

Studies on Catalytic C–H Functionalization Reactions and Their Enantiocontrol

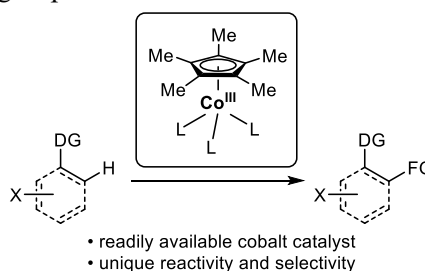
(Faculty of Pharmaceutical Sciences and Global Station for Biosurfaces and Drug Discovery, Hokkaido University) ○Tatsuhiko Yoshino

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Direct functionalization of inert C–H bonds using transition metal catalysts enables streamlined syntheses of valuable and complex organic molecules from readily available feedstocks. In this presentation, I would like to talk about our studies on Cp*Co(III)-catalyzed C–H functionalization reactions, enantioselective C–H functionalization using Rh(III) or Co(III) catalysts hybridized with chiral disulfonates or chiral carboxylic acids, and the development of chiral paddle-wheel diruthenium catalysts and their application for C–H amination reactions.

(1) Cp*Co(III)-catalyzed C–H Functionalization Reactions

Rhodium complexes bearing a pentamethylcyclopentadienyl ligand, Cp*Rh(III), have been widely used for C–H functionalization reactions since 2007. In 2013, we first reported that a Cp*Co(III) complex also catalyzes directing group-assisted C–H functionalization reactions.¹ After this discovery, we and other many research groups have developed various kinds of C–H functionalization reactions using Cp*Co(III) catalysts. Notably, Cp*Co(III) catalysts often exhibit distinctive reactivity and selectivity compared with Cp*Rh(III) catalysts due to the low electronegativity, small ionic radius, and hard nature of cobalt.²



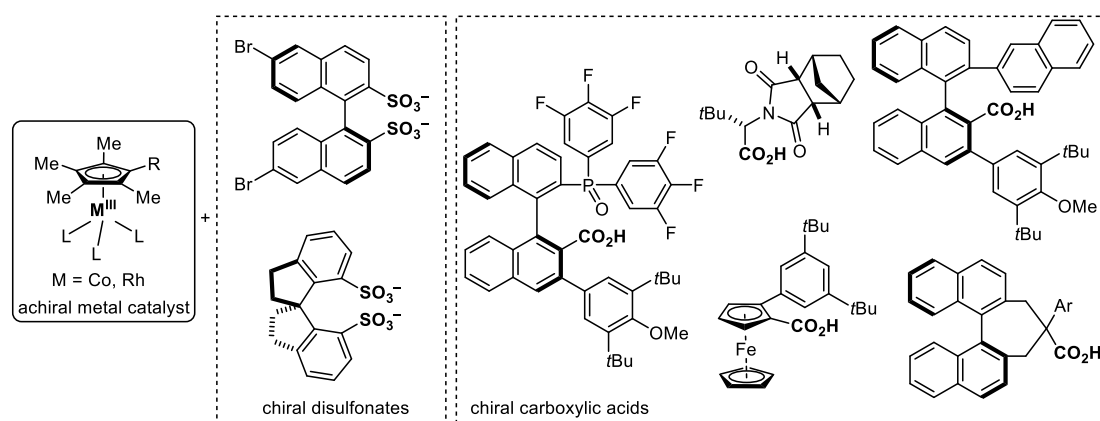
(2) Enantioselective C–H Functionalization Reactions Using Rh(III) or Co(III) Catalysts Hybridized with Chiral Disulfonates or Chiral Carboxylic Acids.

While Cp*M(III) (M = Co, Rh, Ir) complexes are highly reactive and versatile catalysts for C–H functionalization reactions, the presence of the auxiliary Cp* ligand impedes the use of standard chiral bidentate ligands for enantiocontrol of their catalytic processes. Although the introduction of well-designed chiral Cp^x ligands has successfully realized catalytic enantioselective C–H functionalization reactions, the design, synthesis, and derivatization of such elaborated chiral Cp^x ligands and their metal complexes are laborious work, and thus could be a major obstacle for further development of enantioselective C–H functionalization.

In 2018, we reported that the combination of a Cp*Rh(III) catalyst and a chiral anion, 1,1'-binaphthyl-2,2'-disulfonate (BINSate) or 1,1'-spirobiindane-7,7'-disulfonate (SPISate),

catalyzes enantioselective C–H alkylation of 2-phenylpyridines and 6-arylpyridine derivatives with high selectivity.³ The chiral anions might control the enantioselectivity via the formation of a chiral proton source in situ, although the mechanism is still unclear.

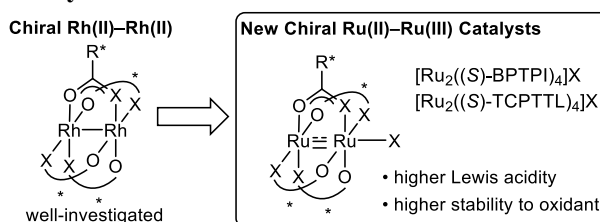
A C–H cleavage step under electrophilic metal catalysis often proceeds via a concerted metalation-deprotonation (CMD) mechanism assisted by a carboxylate base coordinating to a metal center, indicating that the introduction of a chiral carboxylic acid is a straightforward approach to realize selective activation of enantiotopic C–H bonds. Based on this notion, we developed a variety of new chiral carboxylic acids suitable for enantioselective C–H bond cleavage of various prochiral substrates.⁴ The combination of these chiral acids with Rh(III) or Co(III) is an efficient catalytic system for enantioselective C(sp²)-H functionalization as well as C(sp³)-H functionalization.



(3) Chiral Paddle-Wheel Diruthenium Catalysts

Inspired by well-investigated chiral paddle-wheel dirhodium catalysts, we recently developed new chiral paddle-wheel diruthenium catalysts, which exhibit higher Lewis acidity and higher stability under

oxidizing conditions than dirhodium catalysts probably due to the higher oxidation state of the dimetal center (Ru(II)–Ru(III)).⁵ These ruthenium catalysts were applied to enantioselective intramolecular C–H amination reactions and other transformations.



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