HETEROCYCLES, Vol. 90, No. 1, 2015, pp. 3 - 5. © 2015 The Japan Institute of Heterocyclic Chemistry
DOI: 10.3987/COM-14-S(K)Foreword_2

PREFACE TO HETEROCYCLES ISSUE HONORING THE 77TH BIRTHDAY OF PROFESSOR ISAO KUWAJIMA

This issue of HETEROCYCLES is dedicated to Dr. Isao Kuwajima, the Emeritus Professor of Tokyo Institute of Technology, on the occasion of his 77th birthday. It is my tremendous honor to celebrate his "Ki-Ju" by offering this preface as an old boy of the "Kuwajima School".

Dr. Kuwajima was born in 1937 in Naoetsu of Niigata Prefecture, a small town with a long history facing the Sea of Japan. After graduating from the high school of Naoetsu, Dr. Kuwajima entered the Department of Chemistry of Tokyo Institute of Technology where he started his scientific career under the guidance of Prof. Teruaki Mukaiyama. After receiving his Ph.D. from Tokyo Institute of Technology, Dr. Kuwajima continued his research as an Assistant Professor of Mukaiyama's Lab from 1966 to 1970, during which he worked as a post-doctoral fellow for two years in the research group of Prof. E. J. Corey at Harvard University. In 1970, Dr. Kuwajima was appointed as an Associate Professor of Aoyama Gakuin University where his own independent research was initiated. He moved back to Tokyo Institute of Technology after three years and was promoted to Full Professor in 1985.

In the early days of Kuwajima's Lab, very important research projects based on the chemistry of organosilicon compounds were launched. For example, the use of chlorotrimethylsilane in Bouveault-Branc reduction, acyloin condensation, and reductive silylation of organosulfur compounds provided direct access to valuable organosilicon compounds including enol silyl ethers, acylsilanes, and silyloxy cyclopropanes. Even more important is that each of these findings opened the next doors to unique and truly useful synthetic reactions. Dr. Kuwajima expanded the utility of enol silyl ethers dramatically by introducing the activation effect of a fluoride ion, realizing substitution reactions with alkyl halides as well as aldol reactions with aldehydes under mild neutral conditions.

In the same period, Dr. Kuwajima carried out another pioneering work in the chemistry of homoenolate anion. The unique transformation of α-silyl allyl alcohols through Brook rearrangement was designed for generating homoenolate anion equivalents that reacted with electrophiles to form substituted enol silyl ethers in a highly stereoselective fashion. In addition, generation of an ester homoenolate anion was realized by the reaction of 1-alkoxy-1-silyloxycyclopropane with a suitable Lewis acid like zinc chloride. It is noted that his "ester zinc homoenolate" represents one of the very early examples of organozinc compounds possessing a reactive functional group.

Dr. Kuwajima also made significant contribution on development of highly efficient methods for constructing carbocycles with various ring sizes through the cyclization reactions of carbocation species. For example, the regio- and stereoselective [3+2] cycloaddition reaction of a vinyl sulfide derivative, the intramolecular Nicholas reaction of an acetylene dicobalt complex, and the intramolecular cyclization reaction of a dienol silyl ether were designed for the synthesis of five-, seven-, and eight-membered carbocyclic compounds, respectively. While the development of new synthetic reactions remained to be the main objective in Kuwajima's Lab, his research interest gradually shifted toward the total synthesis of natural products with an extremely complex structure.

As the professor of Tokyo Institute of Technology, Dr. Kuwajima accomplished the total synthesis of natural products involving Showdomycin, Cortisone, Taxusin, Taxol, Coriolin, and Ingenol. Because of the contribution in natural product synthesis, Dr. Kuwajima was appointed as the project leader of Grant-in-Aid for Scientific Research on Priority Areas "Exploration of Useful Methodologies and Synthesis of Complex Natural Products" from 1996 to 1999. It should be noted that each of these total synthesis was achieved on the basis of the original reactions and methodologies. Thus, the [3+2] cycloaddition reaction was utilized twice in the total synthesis of Coriolin, and the key step in the Ingenol synthesis was the intramolecular Nicholas reaction. Construction of the highly strained Taxane skeleton was realized through the intramolecular cyclization reaction of a dienol silyl ether, that led to the successful total synthesis of Taxusin and Taxol.

These outstanding achievements clearly show that the extreme originality of Kuwajima's chemistry is based on deep understanding of the molecules and an intimate knowledge of reactions. I remember that Dr. Kuwajima particularly detested his student expecting to get successful results by chance or by monotonous experiments, not by logical strategy. Indeed, his chemistry is constructed on the unique methodologies that come from his philosophy and firm conviction. He often told us about "bigaku (美学)", a Japanese word which refers to aesthetics, in chemistry. The word continues to be the most important one for me, a synthetic organic chemist who is trying to develop unique and truly useful synthetic reactions for natural product synthesis.

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Keiji Tanino is a Professor of Hokkaido University. He was born in Hyogo, Japan in 1963. He received his B.S. in 1985 and his M.D. in 1987 from Tokyo Institute of Technology under the direction of Professor Isao Kuwajima. He was appointed as a Research Associate of the Kuwajima's group at Tokyo Institute of Technology in 1989 and received his Ph.D. in 1994 from the Institute. In 1998, he joined the Department of Chemistry, Hokkaido University and was promoted to Associate Professor in 1999 and then Professor in 2006. His research interest centers around the development of highly selective C-C bond-forming reactions and total synthesis of complex natural products.