Japan Academy Prize to:

Keisuke SUZUKI
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For "Studies on Synthesis of Complex Natural Products"

Outline of the work:

Synthetic organic chemistry is a scientific discipline, enabling access to useful organic compounds from easily available starting materials, where the molecular complexity is made increased through elaboration of the carbon framework and the functional groups. It is important not only as a basic science, but also as the technological background for providing new functional molecules to various related scientific fields, such as biosciences and materials science.

Prof. Keisuke Suzuki is one of the international leaders in organic synthesis with a significant contribution to the area of total synthesis of complex natural products and development of new synthetic reactions. By ingenious use of reactive species, he developed various new stereoselective processes to construct complex molecular architectures. His synthetic studies directed toward the challenging targets with stereochemical and functional complexities have culminated in various total syntheses of biologically active natural products, including glycoconjugates, antibiotics and polycyclic compounds. These achievements are based on the finding of unique solutions to a variety of issues emerged along the lines.

(1) Stereoselective reactions based on molecular rearrangements

One of the keys to organic synthesis is selective construction of the carbon-based molecular frameworks with precise control of three-dimensional structures. Prof. Suzuki developed useful strategies to address these problems based on 1,2-anionotropic reactions. Contrary to the traditional belief that such processes suffer from stereochemical deterioration, he showed that the Lewis acid-mediated 1,2-shifts proceed in stereospecific manner, which was applied to the asymmetric syntheses of chiral pheromones and macrolide antibiotics. He exploited organometallic complexes and heterocycles to enable the stereoselective construction of quaternary chiral centers via 1,2-rearrangements with full stereochemical integrity, which was utilized for the total synthesis of some antibiotic compounds.

(2) Synthesis of glycoconjugates and new glycosylation reactions

In view of the significant roles of the carbohydrate partial structures in various bioactive organic compounds, Prof. Suzuki carried out extensive studies on carbohydrate synthesis and developed new synthetic methods that have been exploited in total synthesis. He developed an efficient *O*-glycosylation reaction by using cationic hafnium complexes for activating glycosyl fluoride, which was used in the total synthesis of macrolide antibiotics. This unique reaction method has found many applications in oligosaccharide synthesis relevant to the cell biology research. He led the chemical synthesis of the aryl *C*-glycoside antibiotics, an emerging class of compounds since 1970. Among others, he developed a bio-inspired reaction ($O \rightarrow C$ glycoside rearrangement), which has been utilized by many researchers and this reaction allowed him to achieve the total syntheses of several antitumor antibiotics, including gilvocarcin and saptomycin.

(3) Synthesis of polycyclic compounds

Prof. Suzuki studied the synthesis of various complex polycyclic compounds derived from the type II polyketide biosynthesis, a rich source of biologically active molecules. These compounds feature multiple stereogenic centers and oxygen functionalities and have been regarded as a class of highly challenging targets in chemical synthesis. However, he developed an efficient method for assembling polycyclic structures based on rapid generation of benzyne species and an excellent synthetic planning. For the stereoselective assembly of polycycles, he developed stereocontrolled pinacol and benzoin cyclizations. His recent study has been also directed to the catechin-class polyphenols. In spite of the wide distribution in nature, these compounds have been regarded as inaccessible in scientific research by the difficulties in handling. However, he developed facile methods for the selective preparation of catechin monomers and the oligomers, opening a newer phase in the polyphenol research.

In summary, Prof. Suzuki carried out an extensive research on organic synthesis with particular emphasis on the total synthesis of biologically active natural products, posing significant impacts to related areas including biosciences and materials sciences. Awards and honors he has received include Synthetic Organic Chemical Society, Japan Award (2003), MEXT Award (2009), Humboldt Research Award (2009), Medal with Purple Ribbon (2010). He was a President of the Synthetic Organic Chemical Society, Japan (2013–2015).

Selected publications

(1) **K. Suzuki**, K. Tomooka, E. Katayama, T. Matsumoto, and G. Tsuchihashi, Stereocontrolled Asymmetric Total Synthesis of Protomycinolide IV, *J. Am. Chem. Soc*., **108**, 5221–5229 (1986).

(2) T. Matsumoto, H. Maeta, **K. Suzuki**, and G. Tsuchihashi, First Total Synthesis of Mycinamicin IV and VII. Successful Application of New Glycosidation Reaction, *Tetrahedron Lett*., **29**, 3575–3578 (1988).

(3) T. Matsumoto, M. Katsuki, and **K. Suzuki**, New Approach to C-Aryl Glycosides Starting from Phenol and Glycosyl Fluoride. Lewis Acid-Catalyzed Rearrangement of *O*-Glycoside to *C*-Glycoside, *Tetrahedron Lett*., **29**, 6935–6938 (1988).

(4) T. Matsumoto, M. Katsuki, H. Jona, and **K. Suzuki**, Convergent Total Synthesis of Vineomycinone B_2 Methyl Ester and Its C(12)-Epimer, *J. Am. Chem. Soc*., **113**, 6982–6992 (1991).

(5) T. Matsumoto, T. Hosoya, M. Katsuki, and **K. Suzuki**, New Efficient Protocol for Aryne Generation. Selective Synthesis of Differentially Protected 1,4,5-Naphthalenetriols, *Tetrahedron Lett*., **32**, 6735–6736 (1991).

(6) T. Matsumoto, T. Hosoya, and **K. Suzuki**, Total Synthesis and Absolute Stereochemical Assignment of (+)-Gilvocarcin M, *J. Am. Chem. Soc*., **114**, 3568–3570 (1992).

