Asymmetric synthesis of heterocyclic compounds and their synthetic applications by cyclic ylides formation followed by enantioselective addition sequences

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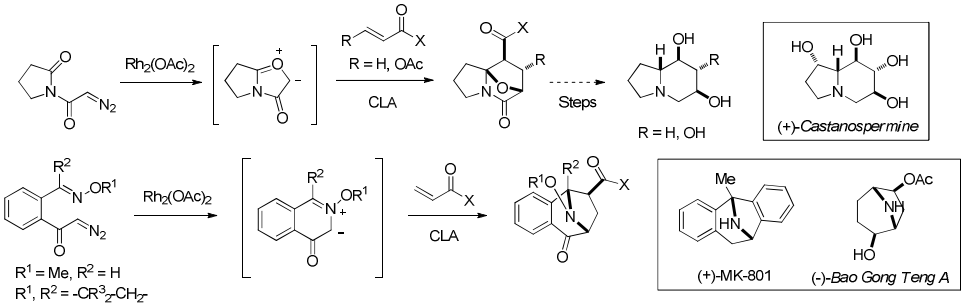
During the past decade, we developed enantioselective carbonyl ylide cycloaddition reactions featuring dual-activation methodology involving Rh-catalyzed cyclic carbonyl ylide formation followed by chiral Lewis acid-catalyzed cycloadditions, which have exhibited high levels of asymmetric induction.[1,2)] To evaluate the efficiency of the dual-activation methodology for the asymmetric synthesis of several other biologically important heterocyclic compounds such as optically active polyhydroxy Indolizidine derivatives and 8-azabicyclo[3.2.1]octanes, we have investigated asymmetric cycloaddition reactions of the corresponding cyclic ylides derived from *N*-diazoacetyl lactams, 2-(2-diazoacetyl)-benzaldehyde *O*-methyloximes and related isoxazoline derivatives as diazo substrates based on the dual-activation methodology. Details of their enantioselectivities (good to high %ees) and synthetic applications will be reported.



This methodology could apply to the addition reaction of benzylalcohol to the cyclic carbonyl ylides derived from 2-diazo-3-alkanoyl-2-oxazolidinone derivatives. Relatively high enantioselectivities were observed for the addition products, which could be hydrolyzed to the corresponding water insertion products.

References

1) Suga, H. et al. *J. Am. Chem. Soc.* **2002**, *124*, 14836. *J. Org. Chem.* **2013**, *78*, 10840.

2) Suga, H. et al. *Org. Lett.* **2007**, *9*, 4359. *Tetrahedron* **2010**, *66*, 3070.