Development Strategy of SEGPHOS and Smart Approaches to β-Amino Acids

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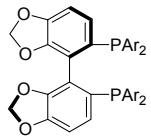
Introduction

Two topics out of our continuous efforts in development of asymmetric hydrogenation are reported. Presented herein are: 1) development of SEGPHOS family, a series of biaryl diphosphine ligands with narrow dihedral angle and 2) new and effective method to access to β-amino acid derivatives via asymmetric hydrogenation of corresponding unprotected enamines.

Results and Discussion

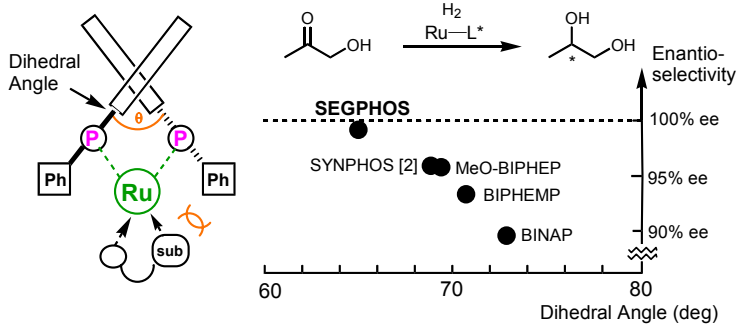
1. Development of SEGPHOS

We have developed SEGPHOS, powerful tool in asymmetric hydrogenation.[1]



Ar = C_6H_5:	**SEGPHOS**
4-$CH_3C_6H_4$:	**T-SEGPHOS**
3,5-$(CH_3)_2C_6H_3$:	**DM-SEGPHOS**
4-CH_3O-3,5-$(CH_3)_2C_6H_2$:	**DMM-SEGPHOS**
4-CH_3O-3,5-$(t\text{-}C_4H_9)_2C_6H_2$:	**DTBM-SEGPHOS**

The design of the ligands is based on dihedral angle control. Inspired by the observation that ligands with narrower dihedral angles give higher enantioselectivities in asymmetric hydrogenation of hydroxyacetone, we searched for ligands with narrower dihedral angle, leading to SEGPHOS. As expected, SEGPHOS afforded the highest enantioselectivity in hydrogenations.



Featured performances of SEGPHOS in asymmetric hydrogenation include:

- Highest enantioselectivities with functionalized ketones
- Much higher catalytic activity (5-10 times more than that of BINAP)

Applications of SEGPHOS to other asymmetric reactions such as hydrosilylation and cyanomethylation are also outlined.

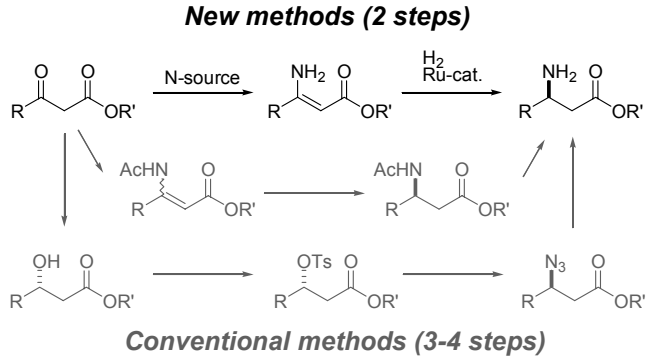
2. β-amino acids via asymmetric hydrogenation of enamines

β-amino acids are attracting increasing attentions in pharmaceutical industry. Recently, we have developed an effective system to hydrogenate unprotected enamines to the corresponding β-amino acid derivatives in high enantioselective fashion. [3]

The system is advantageous than conventional method because of:

- Shorter reaction steps
- No need of protection / deprotection steps
- Lower wastes

Scope and applicability will be discussed in detail.



Significance

These two technologies would achieve great contribution in reducing cost and environmental impact in obtaining optically active compounds.

References

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2. Duprat de Paule, S.; Jeulin, S.; Ratovelomanana-Vidal, V.; Genêt, J.-P.; Champion, N.; Deschaux, G.; Dellis, P. *Org. Proc. Res. Dev.* **2003**, *7*, 399.
3. Matsumura, K.; Zhang, X.; Saito, T. US 0023344 A1, 2004.