The Development of Organic Chemistry in Japan: Riko Majima and His Research School of "Natural Product Chemistry" in the First Half of the Twentieth Century

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1. Chemistry before the Meiji Restoration

In Japanese history, the year 1868 is usually considered to be the beginning of modern Japan. In that year, the Tokugawa government, ruled by the shoguns of the Tokugawa family, based in Edo (today's Tokyo) was replaced by a modern government ruled by an Emperor, who was formerly confined to Kyoto. This revolutionary political change is called the Meiji Restoration, because the ancient Imperial system was nominally restored under Emperor Meiji. Although initially mixed in its leanings, the new government soon adopted a policy of full-fledged modernisation.[1]

The introduction of western science had already started long before the Meiji Restoration. From the middle of the 17th century until 1853, the Netherlands was the only European country with which Japan traded; some books in Dutch on science, technology, and medicine were imported into Japan during that period. In the 1770s, some Japanese medical doctors, including Genpaku Sugita (1733-1817), Ryoutaku Maeno (1723-1803), Junan Nakagawa (1739-86), Hoshu Katsuragawa (1751-1809), began to learn Dutch and translated a Dutch introductory anatomy textbook, *Ontleedkundig Tafelen,*[2] into Japanese. This was the beginning of the so-called "Dutch learning (*Rangaku*)," that is, learning of about western civilisation through the Dutch language.[3]

By the 1830s-40s, Yoan Udagawa (1798-1846), a scholar of Dutch learning, had already written a textbook "Seimi Kaiso [An Introduction to Chemistry]" –basically Lavoisier's chemistry– using contemporary Dutch chemistry textbooks, including the Dutch translation of Lavoisier's *Traité Elémentaire de Chimie.*[4]

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In 1854, after the feudal government abandoned its policy of tight control over foreign trade, the political situation became destabilised. During the political turmoil and colonisation threats, some intellectuals who belonged to the samurai, the military ruling class, began to study western science and technology, including chemistry and chemical technology, as militarily useful subjects.

During this period scholars studied western knowledge not only in Dutch, but other in other European languages such as English, French and German. They were called scholars of Western learning. Some of them, who were interested in chemistry, followed its development in 19th century, including Dalton's atomic theory, which Udagawa did not pay attention in his textbook. Komin Kawamoto (1810-71), a teacher of chemistry at a governmental school of Western learning, was such a scholar and translated a number of newer chemistry textbooks and wrote a textbook based on Dalton's atomic theory.

2. Institutionalisation of Chemistry in Japan: Joji Sakurai and Organic Chemistry[5]

The institutionalisation of science, including that of chemistry, started after the Meiji Restoration. Then the modern Western education system was introduced to Japan, and many foreign teachers were employed by the new government to teach in higher education. Even though most children studied only up to the elementary education level, some middle- and upper-class children, including those of the former samurai class, studied western languages from an early age and continued their studies at higher educational institutions in which westerners taught. The Meiji government sent the most successful students to Europe and the United States to study further. When they returned, they replaced the foreign teachers to become the first generation of Japanese professors to teach in the new system.

Joji Sakurai (1858-1939) was a chemist who belonged to the first generation of Japanese scientists. He was born in 1858 to a samurai family in Kanazawa, the capital of one of the most powerful feudal lords. He started to learn English at an early age and entered an institution of western learning, founded by the Ministry of Education, in 1871. He studied in the three-year preliminary course and the two-year specialist chemistry course under the English chemist, Robert William Atkinson (1850-1929). Then, he was sent to England and studied at University College London between 1876 and 1881 under a famous chemist and Atkinson's teacher, Alexander William Williamson (1824-1904).

When Sakurai returned to Japan in 1881 at the age of 23, he obtained a teaching position as a lecturer in the Faculty of Science at Tokyo University as the successor of his mentor, Atkinson, and became a professor the next year. He was the second Japanese professor of chemistry after the American-trained chemist Naokichi Matsui (1857-1911), who had been appointed a year earlier.

With the foundation of the Imperial University in Tokyo in 1886, the education system in Japan was fully established. Sakurai became the Head of the Department of Chemistry at the College of Science at the Imperial University. Sakurai taught organic chemistry as well as physical and theoretical chemistry. His lectures, especially those on organic chemistry, were highly praised by students, even though Sakurai researched in physical chemistry rather than in organic chemistry.

