

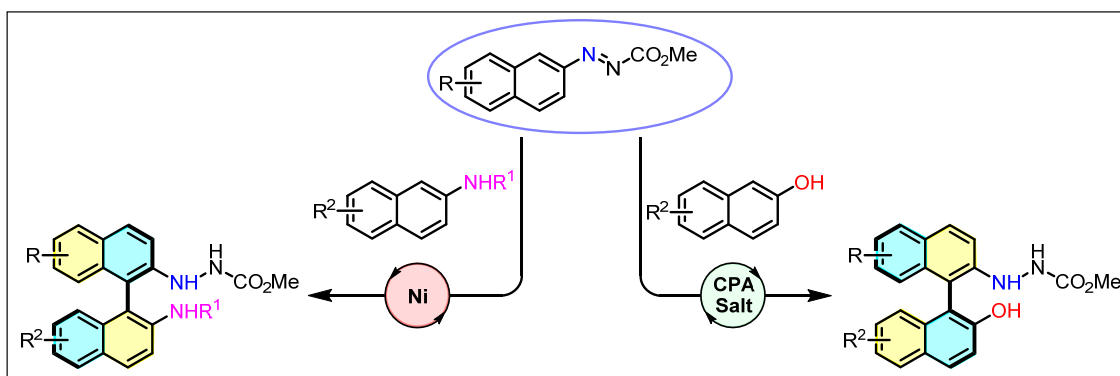
ORGANOCATALYTIC ASYMMETRIC SYNTHESIS OF ATROPISOMERIC BIARYLS

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Optically active atropisomeric biaryl motif is widespread in various bioactive natural products, pharmaceuticals and chiral materials. They also constitute the core structures of a series of important ligands and catalysts which are widely used in asymmetric catalysis. Despite remarkable advance has been achieved in the recent years, universal and facile approaches to access the axially chiral scaffolds are still highly desirable. The lack of concise enantioselective cross-coupling mounts to unacceptably high production cost for their commercialization which in turn greatly impeded their applications in related research area. In this context, our program aims to partially solve the source of useful atropisomerically enriched molecules through pursuing cost-effective and environmental-benign synthetic routes. The central strategy of our proposal is the installation of electron-withdrawing group to activate the arene and the rapid conversion of the unstabilized negative charged intermediate. Aided by the organocatalyst, the asymmetric aromatic nucleophilic substitution could be realized under mild reaction conditions to give the atropisomers with excellent stereocontrol. Two complementary systems were devised employing CPA-salt complex or Ni(OTf)₂/chiral SaBOX ligand catalytic system for accessing representatively atropisomeric biaryls NOBIN as well as BINAM derivatives respectively (Scheme 1).



Scheme 1. Organocatalytic Asymmetric synthesis of NOBIN and BINAM derivatives