The Fifth Green and Sustainable Chemistry Award

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Design of Chiral Organocatalysts and Practical Asymmetric Synthesis of Useful Amino Acids

Recently, the challenge to the green chemistry advances in order to make the better environment with the aim of the environmentally benign chemical synthesis and reactions as well as the environmentally benign molecular design. The change of the quality has been required in the 21st century from the chemistry in the 20th century that wastes resources to prepare necessary materials with spreading the environmental pollution in the field of synthetic organic chemistry. Accordingly, Professor Maruoka investigates the rational design of the environmentally benign chiral organocatalysts, and the application to the practical asymmetric synthesis of useful amino acids.

The phase transfer reactions, where quaternary ammonium salts move between organic and aqueous phases, have been recognized as a convenient and highly useful synthetic tool in both academia and industry because of several advantages of phase transfer reactions (i.e., operational simplicity, mild reaction conditions with aqueous media, environmental consciousness, suitability for large-scale reactions, etc.), which meet the current requirement for practical organic synthesis. In addition, these non-metallic organocatalysts make possible to realize the environmentally benign synthetic reaction processes. Professor Maruoka devised a series of spiro-type chiral phase transfer catalysts derived from commercially available chiral binaphthol, and established practical large-scale synthesis of useful compounds, in particular natural-type and unnatural-type amino acids and peptides for the pharmaceutical purpose. This method allows the large-scale synthesis of various artificial amino acids, which are hitherto difficult to obtain by the previous industrial approaches. Various biologically active amino acids such as L-Dopa, L-Azatyrosine, ACE inhibitor, and dihydro- and tetrahydroisoquinoline alkaloids can be readily synthesized. Moreover, hitherto very difficult, catalytic asymmetric synthesis of α,α-dialkylamino acids can be established by way of sequential double alkylations of glycine derivatives with high enantioselectivity. These chiral catalysts have attracted considerable attention from the industrial world, mainly because about 20% of the top 500 drugs contain amino acids and their derivatives. The chiral phase transfer catalysts, which are now commercially available as Maruoka Catalysts from Sigma-Aldrich Inc. and Wako Pure Chemical Ind., are also applicable to direct asymmetric aldol synthesis, asymmetric alkylation of β-keto esters, asymmetric nitroaldol synthesis, asymmetric conjugate addition, and terminal functionalization of small peptides. Furthermore, a structurally simplified, highly active chiral phase transfer catalyst with the catalysts loading of 0.01 mol% can be designed, and is commercially available from Kanto Chemical Co.

Recently, binapthyl-modified chiral amino acid catalyst and amine catalyst can be also designed as other practical chiral organocatalysts, and successfully applied to the practical asymmetric aldol reaction and asymmetric Mannich reaction.