3. Riko Majima and the Beginning of Reseach in Organic Chemistry[6]

One of Sakurai's students, Riko (Toshiyuki) Majima (1874-1962), was the first organic research chemist in Japan. Majima was born in Kyoto in 1874, the eldest son of an affluent medical doctor. His generation was the first to study fully within a modern educational system. Majima entered the Imperial University in Tokyo ten years after its establishment. Kyoto Imperial University was established the next year. Soon after his graduation in 1899, he remained in the department as a research assistant and a graduate student of the department under the supervision of professor Sakurai. Sakurai gave him total freedom in choosing his research topics, but Majima felt insecure because Sakurai gave no advice on research. Since there was no one to provide advice on research in organic chemistry, he studied well-known German organic chemists' work that had been published in German journals. When he started to conduct research in organic chemistry, he decided to study local natural products that could not be obtained easily in Europe in order to be able to compete with chemists in the West.[7] He first studied the structure of urushiol, the main component of the sap of the Japanese lacquer tree (*Rhus verniciflua* Stokes*, urushi-no-ki* in Japanese). The black glossy varnish is sometimes known as japan, the lacquer tree is an important indigenous commercial source of natural lacquer.

In 1903, Majima was promoted to the position of associate professor. Soon the Ministry of Education sent him to Europe for further study. He conducted research in Kiel under Carl Dietrich Harries (1866-1923) and in Zurich under Richard Willstätter (1872-1942). While in Europe, besides his research on the top-

ics provided by his European supervisors, he continued to study urushiol, using advanced instruments available in the laboratories.

Majima returned to Japan in January 1911 and became a Professor of Organic Chemistry at Tohoku Imperial University, a newly established imperial university in Sendai in northern Japan, in March. After establishing his laboratory, he restarted his research on the structure of urushiol, using newly introduced advanced instruments and methods from Europe, such as highly reduced pressure distillation and a new method of catalytic reduction, Harries ozonolysis. Within six years, he succeeded in elucidating the structure of urushiol as a catechol (o-dihydrobenzene) derivative.

Majima's study of urushiol and local natural products using newly developed European methods was a major research strategy in Japan until the 1960s. Many of his students followed this line of research.

4. Majima's Research School and Tetsuo Nozoe: From Natural Product Research to a New Field of Organic Chemistry

Majima, as a leader of the first generation of organic research chemists, contributed greatly to the establishment of organic chemistry laboratories in higher education institutions as well as in research institutes in Japan including the Imperial Universities at Sendai and Osaka, and the Tokyo Institute of Technology, and a laboratory at the Research Institute of Physical and Chemical Sciences (RIKEN).

Tetsuo Nozoe was one of Majima's students at Tohoku Imperial University, and his research path showed how Majima's research line was developed by his students.[8] Nozoe was born in Sendai in 1902 as the sixth child of a lawyer and local politician. He entered the Department of Chemistry of the Faculty of Science at Tohoku Imperial University in 1923. At the university, Majima became Nozoe's mentor and was to play a decisive role in his life.

After his graduation in March 1926, Nozoe stayed on as Majima's assistant. However, at the end of June 1926, Nozoe left Sendai for Formosa (now Taiwan) to become a researcher at the Monopoly Bureau in Taipei, the capital of Formosa, with Majima's strong recommendation. Nozoe was a candidate for a Professorship at a planned new Imperial University in Formosa. In 1928, Taihoku Imperial University (Taihoku is the Japanese name for Taipei) was established. Young Nozoe was appointed an associate professor the following year. Taihoku Imperial

University was the second Japanese Imperial University in its colonies after Keijo Imperial University in Keijo (now Seoul), founded in 1925. Nozoe's main research interest was the study of natural products, especially those found in Formosa.

Nozoe's well-known work in Formosa concerned the chemical components of *taiwanhinoki* (*Chamaecyparis obtusa var. formosana*, now *C. taiwanensis*), a native conifer that grew in high mountainous areas. Nozoe obtained a new compound, named hinokitiol, from the components and reported it for the first time in 1936 in a special issue of *The Journal of the Chemical Society of Japan* to celebrate Professor Majima's sixtieth birthday.

