【Grant-in-Aid for Scientific Research(S)】
Science and Engineering (Chemistry)

Title of Project：Rapid synthesis of complex molecules using super Brønsted acid catalysis

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Research Area：organic synthesis
Keyword：selective organic synthesis, molecular acid catalysis

【Purpose and Background of the Research】

Selective organic synthesis was refined significantly during the last century and we now have numerous reliable tools for chemical transformations using transition metal catalysis. The recent high demand for green chemistry, however, has required environmentally benign chemical processes, particularly the non-metal catalysis protocols. The present project will attempt to introduce new strong organic non-metal acid catalysis, which is expected to be one of the major tools of organic synthesis of the next generation, and to apply these new catalysts for various organic transformations. Further, the project will attempt to design new super Brønsted acid catalysts, which will give us opportunities to make complex molecules by combining their use with super-silyl reagents. These new processes will establish an unusually short synthetic route to construct complex three-dimensional molecules for which very few synthetic methods are currently available.

【Research Methods】

Combined use of super Brønsted acid catalyst and super-silyl reagent would provide simple and reliable methods to control the otherwise nonstop polymerization process so that it terminates at three or four steps. The super Brønsted acid catalyst serves as an important tool to accelerate and/or decelerate these chemical processes. Further, chiral Brønsted acid catalyst will open a new approach for an asymmetric version of these successive reactions.

Specifically, the super-silyl groups generate a specially designed molecular reaction template within which the polymerization reaction can be stopped by strong stereochemical demands. Thus, we will be able to stop the second, third, and fourth successive reactions for various transformations by choosing the proper reaction conditions and catalysis. For example, the double or triple aldol products could be prepared with high chemoselectivity as well as diastereo stereoselectivity. Using alpha alkoxy or amino silyl enol ethers, we would be able to obtain all the functional polyhydroxy linear carbon chain or amino-hydroxy chains stereo- and regioselectively.

The concept can also be applied to 1,3-butadiene polymerization as well as terminal olefins polymerization processes. Employing these new protocols, we would be able to prepare isoprenoid structures in significantly short steps or 1,3-siloxy derivatives stereoselectively.

【Expected Research Achievements and Scientific Significance】

Flexible and reliable molecular engineering is one of the most sought-after scientific targets of our century. The present proposed strategy would contribute the molecular engineering by providing rapid access of three-dimensional molecules with high stereo- and regioselectivities. The method would be very useful not only for medicinal chemistry but also for material sciences. The Brønsted acid catalyst, which was developed mainly in the principal investigator's laboratories, is the key catalyst for the present proposal. The same catalyst, however, would contribute to numerous other fields of synthesis as an environmentally acceptable green catalyst.

【Publications Relevant to the Project】

(1) Cheon, C.H., Yamamoto, H., A Brønsted Acid Catalyst for the Enantioselective Protonation Reaction, *J. Am. Chem. Soc.*, **2008**,130, 9246-9247.
(2) Boxer, M. B., Yamamoto, H., Ketone Super Silyl Enol Ethers in Sequential Reactions: Diastereoselective Generation of Tertiary Carbinols in One Pot, *J. Am. Chem. Soc.*, **2008**,130, 1580-1583.
(3) Boxer, M. B., Yamamoto, H. "Super Silyl" Group for Diastereoselective Sequential Reactions: Access to Complex Chiral Architecture in One Pot, *J. Am. Chem. Soc.*, **2007**, 129, 2762.

【Term of Project】 FY2011-2015

【Budget Allocation】 165, 600 Thousand Yen

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