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Highly Enantioselective [5+2] Annulations through Cooperative N-Heterocyclic Carbene (NHC) Organocatalysis and Palladium Catalysis

J. Am. Chem. Soc. **2018**, *140*, 3551–3554.

Enantioselective [5+2] Annulations with a Cooperative Catalytic System

Representative examples:

L: Ar = 4-MeC₆H₄

precat. 1: Ar = 2,6-Et₂C₆H₃

Significance: Synthetic chemists have long sought to combine N-heterocyclic carbene (NHC) organocatalysis and metal catalysis. However, because NHCs are excellent ligands for late-transition metals, the design of cooperative catalytic systems remains a formidable challenge (M. H. Wang, K. A. Scheidt *Angew. Chem. Int. Ed.* **2016**, *55*, 14912). Reported is the first highly enantioselective [5+2] annulation between an NHC enolate and a π -allyl palladium intermediate through a dual catalytic process.

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Synfacts 2018, 14(06), 0571 Published online: 17.05.2018
DOI: 10.1055/s-0037-1610019; Reg-No.: V05318SF

Comment: The authors expand their previous studies on NHC/Pd-based catalytic systems (*J. Am. Chem. Soc.* **2016**, *138*, 7840; *ibid.* **2017**, *139*, 4443) by using a bidentate phosphine ligand to prevent NHC coordination to the active palladium catalyst. A matched combination of a chiral NHC and a chiral phosphine ligand promotes high levels of enantioselectivity, which has previously been a challenge for seven-membered rings due to both unfavorable entropy effects and transannular interactions (see, for example: Y.-N. Wang et al. *Angew. Chem. Int. Ed.* **2018**, *57*, 1596).

Category

Synthesis of
Heterocycles

Key words

organocatalysis

N-heterocyclic
carbenes

palladium catalysis

enantioselectivity

[5+2] annulation

lactones

Synfact
of the month