(7) T. Saito, T. Suzuki, C. Akiyama, T. Ochiai, K. Takeuchi, T. Matsumoto, and **K. Suzuki**, Total Synthesis of the Furaquinocins, *J. Am. Chem. Soc*., **120**, 11633–11644 (1998).

(8) M. Kitamura, K. Ohmori, T. Kawase, and **K. Suzuki**, Total Synthesis of Pradimicinone, the Common Aglycon of the Pradimicin–Benanomicin Antibiotics, *Angew. Chem. Int. Ed. Engl*., **38**, 1229–1232 (1999).

(9) T. Matsumoto, H. Yamaguchi, M. Tanabe, Y. Yasui, and **K. Suzuki**, Synthestic Study of Aquayamycin. Part 3: First Total Synthesis, *Tetrahedron Lett*., **41**, 8393–8396 (2000).

(10) T. Hamura, T. Hosoya, H. Yamaguchi, Y. Kuriyama, M. Tanabe, M. Miyamoto, Y. Yasui, T. Matsumoto, and **K. Suzuki**, Facile Access to Versatile Polyaromatic Building Blocks: Selectively Protected Benzocyclobutenedione Derivatives via Regioselective [2+2] Cycloaddition of Benzyne and Ketene Silyl Acetal, *Helv. Chim. Acta*, **85**, 3589–3604 (2002).

(11) Y. Hachisu, J. W. Bode, and **K. Suzuki**, Catalytic Intramolecular Crossed Aldehyde–Ketone Benzoin Reactions: A Novel Synthesis of Functionalized Preanthraquinones, *J. Am. Chem. Soc*., **125**, 8432–8433 (2003).
(12) K. Ohmori, K. Mori, Y. Ishikawa, H. Tsuruta, S. Kuwahara, N. Harada, and **K. Suzuki**, Concise Total Synthesis and Structural Assignment of (+)-TAN-1085, *Angew. Chem. Int. Ed*., **43**, 3167–3171 (2004).
(13) K. Ohmori, N. Ushimaru, and **K. Suzuki**, Oligomeric Catechins: Enabling Synthetic Strategy via Orthogonal Activation and C(8)-Protection, *Proc. Nat. Acad. Sci*., **101**, 12002–12007 (2004).
(14) K. Ohmori, M. Tamiya, M. Kitamura, H. Kato, M. Oorui, and **K. Suzuki**, Regio- and Stereo-Controlled Total Synthesis of Benanomicin B, *Angew. Chem. Int. Ed*., **44**, 3871–3875 (2005).
(15) H. Takikawa, Y. Hachisu, J. W. Bode, and **K. Suzuki**, Catalytic, Enantioselective Aldehyde–Ketone Benzoin Cyclizations, *Angew. Chem. Int. Ed*., **45**, 3492–3494 (2006).
(16) T. Hamura, Y. Ibusuki, H. Uekusa, T. Matsumoto, and **K. Suzuki**, Poly-oxygenated Tricyclobutabenzenes via Repeated [2+2] Cycloaddition of Benzyne and Ketene Silyl Acetal, *J. Am. Chem. Soc*., **128**, 3534–3535 (2006).
(17) **K. Suzuki**, H. Takikawa, Y. Hachisu, and J. W. Bode, Isoxazole-directed Pinacol Rearrangement: Stereocontrolled Approach to Angular Quaternary Stereogenic Centers in Fused Polycyclic Natural Products, *Angew. Chem. Int. Ed*., **46**, 3252–3254 (2007).
(18) M. Tamiya, K. Ohmori, M. Kitamura, T. Arai, H. Kato, M. Oorui, and **K. Suzuki**, General Synthetic Route to Benanomicin–Pradimicin Antibiotics, *Chem. Eur. J*., **13**, 9791–9823 (2007).
(19) H. Takikawa, A. Takada, K. Hikita, and **K. Suzuki**, Formation of α-Hydroxy-β-diketones through Hydroxylation of Isoxazolium Salts: Stereoselective Approach to Angular cis-Diol in Polycyclic System, *Angew. Chem. Int. Ed*., **47**, 7446–7449 (2008).
(20) K. Mori, K. Ohmori, and **K. Suzuki**, Stereochemical Relay via Axially Chiral Styrenes: Asymmetric Synthesis of the Antibiotic TAN-1085, *Angew. Chem. Int. Ed*., **48**, 5633–5637 (2009).
(21) K. Ohmori, T. Yano, and **K. Suzuki**, General Synthesis of epi-Series Catechins and Their 3-Gallates: Reverse Polarity Strategy, *Org. Biomol. Chem*., **8**, 2693–2696 (2010).
(22) A. Takada, Y. Hashimoto, K. Hikita, H. Takikawa, and **K. Suzuki**, Total Synthesis and Absolute Stereochemistry of Seragakinone A, *Angew. Chem. Int. Ed*., **50**, 2297–2301 (2011).
(23) K. Ohmori, T. Shono, Y. Hatakoshi, T. Yano, and **K. Suzuki**, Integrated Synthetic Strategy for Higher Catechin Oligomers, *Angew. Chem. Int. Ed*., **50**, 4862–4867 (2011).
(24) Y. Yamashita, Y. Hirano, A. Takada, H. Takikawa, and **K. Suzuki**, Total Synthesis of the Antibiotic BE-43472, *Angew. Chem. Int. Ed*., **52**, 6658–6661 (2013).
(25) K. Kitamura, Y. Maezawa, Y. Ando, T. Matsumoto, and **K. Suzuki**, Synthesis of the Pluramycins 2: Total Synthesis and Structure Assignment of Saptomycin B, *Angew. Chem. Int. Ed*., **53**, 1262–1265 (2014).