

# A Proton-Responsive Annulated Mesoionic Carbene (MIC) Scaffold on Ir Complex for Proton/Hydride Shuttle: An Experimental and Computational Investigation on Reductive Amination of Aldehyde

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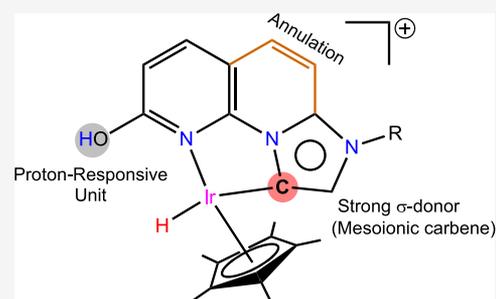
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**ABSTRACT:** A Cp\*Ir(III) complex (**1**) bearing a proton-responsive hydroxy unit on an annulated imidazo[1,2-*a*][1,8]naphthyridine based mesoionic carbene scaffold was synthesized by two different synthetic routes. The molecular structure of **1** revealed an anionic lactam form of the ligand. The acid–base equilibrium between the lactam-lactim tautomers on the ligand scaffold was examined by <sup>1</sup>H NMR and UV–vis spectra. The p*K*<sub>a</sub> of the appendage –OH group in the lactim form of **1** was estimated to assess the proton transfer property of the catalyst. The catalytic efficacy of **1** for reductive amination of aldehyde was evaluated by utilizing three different hydrogen sources: molecular H<sub>2</sub>, <sup>t</sup>PrOH/KO<sup>t</sup>Bu combination, and HCOOH/Et<sub>3</sub>N (5:2) azeotropic mixture. The HCOOH/Et<sub>3</sub>N (5:2) azeotropic mixture protocol was found to be the best among the three different hydrogenation methods. Catalyst **1** hydrogenates imines chemoselectively over carbonyls under the reaction conditions. A range of aldehydes was reductively aminated to the corresponding secondary amines using the HCOOH/Et<sub>3</sub>N (5:2) azeotropic mixture. Further, catalyst **1** showed high efficiency for the reduction of a wide variety of N-heterocyclic imine derivatives. The lactam-lactim tautomerization of the ligand system is proposed for direct hydrogenation, whereas only the lactam form operates in the strongly basic medium (<sup>t</sup>PrOH/KO<sup>t</sup>Bu). Under HCOOH/Et<sub>3</sub>N (5:2) conditions, the lactam scaffold is not protonated; rather, an outer-sphere hydride transfer from formate to the Ir is proposed, which is supported by <sup>1</sup>H NMR and DFT calculations. Finally, ligand-promoted hydride transfer from metal-hydride to the protonated imine affords the corresponding amine. A close agreement between the experimentally estimated and computed thermodynamic/kinetic parameters gives credence to the metal-ligand cooperative mechanism for the imine hydrogenation reaction using the HCOOH/Et<sub>3</sub>N (5:2) azeotropic mixture.



## INTRODUCTION

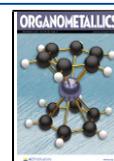
A protic functionality suitably placed on a ligand scaffold accelerates the hydrogenation/dehydrogenation reactions.<sup>1</sup> The protic ligand is capable of adapting between two distinct electronic states on gaining or losing a proton. The ligand electronics influences the proton transfer at the secondary coordination sphere and the hydride transfer at the metal center to/from a suitable partner. Several factors must be considered to develop an efficient hydrogen transfer catalyst that include the spatial position of the proton-responsive unit (PRU) with respect to the metal, the acid/base properties of the PRU, and the metal hydricity.<sup>2</sup> The metal-ligand cooperative action activates a hydrogen molecule (or another hydrogen source) to generate the hydrogenated form of the catalyst that features a nucleophilic hydride at the metal center and a proton on the ligand, which are subsequently transferred to a suitable substrate. The hydrogenated form of the catalyst is then regenerated by abstracting a hydride and a proton from the primary reductant.

In recent years, significant advances have been made on the design and development of protic catalysts for a wide variety of

hydrogenation and dehydrogenation reactions.<sup>3</sup> Among different PRUs, the –OH/–O<sup>–</sup> couple has been exploited widely in (de)hydrogenation related reactions. Shvo's catalyst and its other metal analogues with hydroxy/keto functionality have been studied extensively for a wide range of hydrogenation and transfer hydrogenation reactions of aldehydes, ketones, imines, alkynes, and alkenes.<sup>4</sup> Fujita and Yamaguchi examined the interconversion between lactam and lactim forms of the 2-pyridonate and bipyridonate ligands on Ir for the reversible dehydrogenation/hydrogenation of organic molecules.<sup>1b,5</sup> Himeda has developed an array of bidentate protic ligands based on bipyridine, bipyrimidine, and azole-pyridine/pyrimidine scaffolds and studied the catalytic efficacies of

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