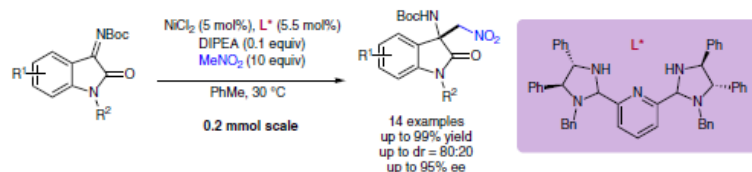
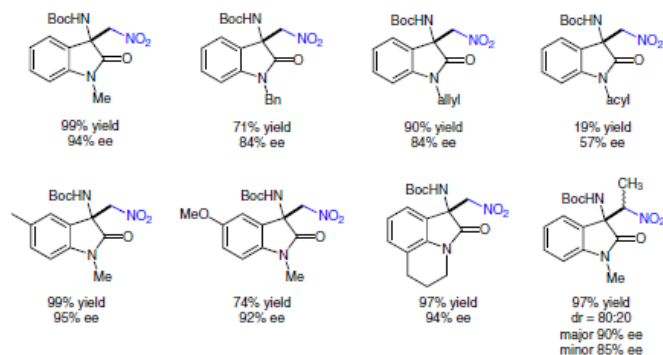


T. ARAI,* E. MATSUMURA, H. MASU (CHIBA UNIVERSITY, JAPAN)
 Bis(imidazolidine)pyridine-NiCl₂ Catalyst for Nitro-Mannich Reaction of Isatin-Derived *N*-Boc Ketimines:
 Asymmetric Synthesis of Chiral 3-Substituted 3-Amino-2-oxindoles
Org. Lett. 2014, 16, 2768–2771.

Nickel-Catalyzed Enantioselective Nitro-Mannich Reaction of Isatin Derivatives



Selected examples:



Significance: 3,3-Disubstituted oxindoles are prevalent scaffolds in a range of biologically active natural products and pharmaceutical targets (see Review below). One common and direct asymmetric approach to these core structures involves nucleophilic additions to isatin-derived ketimines. As an extension of the authors' previous work on Cu- and Co-catalyzed asymmetric Mannich-type reactions, Arai and co-workers currently present a Ni-catalyzed enantioselective nitro-Mannich reaction to isatin-derived ketimines (previous work: *Chem. Eur. J.* 2012, 18, 11219).

Review: B. M. Trost, M. K. Brennan *Synthesis* 2009, 3003–3025.

Comment: The developed protocol provides functionalized oxindole products containing a chiral quaternary aminocarbon center. While the observed enantiomeric excesses range from good to moderate, the yields are generally high. Electron-rich protecting groups on the oxindole nitrogen (e.g., Me, Bn, allyl) are well-tolerated under the reaction conditions. However, substitution with an electron-withdrawing acetyl group on the isatin nitrogen decreases the reactivity of the substrate significantly. The nitro group in the final product can be readily reduced to an amine in high yield with no observable degradation in enantiomeric excess.

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