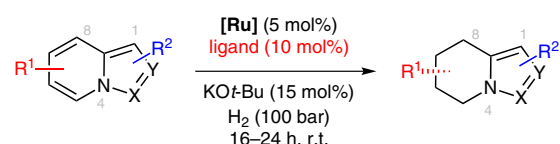
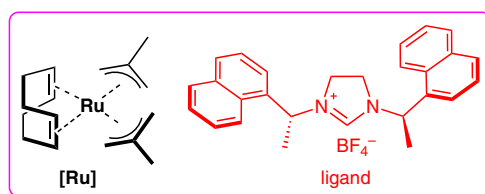


Asymmetric Hydrogenation of Indolizines and 1,2,3-Triazolo[1,5-*a*]pyridines

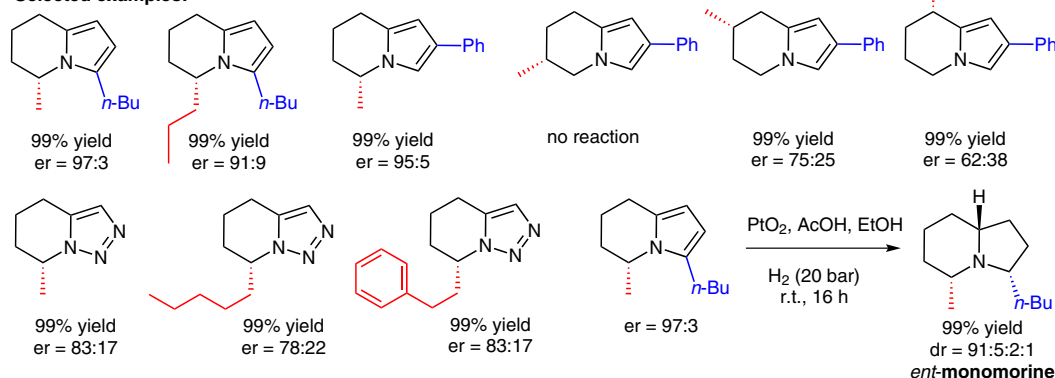


R^1 = H, 5-Me, 5-Et, 5-Pr, 5-C₅H₁₁,
5-(CH₂)₂Ph, 5-C₁₁H₂₃, 6-Me,
7-Me, 8-Me
 R^2 = H, 2-CO₂Et, 2-Ph, 2-(4-FC₆H₄),
2-(4-MeOC₆H₄), 3-Bu
X = Y = CR², N

13 (+ 2) examples
up to 99% yield
er up to 97:3
(0.3 mmol scale)



Selected examples:



Significance: The indolizidine motif, which is characterized by fused six- and five-membered rings containing a bridgehead nitrogen atom, is widely distributed as a core structure in bioactive alkaloids. The authors reported the direct asymmetric hydrogenation of the challenging *N*-bridged heterocycles, represented by substituted indolizine and 1,2,3-triazolo[1,5-*a*]pyridine derivatives. High enantioselectivities and yields were achieved by the application of a chiral ruthenium–NHC complex for the completely regioselective and asymmetric hydrogenation. Additionally, access to indolizidine scaffolds is demonstrated by the efficient synthesis of (–)-monomorine via hydrogenation of the remaining pyrrole ring under Jefford's conditions.

Comment: The high regioselectivity is explained by the unusual aromatic structure of the fused *N*-bridged heterocycle, where the six-membered ring reacts more like a reactive diene rather than a pyridine, furnishing partially hydrogenated products in high yields. Interestingly, the chiral induction is influenced strongly by the substitution pattern on the substrate. In the case of alkyl groups on the 3- and 5-position, high ee values are observed. A similar trend was obtained for substrates substituted with aryl or ester groups on the 2-position. Alkyl groups on the 6-, 7- and 8-position caused no reaction or diminished enantioselectivities. The potential of the procedure was demonstrated by the short two-step synthesis of an alkaloid in an overall yield of 98%.

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