



SYNTHESIS OF NEW CHIRAL BRONSTED ACIDS

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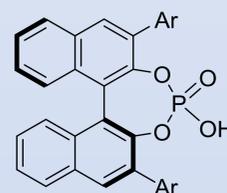
Introduction

In the last decade chiral Brønsted acid catalysts, initially developed by Akiyama⁽¹⁾ and Terada⁽²⁾, have been successfully used as promoters of a wide class of transformations.

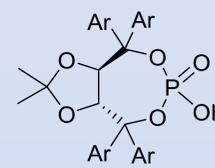
Different families of Brønsted Acids have been developed up to now, but chiral phosphoric acid derivatives have proved to be the most promising one. They can catalyze a great number of reactions such as: reductions of ketoimines and α,β -unsaturated carbonyl compounds, addition of several nucleophiles to imines, hydrophosphonylation reactions, Diels-Alder and aza-Diels-Alder cycloadditions, Friedel-Craft reactions and many others.⁽³⁾

However, at the present, chiral phosphoric acid catalysts are almost exclusively based on the non-natural BINOL scaffold; only one example of TADDOL-derived acids exists: the scarcely active TADDOP (Figure 1).

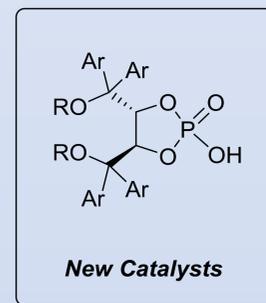
Our aim is to synthesize a new class of enantiomerically pure Brønsted acids based on tartaric acid as cheap chiral scaffold (Figure 1).



BINOL derivatives
(Ar=Ph, 1)



TADDOP



New Catalysts

Figure 1

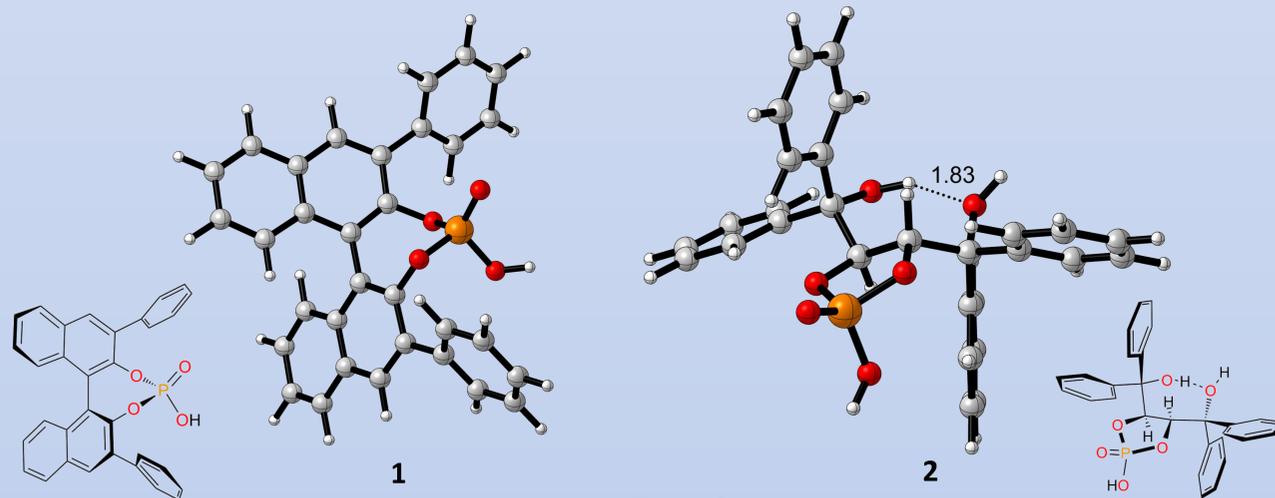


Figure 2

Features

These new catalysts present a very rigid structure due to the presence of a five membered ring; additionally when R=H (Figure 1) an intramolecular hydrogen bond can be formed forcing the aryl groups in a rigid position.

