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

Org. Lett. **2012**, *14*, 5412–5415.

NHC-Catalyzed Annulation of Isatin *N*-Boc Ketimines and Enals

Selected examples:

Removal of the Boc protecting group:

Significance: 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.

SYNFACTS Contributors: Benjamin List, Qinggang Wang
 Synfacts 2013, 9(1), 0104 Published online: 17.12.2012
 DOI: 10.1055/s-0032-1317902; Reg-No.: B11512SF

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.