One-pot enantiodivergent synthesis of axially chiral biaryls using organocatalyst

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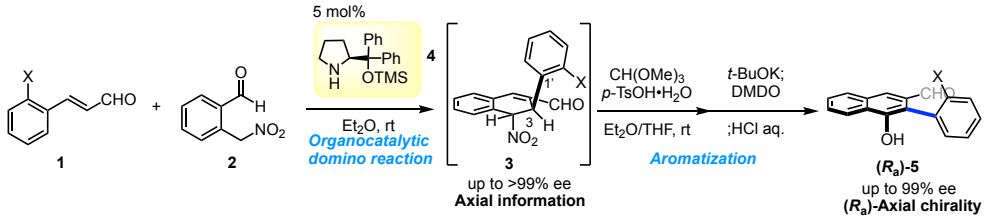
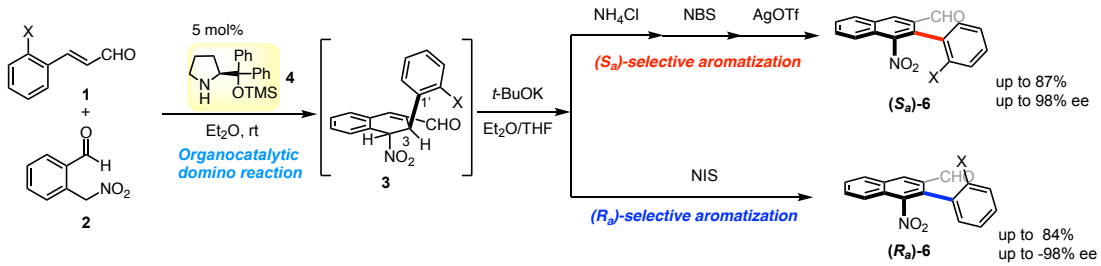
Axially chiral biaryls have broad utility for not only chiral ligands and organocatalysts, but also bioactive molecules in nature. Thus, it is important to develop a new methodology for the enantioselective construction of axially chiral molecules. We have already reported that axially chiral biaryl **5** was obtained with excellent enantioselectivity and complete axial inversion by removal of the central chirality from the enantio-enriched dihydronaphthalene **3**,[1)] which was synthesized as a single axial conformer from nitroaldehyde **2** and unsaturated aldehyde **1** using organocatalyst **4**.[2)] In this presentation, we will report a one-pot enantiodivergent synthesis of axially chiral biaryls using a catalytic amount of the chiral source.



The organocatalyst mediated domino Michael/aldol reaction afforded the enantio-enriched dihydronaphthalene **3**, which was converted to axially chiral biaryl **(*S*$_a$)-6** with excellent enantioselectivity by sequential treatment of *t*-BuOK/NH_4Cl/NBS/AgOTf in one-pot. On the other hand, the treating of **3** with *t*-BuOK/NIS afforded **(*R*$_a$)-6** with excellent enantioselectivity in one-pot. These axially chiral compound **6** were useful as a new chiral building block and could be transformed into other axially chiral biaryls without losing the enantiopurity. The reaction mechanism of enantiodivergence is also investigated by isolation of intermediates and investigation of their reactivities. The plausible reaction mechanism will be proposed.



1) D. Enders, C. Wang, J. W. Bats, *Synlett,* **2009**, *11*, 1777.

2) S. Koshino, A. Takikawa, K. Ishida, T. Taniguchi, K. Monde, E. Kwon, S. Umemiya, Y. Hayashi, *Chem. Eur. J.* **2020**, *26*, 4524.