Highly Diastereo- and Enantioselective Silver-Catalyzed Double [3+2] Cyclization of α-Imino Esters with Isocyanoacetate


Significance: The authors present a double [3+2] cyclization of α-amino esters with isocyanates to produce highly functionalized oxazole-imidazoles. Therefore, a silver oxide quinine derived amino phosphine ligand was used. For the pioneering work regarding isocyanates using a gold catalyst, see: Y. Ito, M. Sawamura, T. Hayashi J. Am. Chem. Soc. 1986, 108, 6405–6406.

Comment: Kinetic studies identified two cyclization processes to be step-wise. The intermediates, mono-[3+2] cyclization products, were isolated. The products can be hydrolyzed to yield functionalized α,β-diamino esters.

Selected examples:

- 99% yield, 98% ee
- 61% yield, 99% ee
- 76% yield, 95% ee
- 69% yield, 37% ee

Isolation of intermediates and three-component reaction:

- 92% yield, dr > 20:1, 99% ee
- 67% yield, 97% ee
- 99% ee

Synthesis of the α,β-diamino ester:

- 95% ee
- 90% yield, 96% ee