HETEROCYCLES, Vol. 103, No. 1, 2021, pp. 1 - 5. © 2021 The Japan Institute of Heterocyclic Chemistry
DOI: 10.3987/COM-20-S(K)Foreword_1

PREFACE TO HETEROCYCLES ISSUE HONORING THE 77TH BIRTHDAY OF PROFESSOR DR. YASUYUKI KITA

I am delighted to express my sincere congratulations to Professor Kita (Kita sensei) on his seventy-seventh birthday, the "Kiju” celebration. I am surprised to know his seventy-seventh birthday, since Kita sensei has been an active leader and top runner in the competitive area of chemical sciences, hypervalent iodine chemistry.[1] He has been an incredibly influential figure in hypervalent iodine chemistry research over the past few decades. It is my great honor and singular pleasure to write in praise and recognition of his notable career as one of his former students at the Faculty of Pharmaceutical Sciences, Osaka University. While he is well-known to be a pioneer of oxidative biaryl coupling reactions using hypervalent iodine reagents under non-metallic conditions, his research contributions cover a wide range of pharmaceutical sciences, including those special to me, heteroatom chemistry such as sulfur (S) and silicon (Si). In the late 1980s, I joined his laboratory, and he suggested that I contribute to the research project entitled the “Silicon-induced Pummerer-rearrangement”. The Pummerer-rearrangement is a reaction of sulfoxides with acids or acid anhydrides which provides α-substituted sulfides, such as the α-acetoxy-sulfides reported by Pummerer in 1909.[2] The Pummerer rearrangement was found to be a general reaction for the preparation of α-substituted-sulfides. Many applications of the Pummerer reaction were carried out to prepare complex molecules, including natural products. Professor Oae disclosed the unique mechanistic details of Pummerer rearrangement in the 1970s (Figure 1a).[3] Professor Kita found that a Pummerer-type rearrangement can also happen with the use of silyl ketene acetals (SKA) rather than acids or acid anhydrides, which enabled Pummerer-type rearrangement to be performed under mild, near-neutral conditions (Figure 1b). His discovery of this silicon-induced Pummerer-type rearrangement was applied to a variety of synthetic applications, exemplified by asymmetric variants of intramolecular and intermolecular Pummerer reactions.[4]

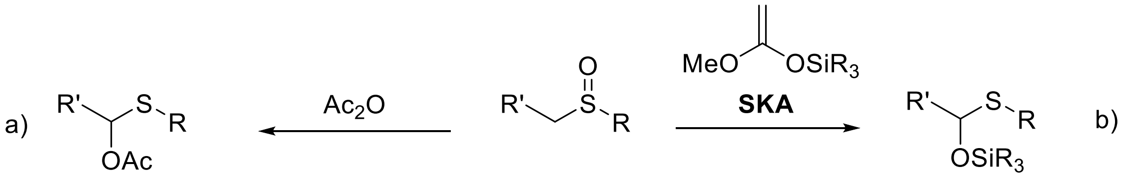

Figure 1. a) Pummerer rearrangement (Pummerer, Oae). b) Pummerer-type rearrangement (Kita)

One of the most impressive contributions of his Pummerer-type rearrangement is a potential relation to the penicillin biosynthesis. Penicillin is an antibiotic derived from penicillium molds discovered by Fleming in 1928. Penicillin is biosynthesized by the enzyme “IPNS” (Isopenicillin N synthase) from a precursor tripeptide “LLD-ACV" consisting of L-aminoadipic acid, L-cysteine, and D-valine. The mechanistic details of the biosynthesis of penicillin had been veiled in mystery for a long time. In the 1980s, Professor J. E. Baldwin had been elucidating the details of one biosynthetic mechanism after another, much to the fascination of many scientists (Figure 2a). We were excited to follow the progression of the state of the art regarding penicillin biosynthesis through Baldwin's work, which was published in many chemical communications.[5] One of the most beautiful parts of the biosynthesis is the mechanistic details of the formation of an unstable *cis*-β-lactam ring rather than the stable *trans*-β-lactam from tripeptide LLD-ACV; that was the long-standing problem of the biosynthesis of penicillin. Among the three potential hypotheses of this process, Professor Kita believed that there could be a relationship between the *cis*-β-lactam ring construction and the Pummerer-type reaction. He therefore proposed some ideas to support the mechanism of penicillin biosynthesis based on the Pummerer reaction, and I devoted all of my attention to carrying out this research during my PhD days (Figure 2b).[6,7] Just before completing my doctoral work, Kita sensei strongly recommended that I go to Oxford to join the J. E. Baldwin group to elucidate the mechanism of the *cis*-β-lactam formation with the state of the art guidance of his organic chemistry and molecular enzymology. I spent a marvelous time with JEB and his fantastic co-workers in Oxford, and the JEB team finally elucidated the full mechanistic details of penicillin biosynthesis at the molecular level in the mid 1990s.[8,9] I clearly remember the day that we got the pictures of X-ray crystallographic structures of LLD-ACV and IPNS complexed with Fe(II). I soon wrote the personal letter to Kita sensei on this exciting news, and he praised me.

