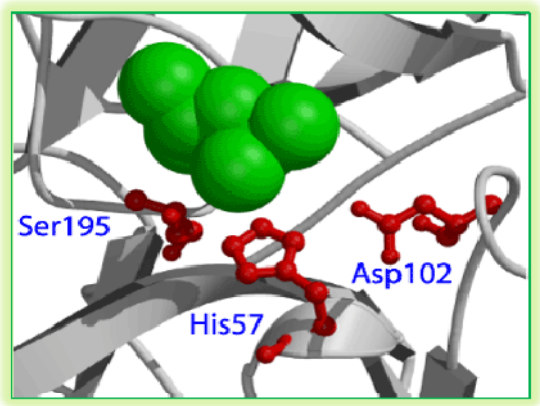
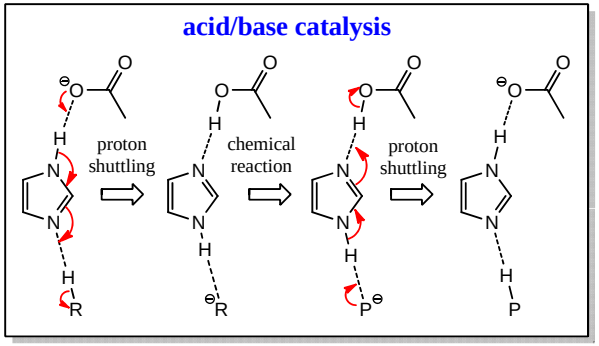
Design of Organocatalysts with Catalytic Acid-Base Dyad Inspired by Serine Proteases

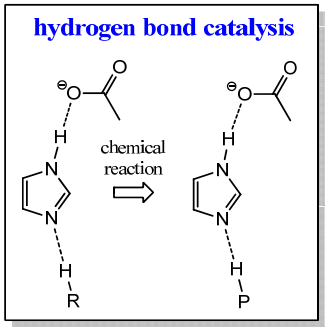


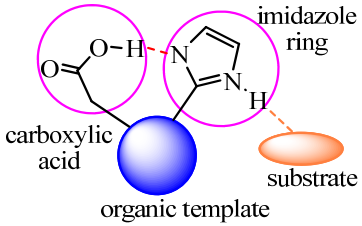
Inspiration: enzyme catalysis of serine protease

A new type of chiral β-amino acid catalyst has been designed computationally mimicking the enzyme catalysis of serine proteases. Our catalyst approach is based on the bio-inspired catalytic acid-base dyad, namely carboxyl and imidazole pair. DFT calculations predict that this designed organocatalyst catalyzes Michael additions of aldehydes to nitroalkenes with excellent enantioselectivities and remarkably high *anti* diastereoselectivities. The unusual stacked geometry of the enamine intermediate, hydrogen bonding network and the adoption of an *exo* transition state are the keys to understand the stereoselectivity.

H. Yang and M.W. Wong, *Journal Organic Chemistry* **2011**, *76*, 7399-7045.





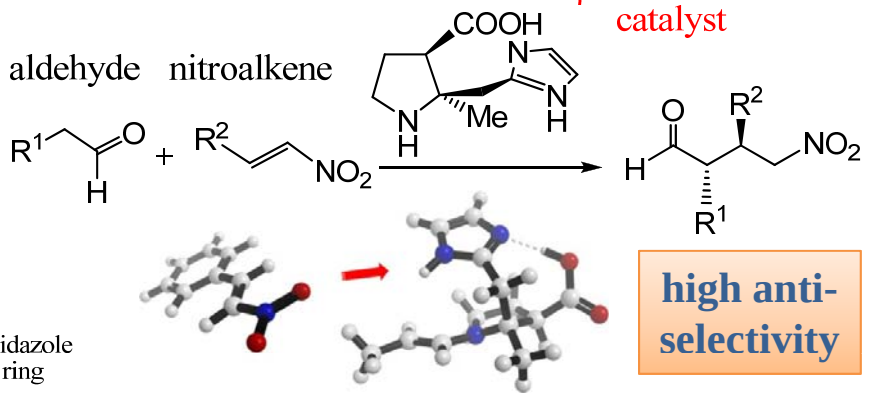


designed acid-base catalytic dyad (carboxyl imidazole pair)

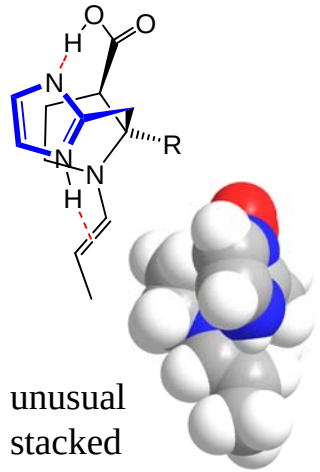
Michael Reaction

aldehyde nitroalkene

β-amino acid catalyst



high anti-selectivity



unusual stacked geometry of *E*-enamine

Prof. Richard M. W. Wong
Department of Chemistry, National University of Singapore