In Figure 2 are depicted the PM6 level-optimized structures of the well known 3,3'-diphenylbinaphthylphosphoric acid (1) and of a new catalyst (2). BINOL-derived catalyst creates a chiral environment because of the phenyl rings in the 3,3' positions of the binaphthyl moiety. Also catalyst (2) may generate a chiral environment defined by the aryl groups; the steric hindrance can be further modulated by simply introducing more bulky groups on the aromatic rings.

Synthesis

A key point in the development of the new chiral phosphoric acids is an easy synthesis starting from commercially available cheap materials (in order to obtain efficient but also convenient catalysts). Indeed only two steps are needed to synthesize these molecules, while at least five steps are required in the synthesis of the simplest BINOL-derived phosphoric acids.

Starting from diethyl tartrate as cheap chiral reagent, a Grignard addition reaction followed by the ring closure with phosphoryl chloride lead to the desired Brønsted acid in good yields, while the use of phosphorous trichloride instead of phosphoryl chloride and consecutive oxidation with iodine afforded a different *non-C₂* symmetric phosphoric acid 3 (Figure 3).

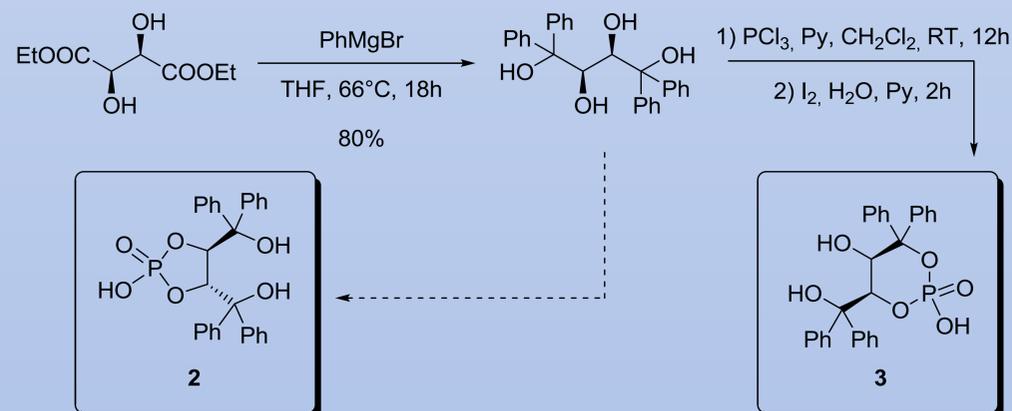


Figure 3

Applications

As mentioned above, the new catalysts could promote a large number of reactions. Typical examples that will be firstly tested are: the nucleophilic addition of acetylacetone to *N*-Boc-aldimines⁽¹⁾, the Hantzsch ester mediated reduction of *N*-aryl-ketoimines⁽⁴⁾ and the aza-Diels-Alder⁽⁵⁾ reaction with Danishefsky's diene (Figure 4).

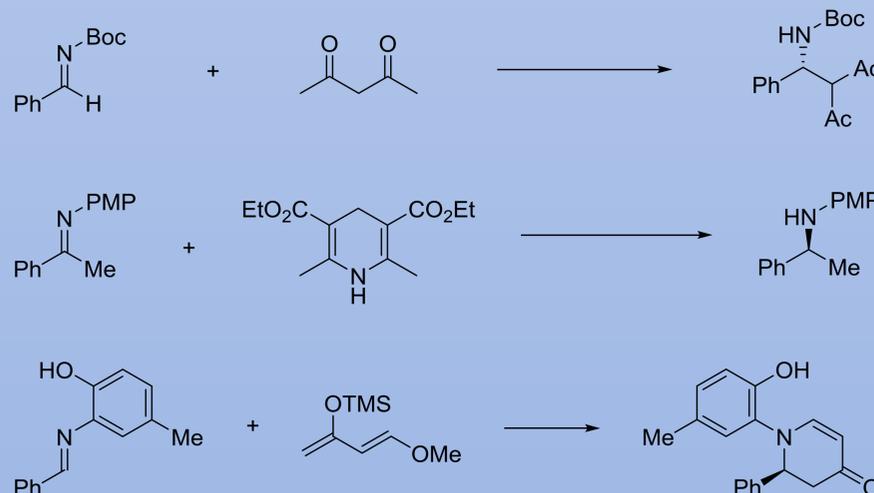


Figure 4

References

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