

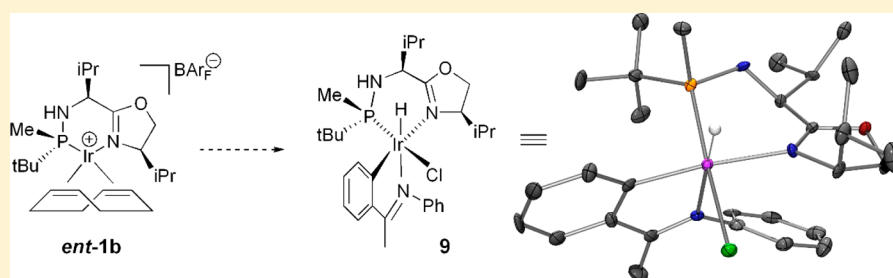
P-Stereogenic and Non-P-Stereogenic Ir–MaxPHOX in the Asymmetric Hydrogenation of *N*-Aryl Imines. Isolation and X-ray Analysis of Imine Iridacycles

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S Supporting Information



ABSTRACT: A small library of Ir–MaxPHOX catalysts has been applied to the asymmetric hydrogenation of *N*-aryl imines. A structure–activity analysis of the three-chiral-center MaxPHOX ligand has been performed. Using complex **1b**, the hydrogenation of *N*-aryl imines took place with up to 96% enantiomeric excess at atmospheric pressure of hydrogen and low temperature. The impact of the stereochemical information at the phosphorus center is small with respect to the selectivity, but large with respect the catalyst activity. Non-P-stereogenic analogs of MaxPHOX were also synthesized and tested, but they provided lower selectivity. The selectivity observed could be explained by taking into account that the actual catalysts were cyclometalated imine complexes formed in situ. [IrHCl(MaxPHOX)(imine)] complexes **9** and **10** were synthesized and characterized by X-ray crystallography. These complexes, via chloride abstraction, provided the active catalytic species with the same levels of selectivity. Finally, the influence of the counterion on the catalyst performance was also studied.

INTRODUCTION

Many active pharmaceutical ingredients and agrochemicals contain chiral amines. In this regard, there is considerable interest in developing efficient methods that provide single enantiomers of such compounds, thus avoiding inefficient racemate resolutions. Metal-catalyzed asymmetric hydrogenation of imines is one of the methods of choice in terms of industrial applicability.¹ While ruthenium has provided excellent results in transfer–hydrogenation reactions, iridium has shown better performance for the direct hydrogenation of imines.² In this field, Pfaltz and others have shown that Ir–P,N catalysts provide an excellent platform for the reduction of *N*-aryl imines.³

We recently developed the MaxPHOX ligand system, which is built from three fragments: an amino alcohol, an amino acid, and a P-stereogenic phosphinous acid (Figure 1).⁴ The Ir–MaxPHOX complexes have shown outstanding selectivity in the hydrogenation of cyclic enamides.⁵ One of the key advantages of the MaxPHOX ligand is the structural diversity arising from its possible configurations and substitution patterns, which can be adapted to a specific reaction. To demonstrate this versatility, here we report on the asymmetric

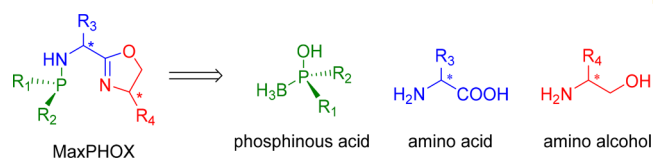


Figure 1. General structure of the MaxPHOX ligands.

hydrogenation of *N*-aryl imines using the Ir–MaxPHOX catalyst system. To study the influence of the stereogenic center of the phosphorus atom, non-P-stereogenic MaxPHOX ligands were also synthesized and evaluated in the asymmetric hydrogenation. We spotted a catalyst that hydrogenates *N*-aryl imines with up to 96% enantiomeric excess (ee) at atmospheric pressure of hydrogen (balloon). The putative imine-cyclometalated catalyst derivatives were also isolated, characterized by X-ray analysis, and tested in the reaction.

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