Highly Enantioselective Addition of Enals to Isatin-Derived Ketimines Catalyzed by N-Heterocyclic Carbenes: Synthesis of Spirocyclic γ-Lactams


Chi and co-workers report an N-heterocyclic carbene (NHC)-catalyzed annulation of isatin N-Boc imines with enals, which affords spirocyclic oxindole-γ-lactams bearing one quaternary chiral center in good diastereo- and excellent stereoselectivities (dr up to >20:1 and er > 99.5:0.5). Ketimines and γ-aryl enals with electron-donating substituents lead to better yield and selectivity compared to electron-withdrawing substituents. The presence of a trace of water is beneficial for the conversion of the reaction. The resulting products can be easily deprotected to free γ-lactams in high yield.

Comment: γ-Lactams are privileged scaffolds found in naturally occurring and synthetic biologically active compounds. Herein, the authors have developed a novel NHC-catalyzed annulation methodology, which allows for a rapid construction of spirocyclic oxindole-γ-lactams with high diastereoselectivity and enantioselectivity. More efficient catalysts and the application to more challenging substrates are expected.