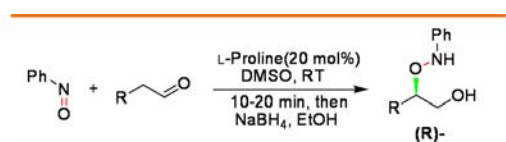


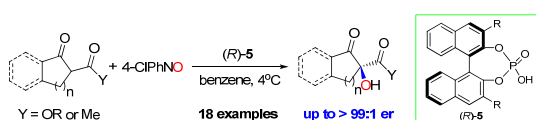
Guofu ZHONG

We are interested in the development of new synthetic methodologies in organic synthesis and asymmetric catalysis as well as their uses in the synthesis of biologically active compounds. Learning from Nature is always inspiring. Our studies started from developing new approaches to mimic the natural Class-I aldolases that use an amine functionality in its active site and a covalent catalysis involving imine and enamine intermediates. Antibody catalysis provided significant conceptual model which promoted our interest to find organocatalysts of similar reactions. New asymmetric routes with organocatalysis were then developed, that can be ideally performed under ambient conditions in benign media using small organocatalysts. With the development of organocatalytic asymmetric reactions, a new asymmetric aminoxylation was discovered. Unmodified aldehydes were reacted with nitrosobenzene in the presence of chiral proline catalyst affording  $\alpha$ -aminoxy aldehydes with excellent enantioselectivities (94 - >99% ee). Since the amino group on aminoxy functional group can be easily removed to give free hydroxy, the reaction provided with a direct methodology to the synthesis of  $\alpha$ -hydroxy aldehydes, a basic element in carbohydrates and sugars.

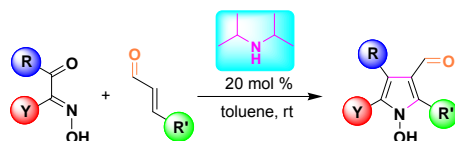


Enantioselective  $\alpha$ -Aminooxylation of Aldehydes (up to  $\geq 99\%$  ee)

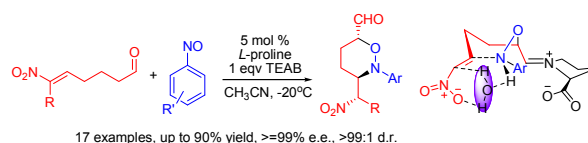
A novel, facile, and highly enantioselective Brønsted acid catalyzed  $\alpha$ -hydroxylation of  $\beta$ -dicarbonyl compounds using nitroso compounds as the oxygen source has been developed in up to 99:1 er. The results disclosed considerably extend the substrate scopes for the  $\alpha$ -aminooxylation, allowing expeditious, straightforward, and efficient access to valuable  $\alpha$ -hydroxy- $\beta$ -dicarbonyl compounds in the highest levels of enantiocontrol.<sup>1</sup>



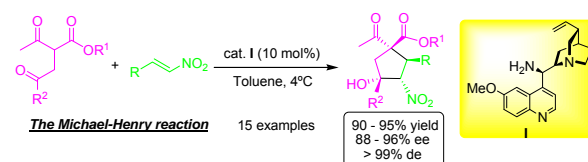
A facile synthesis of N-hydroxy pyrroles, involving sequential Michael addition/intramolecular aldol condensation reactions, has been developed using readily available starting materials. The domino reaction proceeds via an iminium activation of unsaturated aldehydes, Michael addition using oximes as N-selective nucleophiles and aldol condensation. This protocol is associated with mild reaction conditions, good yields, wide substrate scope, high regioselectivities, dense and flexible substitution patterns.<sup>2</sup>



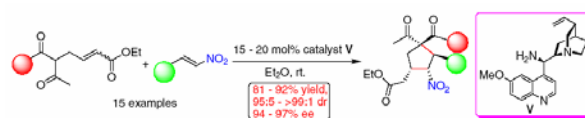
The aminooxylation directed domino reactions have been developed, from which pure aldehyde products could be isolated in good to excellent yields with excellent stereocontrol.<sup>3,4</sup>



The asymmetric construction of a quaternary carbon atom represents one of the most challenging and demanding topics in the synthesis of natural products and chiral drugs. The development of efficient methods to access complex molecules with multiple stereogenic centers also continues to be a substantial challenge in both academic research and industrial applications. We have developed a novel organocatalytic tandem Michael-Henry reaction. The reaction was efficiently catalyzed by readily available 9-amino-9-deoxyepiquinine (**V**) to give synthetically useful, highly functionalized chiral cyclohexanes with four stereogenic centers containing two quaternary stereocenters in good to excellent yields (85-94%), excellent enantioselectivities (97% to >99% ee) and high diastereoselectivities (93:7-99:1 dr).<sup>5,6</sup>



We have also extended the above tandem process to a novel enantioselective and diastereoselective organocatalytic domino double Michael reaction that provides expedited access toward highly functionalized cyclopentane derivatives. Simple operational procedures, excellent enantioselectivity (90-97% ee), diastereoselectivities (95:5 to >99:1 dr), and immense potential of synthetic versatility of the products render this new methodology highly appealing for asymmetric synthesis.<sup>7-10</sup>



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- B. Tan, Z. Shi, P. J. Chua, Y. Li, G. Zhong, *Angew. Chem. Int. Ed.* **48** (2009), 758-761.
- M. Lu, D. Zhu, Y. Lu, Y. Hou, B. Tan, G. Zhong, *Angew. Chem. Int. Ed.* **47** (2008), 10187-10191.
- D. Zhu, M. Lu, P. J. Chua, B. Tan, F. Wang, X. Yang, G. Zhong, *Org. Lett.* **10** (2008), 4585-4588.
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