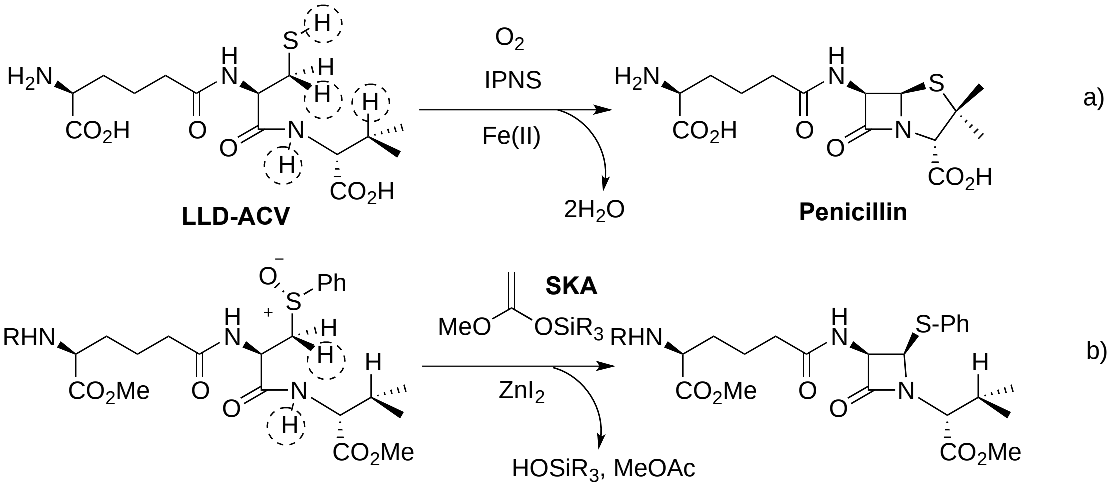

Figure 2. a) Penicillin biosynthesis (Baldwin) b) Biomimetic synthesis of penicillin (Kita)

I recall well my first impression of Kita sensei, back in the late 1980s. He was so cool and tough to approach for me, because of his professional mystique despite his age. Indeed, his suggestion for research work was very sharp and unique, and I was always profoundly enchanted. While considering many of the distinguished achievements of Kita sensei in chemistry and scientific fields, I cannot overlook his personal side. He is a gentleman, and a warm and occasionally amiable teacher. He loves chemistry discussions in academic conferences/meetings, and always encourages us to attend a couple of meetings every year. My first academic presentation was the 109th Annual Meeting of the Pharmaceutical Society of Japan (Nagoya, April, 1989), and I attended the oral presentation with something about my research progress of β-lactam synthesis. A photograph of us during the conference is shown. This photo is one of my treasures. You might suppose the reason for this is because the photo was taken at the conference of my first academic presentation. However, I am afraid that would be incorrect. We took the photo in the gate of the Nagoya Institute of Technology (NITech), in the main hall in the Annual Meeting in 1989. I was 23 and had just started my chemistry career. This is a fantastic coincidence since I am here now, as a professor of NITech. I believe Kita sensei recognized the thread of fate linking me with NITech. I have dedicated my life to fluorine chemistry while Kita sensei works with iodine chemistry. What a nice coincidence again, we are both in halogen chemistry. I was happy to publish our collaboration work for the first catalytic enantioselective fluorination using HF by chiral iodine-based catalysts in 2014 (Figure 4).[10]

Figure 3. Professor Kita, with his friends and students, including me (just the left side of Prof. Kita) at the gate of NITech in 1989 (Nagoya, Japan).

