HETEROCYCLES, Vol. 101, No. 1, 2020, pp. 1 - 3. © 2020 The Japan Institute of Heterocyclic Chemistry
DOI: 10.3987/COM-19-S(F)Foreword_1

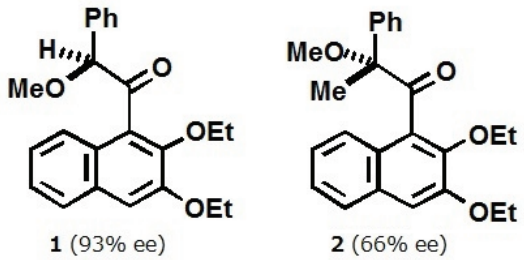
A TRIBUTE TO PROFESSOR KAORU FUJI ON THE OCCASION OF HIS 80TH BIRTHDAY

It is my great honor and pleasure to introduce this special issue of HETEROCYCLES in celebration of the career and 80th birthday of Professor Kaoru Fuji.

I first met Kaoru Fuji at the First Princess Chulabhorn Science Congress, held in Bangkok, Thailand in 1987. Over the more than 30 years since that time, we have developed a very close friendship and have been involved in exciting scientific exchange to this day even though Karou has officially retired from the academic world.

Professor Fuji's research interests over his prolific chemical career have focused on asymmetric synthesis, natural product total synthesis, and the design and synthesis of artificial receptors. I would like to call to your attention here two topics from his seminal contributions to the field of asymmetric synthesis. The first is the asymmetric creation of quaternary carbon centers through addition-elimination processes, which he began soon after he was promoted to the full Professor of the Institute for Chemical Research, Kyoto University in 1983. The most remarkable feature of this reaction is the use of a chiral leaving group in asymmetric synthesis. This was a highly risky idea at that time because asymmetric induction via a chiral leaving group was considered difficult due to the lengthening bond distance between the reacting carbon atom and the leaving group in the transition state in a typical S_N2 reaction. Moreover, the incoming group approaches from the opposite side of the leaving group, which decreases the influences of the chiral leaving group to an incoming nucleophile. Prof. Fuji solved this intriguing problem by designing the reagent with a chiral leaving group at the β-position of nitroolefin to create a quaternary chiral carbon center which pleasingly proceeded with up to 96% enantiomeric excess (*J. Am. Chem. Soc.*, **1986**, *108*, 3855-3856). Based on this interesting asymmetric nitroolefination, a number of enantioselective total syntheses including indole alkaloids were achieved (*J. Am. Chem. Soc.*, **1987**, *109*, 7901-7903).

Another major contribution to the world of asymmetric synthesis was the introduction of the concept "Memory of Chirality" (*J. Am. Chem. Soc.*, **1991**, *113*, 9694-9696, see also *Chem. Eur. J.*, **1998**, *4*, 373-376). As we all know, enolation of a carbonyl group will lead to the loss of chirality at the α-carbon because of the generation of an achiral sp^2 carbon intermediate. Thus, it is necessary to employ chiral electrophiles, auxiliaries or catalysts to produce optically active products even though the starting material is



1 (93% ee) **2** (66% ee)

enantiopure. Prof. Fuji and his co-workers, however, challenged this common understanding and disclosed a conceptually novel reaction where the optically active ketone **1** gave the methylated product **2** with 66% *ee* without any other chiral environments introduced during the enolate formation or the following methylation. In this reaction, chirality of the starting ketone **1** is preserved in the enolate intermediate via axial chirality. The slow rate of racemization of the conformationally chiral intermediate enables chirality transfer in the fast methylation step, which regenerates the nonracemic sp^3 carbon center in the product. This conceptually new reaction was extended to amino acid derivatives (*J. Am. Chem. Soc.*, **1994**, *116*, 10809-10810). Latter studies by Prof. Kawabata and his coworkers refined this reaction to a highly useful synthetic useful protocol. These two examples clearly demonstrate Prof. Fuji's strong will both to challenge common dogma in chemistry and to develop conceptually new, innovative methods throughout his outstanding scientific research career.

In addition to our scientific exchanges, we have enjoyed our private company both in Japan and in the US. Seeing is believing!! I selected several pictures below to demonstrate our close friendship.

Picture 1. Sukiyaki party at the Post Symposium at Kuni-so in Kyoto after the International Symposium on Natural Product Chemistry (1988).

Picture 2. Karaoke time in Kyoto (1993). From the left, me, my wife Janet, Prof. Fuji's wife Chi, and Prof. Fuji.

Picture 3. In my home. With Prof. Frank Davis and his wife, Lynne (1995).

Picture 4. At the restaurant in Philadelphia, Prof. Fuji, his wife, Chi, me and my wife, Janet (2002).

In summary, I would like to express my heart warm congratulations and best wishes to Professor Kaoru Fuji for his 80th birthday. All the very best to you and Chi!

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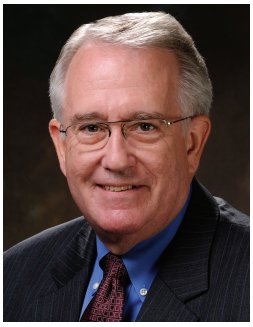

Amos B. Smith, III, born in Lewisburg, PA in 1944, received Bucknell University's first combined B.S.-M.S. degree in chemistry (1966) under the direction of Professor Harold W. Heine. After a year in Medical School at the University of Pennsylvania, he entered Rockefeller University, completing his Ph.D. degree (1972) and a year as a Postdoctoral Associate with Professor William C. Agosta. In 1973 he joined the Department of Chemistry at the University of Pennsylvania where he is currently the Rhodes-Thompson Professor of Chemistry and a Member of the Monell Chemical Senses Center. From 1988-1996 he was Chair of the Department. In addition, Professor Smith served as the inaugural Editor-in-Chief of *Organic Letters* (1999-2018). His research interests include the design of new synthetic methods and their application to the construction of architecturally complex natural products, bioorganic/medicinal chemistry related to the inhibition of HIV-1 viral infection and possible eradication, and peptide/protein folding via stapling and unstapling. In each of these programs, Smith and his group exploit the power of "state of the art" organic synthesis to provide solutions to problems of importance for the improvement of human health.