Abstract of Doctoral Dissertation

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Enantioselective C–H Functionalization using Chiral Carboxylic Acid and d6 Transition Metal Complexes
(キラルカルボン酸と d6 型遷移金属錯体を用いたエナンチオ選択的 C–H 官能基化)

1. Transition-metal/chiral carboxylate ligand catalysts for enantioselective C–H functionalization: Transition-metal-catalyzed asymmetric C–H activation via concerted metalation deprotonation offers a powerful strategy to build up stereochemical complexity from readily available hydrocarbon feedstocks. Most of the stereochemical models of these asymmetric reactions involve destabilizing steric interactions as the primary effect of enantiocontrol. Consequently, the design of the ligands and catalysts primarily focused on the incorporation of rigid structural elements to prevent conformational flexibility. Achiral $Cp^xM(III)$ (M = Co, Rh, Ir)-catalyzed asymmetric C–H functionalization enabled by monodentate chiral carboxylic acids (CCAs) with high enantioselectivity have been realized. Based on this background, I developed Cp*Rh(III)/CCA-catalyzed enantioselective C(sp^3)–H alkylation of 8-ethylquinolines with α,β-unsaturated ketones or acrolein.

While Ru(II)-catalyzed C–H activation has also achieved great success during the last two decades, Ru(II)/CCA-catalyzed asymmetric C–H functionalization reactions has only been reported very recently. Sulfoximines and sulfondiimines are aza-analogs of sulfones with a sulfur chiral center and have attracted attention in organic and medicinal chemistry. Based on these backgrounds, I developed enantioselective Ru(II)/CCA-catalyzed C(sp^2)–H functionalization reactions of sulfoximines and sulfondiimines.

2. Cp*Rh(III)/CCA-catalyzed enantioselective C(sp^3)–H alkylation of 8-ethylquinolines with α,β-unsaturated ketones or acrolein: With the optimized conditions using $[Cp^*RhCl_2]_2$ and a BINOL-derived CCA, various substituted 8-alkylquinolines and vinyl ketones afforded the corresponding products in good yield and er.

3. Ru(II)/CCA-catalyzed enantioselective C(sp^2)–H alkylation of sulfoximines: I found that a pseudo-C_2-symmetric binaphthyl CCA was suitable for Ru(II)-catalyzed enantioselective C–H bond cleavage of prochiral sulfoximines and a subsequent reaction with sulfoxonium ylides to afford benzothiazine 1-oxides in moderate to good er. Suloximines with various substituents and sulfoxonium ylides generally provided the products in moderate to good er.

4. Ru(II)/CCA-catalyzed enantioselective C(sp^2)–H alkylation of sulfondiimines: Finally, I investigated the application of the Ru(II)/CCA catalytic system for enantioselective C–H functionalization of sulfondiimines, which are promising compounds for medicinal chemistry but less investigated in organic synthesis. I developed new CCAs with a spirobiindane backbone, which exhibited higher enantioselectivity than other CCAs for desymmetrization of various

sulfondiimines with sulfoxonium ylides as well as a kinetic resolution of a racemic sulfondiimine. The spirobiindane scaffold is much less flexible than a binaphthyl backbone, which would lead to the construction of a more rigid chiral environment and significantly improved er.

5. Summary: I have developed Rh(III)/CCA- and Ru(II)/CCA-catalyzed enantioselective C–H functionalization reactions for the synthesis of 8-substituted quinolines, sulfur-stereogenic benzothiazine 1-oxides, and 1,2-benzothiazine 1-imines. The reactions showed good functional group compatibility and enantioselectivity. In addition, I have newly developed chiral spiro CCAs, which significantly improved the enantioselectivity.