Direct Catalytic Enantioselective Hydrophosphonylation of N-Unprotected Ketimines

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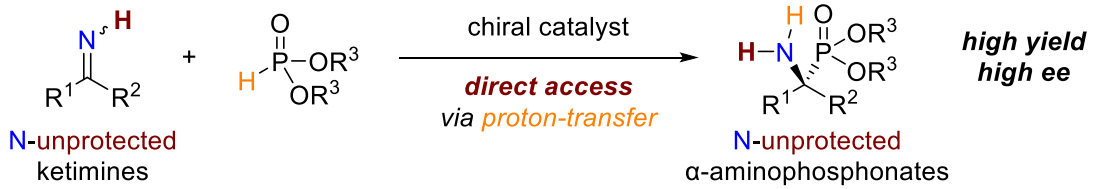
α-Aminophosphonates are useful α-amino acid analogs and important building blocks for bioactive and pharmaceutical compounds. One of the most efficient methods for synthesizing enantioenriched α-aminophosphonates is direct catalytic enantioselective hydrophosphonylation of imines.[1] In particular, hydrophosphonylation of ketimines is useful for synthesizing α-tetrasubstituted α-aminophosphonates. Nevertheless, all the reported reactions use N-protected ketimines for controlling stability, reactivity, and stereoselectivity and require protection/deprotection steps for obtaining N-unprotected α-aminophosphonates.

To circumvent the problem, our group is recently interested in the use of N-unprotected ketimines as a substrate because N-unprotected amines are directly obtained without such protection/deprotection steps, which can contribute to the Sustainable Development Goals (SDGs).[2] To this end, herein we report direct catalytic enantioselective hydrophosphonylation of N-unprotected ketimines.[3] By choosing the appropriate chiral catalyst and reaction conditions, we achieved the direct synthesis of N-unprotected α-aminophosphonates in high yield and high enantioselectivity. Detailed reaction conditions and substrate scope will be disclosed in this presentation.



(1) For reviews of enantioselective hydrophosphonylation of imines, see: (a) P. Merino, E. Marqués-López, R. P. Herrera, *Adv. Synth. Catal.* **2008**, *350*, 1195–1208; (b) M. Ordóñez, H. Rojas-Cabrera, C. Cativiela, *Tetrahedron* **2009**, *65*, 17–49.

(2) For a review, see: (a) K. Morisaki, H. Morimoto, T. Ohshima, *ACS Catal.* **2020**, *10*, 6924–6951. For selected our contributions, see: (b) R. Yonesaki, Y. Kondo, W. Akkad, M. Sawa, K. Morisaki, H. Morimoto, T. Ohshima, *Chem. Eur. J.* **2018**, *24*, 15211–15214; (c) T. Kadota, M. Sawa, Y. Kondo, H. Morimoto, T. Ohshima, *Org. Lett.* **2021**, *23*, 4553–4558.

(3) Y. Kondo, K. Yamada, T. Kadota, H. Morimoto, T. Ohshima, *manuscript in preparation*.