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Stereoselective Synthesis of *N*-Containing Heterocycles via Ir-Catalyzed Intramolecular α-Alkylation of Carbonyl Compounds

Romi S. Aggarwal[1*], Hassan Abbas[1], Changcheng Jing[1], Craig M. Robertson[1], John F. Bower[1]
1) Department of Chemistry, University of Liverpool, Crown Street, Liverpool, L69 7ZD, United Kingdom
****e-mail:** romi.aggarwal@liverpool.ac.uk*

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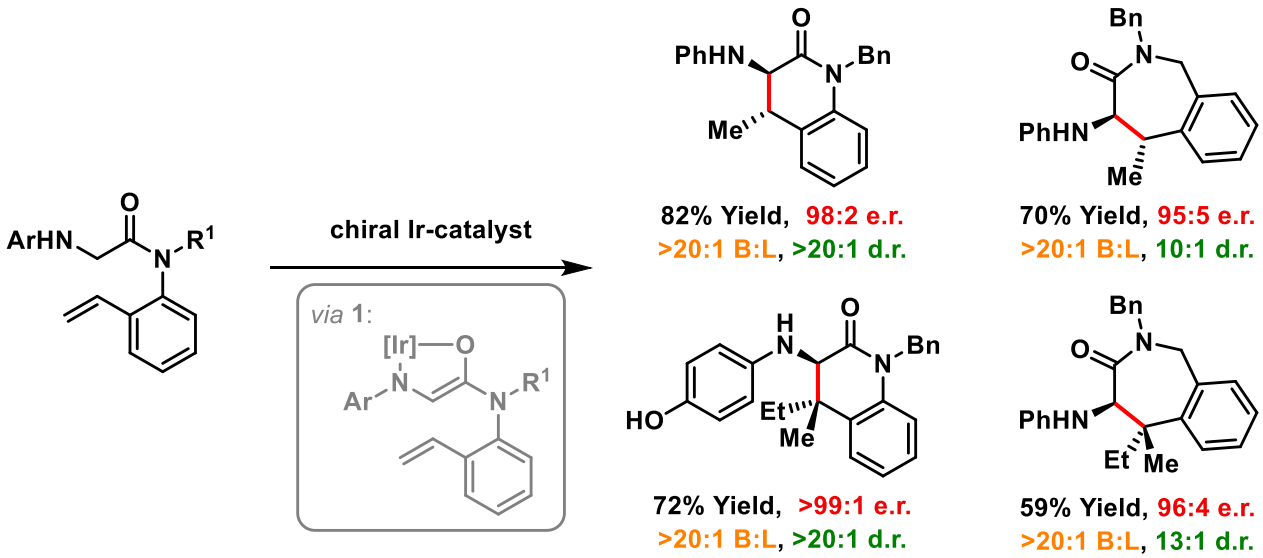
ABSTRACT

Chiral nitrogenous heterocycles are prevalent in many biologically active molecules, with 59% of U.S. FDA approved small-molecule drugs possessing a nitrogen-containing heterocycle.[1] Many synthetic methodologies have been developed to access these scaffolds.[2] However, the asymmetric synthesis of highly substituted *N*-containing heterocycles from achiral, acyclic starting materials is still extremely limited.[3] Here, we demonstrate an intramolecular iridium-catalyzed cyclization of α-amino amides onto unfunctionalized alkenes, installing adjacent stereocenters. This method utilizes the directing group ability of a glycine-derived N–H unit to facilitate Ir-catalyzed enolization of the carbonyl unit (**1**).[4] The resulting stereodefined enolate undergoes branch-selective C–C bond formation with complete regioselectivity. The process occurs with complete atom economy and excellent diastereo– and enantiocontrol (up to >20:1 d.r. and >99% e.r.), which is retained when accessing sterically challenging contiguous stereocenters. This method allows 6– and 7– membered *N*-containing heterocycles and 5– and 6– membered carbocycles to be constructed stereoselectively.



- unique directing-group-based strategy
- high regio-, enantio- and diastereoselectivity
- contiguous stereocenters
- complete atom economy
- non-activated alkenes
- different ring sizes (n = 5–7) and ring classes accessible

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