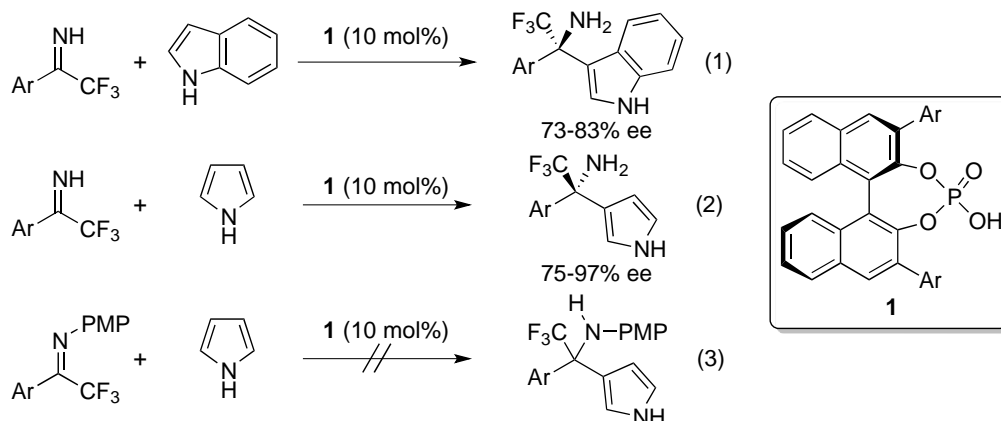


# ENANTIOSELECTIVE FRIEDEL-CRAFTS ALKYLATION REACTION OF TRIFLUOROMETHYLATED N-H KETIMINE WITH HETEROARENES BY MEANS OF CHIRAL PHOSPHORIC ACID

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Construction of  $\alpha$ -trifluoromethylated amines in optically pure form is one of the important topics of research interest because of its interesting biological activity. Nucleophilic addition to *N*-protected trifluoromethylated ketimine, and subsequent deprotection of the *N*-protecting group will furnish  $\alpha$ -trifluoromethylated *N*-free amines.<sup>[1]</sup> Trifluoromethylated *N*-H ketimine is known to be relatively stable among *N*-H ketimines. Nucleophilic addition toward trifluoromethyl *N*-H ketimine will provide a straightforward method for the preparation of  $\alpha$ -trifluoromethylated *N*-free amines because deprotection of the *N*-protecting group is obviated. As part of our continued interest in the chiral phosphoric acid catalysis, we investigated Friedel-Crafts alkylation reactions of heteroarenes, such as indole and pyrrole, with trifluoromethylated *N*-H ketimines by means of chiral phosphoric acid. Corresponding  $\alpha$ -trifluoromethylated amines were obtained in good yields and with good to excellent enantioselectivity (Schemes 1 and 2).<sup>[1]</sup> Interestingly, *N*-PMP (*p*-methoxyphenyl) substituted ketimine did not participate in the reaction and the corresponding *N*-PMP amine was not obtained (Scheme 3). It was found that *N*-H ketimines are more reactive than *N*-PMP ketimine.



[1] Henseler, A.; Kato, M.; Mori, K.; Akiyama, T. *Angew. Chem. Int. Ed.* **2011**, *50*, 8180–8183.

[2] Miyagawa, M.; Yoshida, M.; Kiyota, Y.; Akiyama, T. *Chem. Eur. J.* **2019**, DOI:10.1002/chem.201901020.