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PREFACE TO HETEROCYCLES ISSUE HONORING THE 70TH BIRTHDAY OF PROFESSOR TOHRU FUKUYAMA

This issue of HETEROCYCLES is dedicated to Dr. Tohru Fukuyama, Professor Emeritus of the University of Tokyo, on the occasion of his 70th birthday, “Ko-Ki” in Japanese. It is my great honor to celebrate this occasion by delivering the preface as his first student in Japan.

Dr. Fukuyama was born in 1948 in Anjo, Aichi. After graduating from Okazaki Senior High School, he entered the School of Agricultural Sciences, Nagoya University where he received his Bachelor’s and Master’s degrees in 1971 and 1973, respectively. He then moved to Harvard University as a graduate student and received his Ph.D. in 1977 under the direction of Professor Yoshito Kishi. After a year and a half of postdoctoral studies in the Kishi group, he started his independent career in 1978 as an Assistant Professor of Chemistry at Rice University, where he was promoted to Associate Professor in 1982 and to Professor in 1988. He moved back to Japan in 1995 and started his research at the Graduate School of Pharmaceutical Sciences, the University of Tokyo. In 2013, he returned to his alma mater as a Designated Professor of the Graduate School of Pharmaceutical Sciences, Nagoya University.

The research interests of Dr. Fukuyama have centered around the total synthesis of natural products. His outstanding total syntheses have often been realized through his own efforts in developing novel synthetic methodologies. Antibiotic 593A was synthesized via dimerization of a β-lactam intermediate. In this synthesis, a *p*-hydroxyphenyl group was employed for the first time as a protecting group of the β-lactam, which could be cleaved under mild conditions with ceric ammonium nitrate (CAN). Dr. Fukuyama discovered a reduction of thiol esters with triethylsilane in the presence of a palladium catalyst to form the corresponding aldehydes. This reaction proceeds under neutral conditions at room temperature and has played key roles in the total syntheses of the neothramycins A and B, cyanocycline A, leinamycin, to name a few. This reaction was later expanded to ketone syntheses using organozinc reagents, leading to the total synthesis of CP-263,114. Two generations of radical-mediated indole syntheses starting from isocyanides or thioamides have been developed. A variety of functional groups are compatible with the conditions, thus permitting the total syntheses of such complicated indole alkaloids as vindoline, catharanthine, aspidophytine, and vinblastine. The copper-mediated amination of aryl halides has provided a method for constructing *N*-heterocycles, resulting in the total synthesis of the duocarmycins and yatakemycin.

The discovery of 2- and 4-nitrobenzenesulfonyl (Ns, nosyl) groups for activation of primary amines is one of the most prominent achievements of Dr. Fukuyama. *N*-Alkylation of nosylamides and the subsequent removal of the nosyl group in the alkylated products can be performed under extremely mild conditions. This process realizes the facile transformation of primary amines into secondary amines and has been employed in a variety of total syntheses of alkaloids, such as HO-416b, lipogrammistin-A, ephedradine A, strychnine, and manzamine A. The 2,4-dinitrobenzenesulfonyl (DNs) group is more reactive than the nosyl groups and can be cleaved under even milder conditions. The unique group found a niche in the total syntheses of vindoline and morphine.

On the other hand, his creative synthetic designs in total synthesis have attracted much attention. The total syntheses of mitomycins A and C were achieved via the mitomycin rearrangement of isomitomycin A, which was prepared through an intramolecular cycloaddition between an azide and an olefin to form an aziridine. Gelsemine was synthesized via divinylcyclopropane rearrangement, which constructed a highly functionalized bicyclo[3.2.1]octane skeleton. Eudistomin C was synthesized via the efficient formation of the oxathiazepine ring. The synthesis of oseltamivir starting from pyridine featured an asymmetric Diels–Alder reaction, a bromolactonization, and a Hofmann rearrangement as the key transformations. The total synthesis of ecteinascidin 743 was achieved with the efficient construction of tetrahydroisoquinoline rings via an intramolecular Heck reaction or the addition of an electron-rich aromatic ring to an *N*-acyliminium ion. The enantioselective total synthesis of tetrodotoxin was accomplished from *p*-benzoquinone and a cyclopentadiene derivative, in which the six contiguous stereogenic centers were stereoselectively introduced through Ogasawara’s method, [3,3]-sigmatropic rearrangement of an allylic cyanate, and intramolecular 1,3-dipolar cycloaddition of a nitrile oxide.

Dr. Fukuyama’s continued achievements in the total synthesis of natural products arose from enjoyable discussions with his students. He always wanted to know the latest news from them and kept thinking about how to improve their projects based on the close discussions. We students have been deeply influenced by every aspect of his research style and appreciate the extent to which these insights have made us grow.

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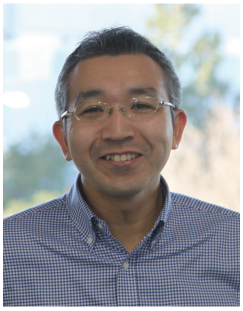

Satoshi Yokoshima was born in Tokyo, Japan in 1974. He received his B.S. in 1997, and his Ph.D. in 2002 from the University of Tokyo under the guidance of Professor Tohru Fukuyama. After working for Mitsubishi Pharma Corporation (2002–2004), he joined the Graduate School of Pharmaceutical Sciences, the University of Tokyo as an Assistant Professor. He was promoted to Lecturer in 2008 and to Associate Professor in 2011. In 2012 he moved to the Graduate School of Pharmaceutical Sciences, Nagoya University, and was promoted to Professor in 2017. He has received the Young Scientist's Research Award in Natural Product Chemistry (2009) and the Pharmaceutical Society of Japan Award for Young Scientists (2012). His current research interests focus on the synthesis of natural products with polycyclic systems.