

SYNFACTS Highlights in Current Synthetic Organic Chemistry

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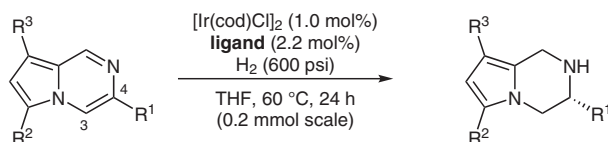
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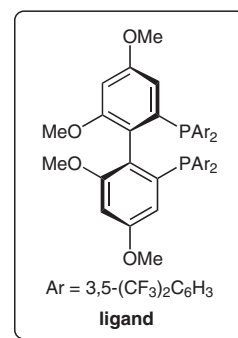
S.-B. HU, Z.-P. CHEN, B. SONG, J. WANG, Y.-G. ZHOU* (DALIAN INSTITUTE OF CHEMICAL PHYSICS, P. R. OF CHINA)

Enantioselective Hydrogenation of Pyrrolo[1,2-*a*]pyrazines, Heteroaromatics Containing Two Nitrogen Atoms
Adv. Synth. Catal. **2017**, 359, 2762–2767.

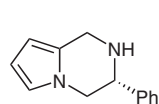
Synthesis of Tetrahydropyrrolo[1,2-*a*]pyrazines by Asymmetric Hydrogenation



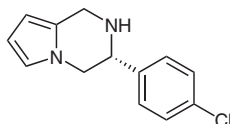
19 examples
90–98% yield
50–96% ee



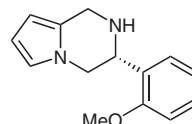
Selected examples:



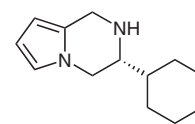
98% yield
94% ee



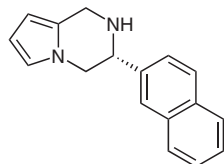
95% yield
91% ee



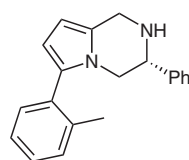
92% yield
50% ee



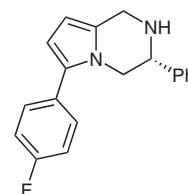
95% yield
54% ee



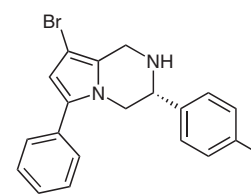
95% yield
91% ee



90% yield
96% ee



94% yield
94% ee



94% yield
91% ee

Significance: Although the asymmetric hydrogenation of nitrogen-containing heterocycles has been studied extensively over the past years, the same strategy remains underinvestigated for heterocycles with multiple nitrogen atoms. One of the hurdles to overcome is the low reactivity of these substrates. To date, common approaches to achieve the enantioselective hydrogenation use more active substrates such as the benzylated or protonated forms. In the present paper, the authors disclose the asymmetric hydrogenation of substituted and unactivated heterocycles.

Comment: The reaction generally delivers the desired products in excellent yields and enantioselectivities, although some examples show diminished enantiomeric excess. In one example, enantioselective hydrogenation of a 3,4-disubstituted substrate has been achieved with excellent diastereoselectivity, albeit with acid as an activator. Deuterium-labeling studies, in combination with reaction monitoring by NMR, suggest that the first hydrogenation takes place at the 3- and 4-position of the heterocycle.

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