DIASTEREODIVERGENT SYNTHESIS OF ENANTIOENRICHED α,β-DISUBSTITUTED γ-BUTYROLACTONES VIA COOPERATIVE CATALYSIS

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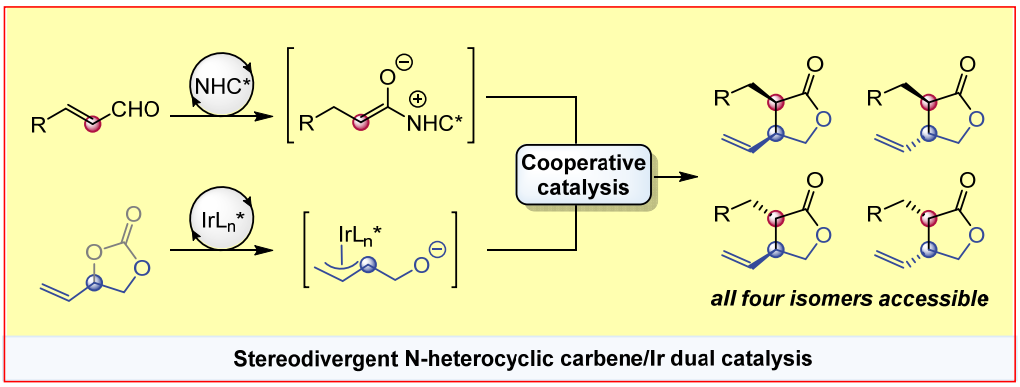
The cooperativity of N-heterocyclic carbene (NHC) organocatalysis with transition-metal catalysis has recently emerged as a new strategy to harness the synthetic potential of NHC-bound nucleophiles [1]. Despite a few methods reported, the merger of these two catalytic manifolds is still limited due to the strong affinity of NHCs to transition metals, which results in the irreversible formation of NHC-transition metal complexes. Herein, we report the first dual catalytic system that combines NHC organocatalysis with iridium catalysis for the diastereodivergent synthesis of enantioentriched α,β-disubstituted-γ-butyrolactones [2]. The use of two chiral catalysts allowed control over the relative and absolute configuration of the two formed stereocenters, thereby providing selective access to all four possible stereoisomers of the γ-lactone products [3]. The synthetic utility of the developed methodology was illustrated in the concise synthesis of a naturally occurring lignan.



Stereodivergent N-heterocyclic carbene/Ir dual catalysis

[1] Wang, M. H.; Scheidt, K. A. *Angew. Chem. Int. Ed.* **2016**, *55*, 14912.

[2] a) Singha, S.; Serrano, E.; Mondal, S.; Daniliuc C. G.; Glorius, F. *Manuscript submitted*. b) Singha, S.; Patra, T.; Daniliuc, C. G.; Glorius, F. *J. Am. Chem. Soc.* **2018**, *140*, 3551.

[3] Krautwald, S.; Carreira, E. M. *J. Am. Chem. Soc.* **2017**, *139*, 5627.