By studying hinokitiol's structure, he arrived at the idea that it could be a new type of aromatic compound stabilised by resonance, involving an intramolecular hydrogen bond, after reading Linus Pauling's *The Nature of the Chemical Bond* (1939), which was probably one of the last academic publications imported into Formosa before World War II started. Even though it turned out later that hinokitiol existed not as a resonance hybrid, but as a pair of tautomers that interconverted through intramolecular hydrogen bonding, this idea was the first step in opening the new research area of non-benzenoid aromatic compounds. Nozoe presented his ideas for the first time at a local meeting of chemists in Taiwan in 1941, but the audience was skeptical about his seven-membered structure.

After World War II, Formosa was returned to the Republic of China and Taihoku Imperial University was renamed Taiwan National University. Most Japanese left Taiwan for Japan, but Nozoe, who had to stay in Taiwan, worked as a Professor of Chemistry at Taiwan National University under the orders of the Chinese government, which needed such specialists.

Since Nozoe regarded hinokitiol as a compound with a novel aromatic system, he examined various substitution reactions: halogenation, nitration, and azo coupling. He managed to return to Japan at the end of May 1948. His *alma mater*, Tohoku University, offered him a position. The results of his group's research on hinokitiol at National Taiwan University were first published in 1949 in a Japanese journal.[9] His group in Tohoku University began to produce many papers on chemistry of hinokitiol and its derivatives in English, first in the Proceedings of the Japan Academy and then other journals.[10]

In 1945, Michael J.S. Dewar (1918-97), later a leading theoretical chemist, proposed a new kind of aromatic structure with a seven-membered ring for which he coined the term "tropolone". At the end of 1948, Nozoe received a copy of a letter written by Holger Erdtman (1902-89), a Professor of Organic Chemistry at the Royal Institute of Technology in Stockholm, along with a reprint of Erdtman's

paper on the structure of thujaplicins, published in *Nature* in 1948, from his Japanese colleague at the Faculty of Pharmacy at the University of Tokyo, who had once worked under Professor Robert Robinson at Oxford along with Erdtman. Erdtman had isolated three isomeric monoterpenoids (named the α–, β–, γ-thujaplicins) from the Western red cedar (*Thuja plicata*). Erdtman and Nozoe corresponded and discovered that hinokitiol was identical to β-thujaplicin.

When a symposium, "Tropolone and Allied Compounds", was organized by the Chemical Society of London in November 1950, Erdtman mentioned Nozoe's work on hinokitiol as a pioneering contribution to tropolone chemistry, thus helping Nozoe's research to gain recognition in the West. Nozoe was able to publish his work on hinokitiol and its derivatives in *Nature* in 1951 thanks to J. W. Cook, the chairman of the symposium.[11]

Nozoe's work, which started with natural products research in Taiwan and developed fully in Japan in the 1950s and 60s, opened a new field of organic chemistry, the chemistry of non-benzenoid aromatic compounds. His work was good example of how Majima's students developed his line of research and demonstrated that organic chemistry research in Japan had reached a world-class level by the 1950s.

Notes

[1] See, for example, Andrew Gordon, *A Modern History of Japan: From Tokugawa Times to the Present* (New York and Oxford: Oxford University Press, 2003).

[2] This was the Dutch translation in 1734 by Gerrit Dickten, a Dutch surgeon, from Johann Adam Kulmus's small anatomy texbook, *Anatomische Tabellen*. Kulmus (1689-1745) was a teacher of medicine and physics in a Gynasium in Danzig (Gdańsk) and wrote the anatomy book in German in 1722 and his book ran several editions in German and was translated into Latin, French and Dutch. See Sumio Ishida, *Oranda ni okeru Rangaku Isho no Keisei* [in Japanese, The Formation of Books on Dutch Medicine in the Netherlands] (Kyoto: Shibun-kaku Shuppan, 2007).

[3] For an overview of the history of "Dutch learning," see Jiro Numata, *Yogaku* [in Japanese, Western Learning in Japan] (Tokyo: Yoshikawa Kobunkan, 1989); Shosuke Sato, *Yogakushi no Kenkyu* [in Japanese, A Study of Western Learning in Japan] (Tokyo: Chuo Koron-sha, 1980); Tadashi Yoshida, "Tenbo: Rangakushi [in Japanese, Overview: History of Dutch Learning in Japan]," *Kagakusi Kenkyu* 23 (1984): 73-80; Grant K. Goodman, *Japan and the Dutch, 1600-1853* (Richmond, Surrey, England: Curzen Press, 2000).

