

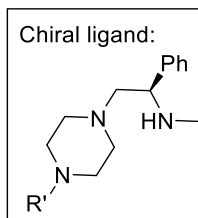
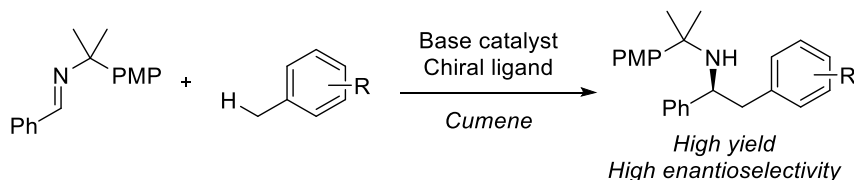
Development of Chiral Strong Brønsted Base Catalyst Systems for Asymmetric Addition Reactions of Various Alkylarenes with Imines

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Keywords: Alkylarene; Imine; Strong Base Catalysis; Chiral Amine Ligand; Asymmetric

Highly abundant, stable, and available unactivated alkylarenes such as toluene and xylenes are ideal building blocks for introduction of aromatic ring moieties into organic frameworks. This makes direct functionalization of their benzylic carbon – hydrogen (C–H) bonds an attractive field of research. Various strategies to achieve direct C–H functionalization have been investigated, one of which is deprotonation to form a benzyl anion by using a strongly basic mixture of t -BuLi and KO t Bu called Schlosser's base. However, achieving catalytic reactions is considered to be difficult because an intermediate formed after the addition of benzyl anion to an electrophile is not basic enough to deprotonate the next alkylarene molecule. On the other hand, our group's strategy to design a strongly basic anionic reaction intermediate was successful, and it was applied to weakly acidic pronucleophiles, such as esters, amides, nitriles as well as alkylarenes ¹. Asymmetric reactions were also made possible by chiral modification of counter cations.

In our previous reports, asymmetric addition reactions of alkylarenes with various imines proceeded smoothly in high yields and enantioselectivities using an alkylpotassium salt and KHMDS base catalyst system, solvent amount of alkylarene and a chiral ligand with N-methylpiperazine moiety ². However, scope of alkylarenes was limited due to their generally high freezing points, making them incompatible with low reaction temperature. We hypothesized that expansion of alkylarene scope for asymmetric addition reactions might be achieved by developing a new catalyst system that employed a non-competing, low freezing point solvent. Here, we report examination of solvents, catalyst preparation conditions optimization and chiral ligand screening for the asymmetric addition reaction of toluene with *p*-methoxycumyl imine. It was found that cumene was a suitable solvent and that, under newly optimized catalyst preparation conditions, the catalyst system with chiral diamine ligands containing an N-alkylpiperazine moiety favored higher yields and enantioselectivities. Interestingly, the enantioselectivities were further improved by increasing steric bulkiness of the N-alkyl substituent.



- 1) Yamashita, Y. Kobayashi, S. *Synlett*, **2020**, 31, 14.
- 2) Kobayashi, S. *et al. Commun Chem*, **2021**, 4, 36.