsted acid. (B) Borderline reaction mechanisms - BA-catalysis & hydrogen-bond catalysis. (C) Specific vs. general acid catalysis - role of BA in the rate determining step. Y = O, NR'

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