[4] Masao Sakaguchi, Tatsumasa Doke, Toshihiko Kikuchi and Minoru Tanaka, *Seimi Kaiso Kenkyu* [in Japanese, Studies on *Seimi Kaiso*] (Tokyo: Kodan-sha, 1975); Togo Tsukahara, *Affinity and Shinwa Ryoku: Introduction of Western Chemical Concepts in Early Nineteenth-Century Japan* (Amsterdam: J.C. Gieben, 1993).

[5] On Joji Sakurai, see Yoshiyuki Kikuchi, "Redefining Academic Chemistry: Joji Sakurai and the Introduction of Physical Chemistry into Maiji Japan," *Historia Scientiarum* 9 (2000): 215-56;

idem, "Sakurai Jôji to Igirisu jin Kagakusha Konekushon [in Japanese, Joji Sakurai and His Connections with British Chemists]", *Kagakushi Kenkyu (the Journal of the Japanese Society for the History of Chemistry)* 31 (2004): 239-67; idem, "The English Model of Chemical Education in Meiji Japan: Transfer and Acculturation." PhD diss., The Open University, 2006.

[6] On Riko Majima, see Takashi Kubota, "*Hihon no Yuki-Kagaku no Kaitaku-sha Majima Riko* [in Japanese, Riko Majima: Founder of Organic Chemistry in Japan]," *Kagakushi Kenkyu (Journal of the Japanese Society for the History of Chemistry*) 30 (2003): 36-51, 93-105, 159-176, 231-255; Majima Riko Sensei Iko Kanko Iinkai, ed., *Majima Riko Sensei no Iko to Tsuioku* [in Japanese, Professor Riko Majima's posthumous manuscript and Remembrance of Him] (Tokyo: Tokyo Kagaku-Dojin, 1970).

[7] Riko Majima, "Waga Shogai no Kaiko [in Japanese, Reminiscences of My Life]," *Kagaku no ryoiki* 8 (1) (1954): 1-11; (3): 137-146, p. 6.

[8] On Tetsuo Nozoe, see T. Nozoe, *Seventy Years in Organic Chemistry* (Washington, D. C.: American Chemical Society, 1991); Nozoe Tetsuo Kyoju Go-taikan Kinen-kai, ed., *Nozoe Tetsuo Kyoju Ronbun Mokuroku-shu* [in Japanese, Bibliography of Professor Tetsuo Nozoe's Papers] ([Sendai, Japan], 1966); Nozoe Tetsuo Sensei Tsuito Jigyo-kai, ed., *Hitosuji no Michi: Tsuioku Nozoe Tetsuo Sensei* [in Japanese, One way: For the memory of Professor Tetsuo Nozoe] ([Sendai, Japan], 1997); *Nozoe Tetsuo Sensei Kenkyu Ronbun-Chosaku Mokuroku* [in Japanese, Bibliography of Professor Tetsuo Nozoe's Work] ([Sendai, Japan], 1999); Shinji Takashima and Public Relations Department of *Hinoki Shinyaku, Ltd.*, *Hinokitiol Monogatari* [in Japanese, The Story of Hinokitiol] (Tokyo: Hinoki Shinyaku, Ltd., 1996); T. Asao, S. Ito, and I. Murata, "Tesuo Nozoe (1902-1996)," *European Journal of Organic Chemistry* (2004): 899-928; Masanori Kaji, "Tesuo Nozoe (1902-1996)", in *New Dictionary of Scientific Biography,* ed. Noretta Koertge (Detroit, New York et al.: Charles Scribner's Sons, 2008), vol. 5, 287-293.

[9] T. Nozoe, "Hinokitiol ni kansuru Kenkyu [in Japanese, Studies on Hinokitiol]," *Yakugaku* 3 (1949): 174-198.

[10] In the early 1950s, soon after the World War II, *the Proceedings of the Japan Academy* were one of a few journals in Japan, published in European languages. Riko Majima, a member of the Japan Academy, was communicated almost every month to the Academy for Nozoe (note 8, Nozoe, *Seventy Years in Organic Chemistry*, p.110). More than sixty papers in English were published in *the Proceedings of the Japan Academy* during 1950 and 1953.

[11] T. Nozoe, "On the Substitution Products of Tropolone and Allied Compounds," *Nature* 167 (1951): 1055-1060.