His significant contributions as a scientist, a teacher, and as a noble human being will continuously influence us for many more years. I am delighted to present this manuscript in a special issue as a gift to Kita sensei on his 77th birthday. I wish Kita sensei many long years of continued success, good health, and a fruitful, happy life. Finally, I must also thank Professor Kunio Ogasawara for his considerable assistance in the production of this Special issue.

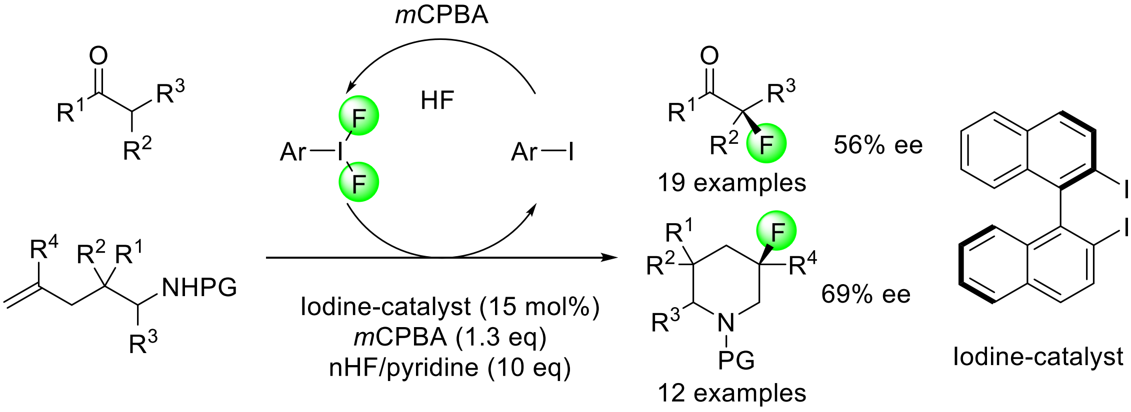

Figure 4. Iodoarene-catalyzed enantioselective fluorination and aminofluorination by an Ar-I/HF/pyridine/*m*CPBA system (Kita & Shibata)

ACKNOWLEDGEMENT

I thank Dr. Daniel M. Sedgwick (Universitat de València) for editing the manuscript.

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Norio Shibata is a Professor at the Nagoya Institute of Technology (NITech) since 2008. He received a Ph.D. (1993) in pharmaceutical sciences from Osaka University under the direction of Professor Yasuyuki Kita. He worked at Dyson Perrins Laboratory (Professor Sir Jack. E. Baldwin), Oxford University (JSPS fellow, 1994−1996), Sagami Chemical Research Institute (Dr. Shiro Terashima, 1996), after which he was a lecturer at Toyama Medical & Pharmaceutical University (1997−2003), and an associate professor at the Nagoya Institute of Technology (2003−2008). His research interests are synthetic and medicinal fluorine chemistry. He is a recipient of the “Incentive Award in Synthetic Organic Chemistry, Japan (2004)”, “RSC Fluorine Prize (inaugural prize in 2005)”, “Fluorine Chemistry Research Incentive Award in Research Foundation ITSUU Laboratory (inaugural prize in 2009)”, “The Pharmaceutical Society of Japan Award for Divisional Scientific Promotions (2010)”, “Prizes for Science and Technology, The Commendation for Science and Technology by the Minister of Education, Culture, Sports, Science and Technology (2014)”, “CSJ Award for Creative Work in Chemical Society of Japan (2015)”, “Chinese Chemical Society, W.-Y. Huang Fluorine Prize (2015)”, “ACS Award for Creative Work in Fluorine Chemistry (2019)”, “The 18th (2018) Green and Sustainable Chemistry Awards by the Minister of Education, Culture, Sports, Science and Technology (2019), and “The Society of Iodine Science Award (2019)”. He serves on the editor of *Cogent Chemistry* (2015−present), associate editor of *Frontiers in Chemistry* (2016−present), editorial board of *Journal of Fluorine Chemistry* (2013−present), *ChemistryOpen* (2012−present), *ScienceOpen* (2013−present), *Fluorine Notes* (2014−present), *RSC Advances* (2019-present) and *Molecules* (2019-present).