【Grant-in-Aid for Scientific Research (S)】

Science and Engineering (Chemistry)

Title of Project : New Frontier of Substrate-Controlled Chemical Reaction

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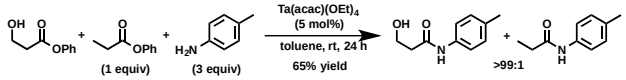
Research Area : Basic Chemistry, Organic Chemistry
Keyword : Substrate Controlled Chemical Reaction

【Purpose and Background of the Research】

Unlike reagent controlled reactions which played significant role in organic synthesis in the past, substrate controlled reactions are relatively newer approach. Nevertheless, since its discovery the latter has become an indispensible tool in modern organic synthesis. In these reactions, an electron donor polar substituent in the substrate, namely a "directing group", actively facilitates the transient interplay between the achiral substrate and the chiral catalyst via nonbonding interaction, in such a fashion that the incoming group attacks from a particular regio-position with enantiotopic face. Thus the region- and stereochemical outcome of an organic reaction is largely dependent on the nature of the substrate.

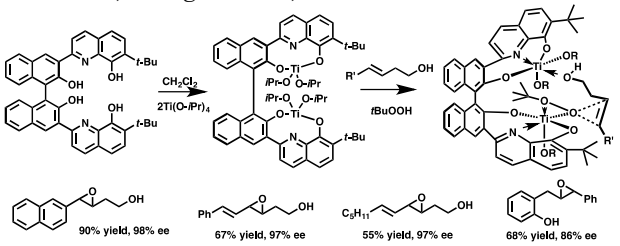
【Research Methods】

In 2016, we observed that the transformation of ester to amide is able to proceed efficiently using a new tantalum catalyst. Substrate having a β-OH group is selectively transformed to amide even in the presence of an equimolar amount of structurally related ester lacking β-OH group. This result indicates that the reaction should proceed *via* the formation of metal hydroxyl ester as the transition state (*J. Am. Chem. Soc.* 2016).



Using our new Ta catalyst system, we have tested the possible transformation of serine methyl ester or threonine methyl ester to the corresponding dipeptides. As expected, the desired dipeptides are prepared in high yields. After the reaction, the Boc protecting group can be removed without any problems.

The new Ti-complex developed in our group acts as a bimetallic catalyst for regio- and enantioselective epoxidation, sulfoxidation, and amine oxide synthesis. The selective binding abilities of the ligand with metal ions in the bimetallic catalyst-scaffold bear a resemblance to biological enzymatic systems. We are planning to prepare various ligands with not only 8-hydroxyl quinolone as the metal folding site but also orthophenanthroline, dipyridyl, and various heterocyclic sub-unites. Hence, the new ligand system will offer numerous opportunities for various transformations, including epoxidation, sulfoxide synthesis, C-H activation, Diels-Alder reactions, halogenation, etc.



【Expected Research Achievements and Scientific Significance】

Enzyme reaction is one of the long-standing targets for organic synthesis. Unfortunately, however, organic transformation is still much less selective compare to the biological processes. I believe substrate controlled reaction will be able to make a breakthrough for this situation. The concept of this project hopefully may provide one possibility for this future problem.

【Publications Relevant to the Project】

Tsuji,H.;Yamamoto,H. 、 Hydroxy-Directed Amidation of Carboxylic Acid Esters Using a Tantalum Alkoxide Catalyst、J. Am. Chem. Soc.、138、14218-14221、2016

Bhadra,S.;Akakura,M.;Yamamoto,H.、Design of a New Bimetallic Catalyst for Asymmetric Epoxidation and Sulfoxidation、J. Am. Chem. Soc.、137、15612-15615、2015

【Term of Project】 FY2017-2021

【Budget Allocation】 159,200 Thousand Yen

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