Nickel-Catalyzed Enantioselective Pyridone C-H Functionalizations Enabled by a Bulky N-Heterocyclic Carbene Ligand

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2- and 4-pyridone rings are prevalent heteroaromatic structures, which are found in a broad variety of natural products, bioactive agents and approved drugs.¹ Over the past decade, rapid advances in C-H functionalization technology have been demonstrated to be of utility for the preparation of functionalized pyridones.² However nickel-catalyzed enantioselective C-H functionalizations are very rare and underdeveloped. Previously, we reported an endo-selective annulation protocol of N-alkenyl-2-pyridones.³ Cooperative Lewis acid/nickel(0)-catalysis⁴ and application of N-heterocyclic carbene ligands (NHCs) enabled C-H activation and regioselective cyclization under formation of chiral annulated 2-pyridones. A variety of known chiral NHCs have failed to achieve a synthetically useful control of enantioselectivity.⁵ Here, we introduce a class of sterically demanding chiral NHCs with large modulation opportunities, enabling the nickel(0)-catalyzed C-H functionalization of 2- and 4-pyridones in excellent yields and enantioselectivities.⁵ Their close relationship to the achiral privileged ligand IPr holds the promise of enabling further catalytic enantioselective transformations with different transition metals.