Retirement

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– Synthetic Organic Chemistry –

On March 31st 2021, Dr. Takeo Kawabata retired from Kyoto University after 32 years of service and was honored with the title of Professor Emeritus of Kyoto University.

Dr. Kawabata was born in Osaka Prefecture on June 12, 1955. He graduated from Faculty of Pharmaceutical Sciences, Kyoto University in 1978, and entered the graduate school. He received the doctoral degree under the direction of Professor Eiich Fujita and Professor Kaoru Fuji in 1983. He studied total synthesis of natural products as a post-doctoral fellow at Indiana University with Professor Paul A. Grieco in 1983–1985. He moved to Sagami Chemical Research Center in 1985, and studied enolate chemistry and asymmetric synthesis of β-lactams with Professor Tamejiro Hiyama and Professor Shiro Terashima. He was appointed an Assistant Professor at ICR in 1989, promoted as Associate Professor in 1998, and Professor in 2004.

Throughout his academic career, Dr. Kawabata's research has been focused on "dynamic chirality" and "dynamic molecular recognition". He proposed dynamic chirality in enolate structure in 1991, and proved that enolates can exist as a chiral form in a limited time scale based on restricted bond rotation around C-C, C-N, and C-O bonds. Since enolates are representative synthetic intermediates, the discovery of dynamic chirality in enolate structure brought a conceptually novel strategy for asymmetric synthesis. The concept of "memory of chirality" was generally recognized, and widely applied in various types of asymmetric syntheses. As an extreme example, asymmetric reactions took place in up to 99% enantiomeric excess via a short-lived chiral enolate intermediate based on the restricted C-O bond rotation, whose half-life of racemization was assumed to be ~ 1 sec at –78 °C. The methods were also applied to industrial production of an anti-tumor drug, veripalib (AbbVie (former Abbott)).

He developed an organocatalyst for asymmetric acylation of alcohols in 1997. The salient feature of the catalyst is conformational change triggered by binding with the reagent (anhydride) via an "induced fit process". In 2007, he developed a catalyst for site-selective acylation of glucose derivatives. The catalyst enables to deliver acyl groups into a secondary hydroxy group at C(4) of the glucose core even in the presence of intrinsically more reactive primary hydroxy group at C(6). The molecular recognition process is highly functional group-tolerant, and the acylation takes places with the desired site-selectivity in the presence of various hydrogen bond donors and acceptors. Recognition of the transition state structure (dynamic molecular recognition) seems to be the key to achieve the catalyst-controlled site-selectivity. The outstanding properties of the catalyst realized extremely short-step total syntheses of natural glycosides. An anti-viral natural glycoside, strictinin (MW 634), has been synthesized from naturally abundant glucose in only 5 steps. The overall synthetic steps were less than half compared with those (11~13 steps) in the previous reports because the the present synthetic route can eliminate the use of protective groups for glucose. Accordingly, he proposed a non-conventional retro-synthetic analysis for total synthesis of natural products based on site-selective and sequential functionalization of unprotected glucose. The strategy was further applied to total syntheses of middle-weight natural glycosides such as tellimagrandin II (MW 938), pterocarinin C (MW 938), cercidinin A (MW 938), punicafolin (MW 938), macarangganin (MW 938), and coriariin A (MW 1874) in only 6 or 7 overall steps from glucose.

He then applied the catalytic strategy to remote asymmetric induction, and found that the related catalysts were quite useful in asymmetric desymmetrization of long chain linear diols by asymmetric acylation as well as asymmetric silylation. Asymmetric desymmetrization of bisphenol derivatives by catalytic bromination was also performed in a highly enantioselective manner. Finally, the strategy for remote asymmetric acylation was successfully applied to asymmetric synthesis of rotaxanes. Highly enantioselective synthesis of chiral mechanically interlocked molecules has been a long-standing dream in organic synthesis. Preparation of an enantiopure rotaxane was achieved by kinetic resolution of the racemate via remote asymmetric acylation promoted by the catalyst.

His educational contribution to Kyoto University is also noteworthy. He has supervised 82 graduate students (40 Ph. D. degrees and 42 Master degrees) and 8 undergraduate students and sent them out to academia and industry.

For his achievements, he was awarded the Pharmaceutical Society of Japan Award for Young Scientists from the Pharmaceutical Society of Japan in 1996, Molecular Chirality Award from Molecular Chirality Research Organization in 2012, the Pharmaceutical Society of Japan Award from the Pharmaceutical Society of Japan in 2017, and the Commendation for Science and Technology by the Minister of Education, Culture, Sports, Science and Technology in 2018.

Dr. Kawabata's contribution to Kyoto University and ICR through his scientific research and education is highly appreciated. His sincere attitude toward science will remain in the memory of the people knowing him for a long time in the future.