Enantioselective Hydrophosphonylation of *in Situ* Generated *N*-Acyl Ketimines Catalyzed by BINOL-Derived Phosphoric Acid

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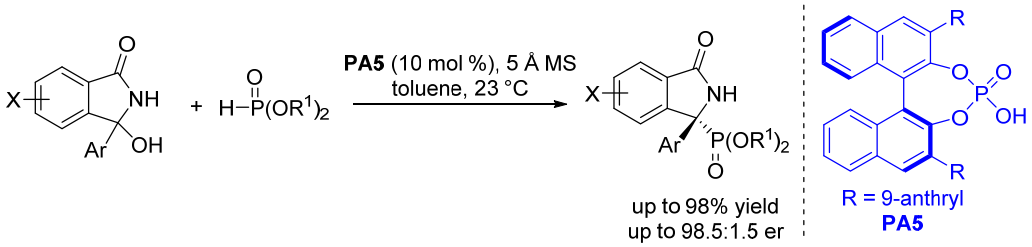
Abstract:
Enantiomerically enriched α-amino phosphonates, and phosphonic acids are considered as important surrogates for α-amino acids with an impressive diversity of biological activities. On the other hand, isoindolinones are important structural scaffolds from a synthetic perspective.



Scheme: Organocatalytic Enantioselective Phospha-Mannich Reaction.

Herein, an efficient route to pharmacologically interesting isoindolinone-based α-amino phosphonates is described *via* asymmetric hydrophosphonylation of *in situ* generated ketimines catalyzed by BINOL-derived phosphoric acid. The reaction proceeds smoothly at ambient temperature affording a variety of α-amino phosphonates with a quaternary stereogenic center embedded in isoindolinone motif in high yields with excellent enantiomeric ratios (up to 98.5:1.5 er). The usefulness of this protocol has also been demonstrated by the synthesis of biologically interesting α-amino phosphonic acid, monoester and other valuable synthetic intermediates based on isoindolinones.

References:

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