

PROFILE AND SCIENTIFIC CONTRIBUTIONS OF PROFESSOR TETSUJI KAMETANI

Ken'ichi TakedaShionogi Research Laboratories, Shionogi & Co., Ltd.,
Fukushima-ku, Osaka, 553 Japan

Professor Tetsuji Kametani was born in August, 1917, in the Asakusa area of downtown Tokyo, and spend his childhood there. The so-called "Edokko-spirit", an openhearted aggressive and artisan spirit with a somewhat stubborn mind, was born from the people living in the downtown of Edo (till about 100 years ago Tokyo was called Edo) and it is still vividly prevalent today. His spiritual character was cultivated under such atmosphere and that Edokko-spirit not only strongly affected him but also can be seen throughout his scientific works.

After graduating the Urawa High School he entered to the Pharmaceutical Institute, Medical Faculty, Tokyo Imperial University (now the Pharmaceutical Faculty, University of Tokyo) and was trained under the guidance of Professor Shigehiko Sugawara as an organic chemist. After graduation from Tokyo Imperial University in September, 1943, Professor Kametani entered the Tokyo Laboratory of the Tanabe Pharmaceutical Company for a while and about two years later he was appointed as assistant professor of Tokyo College of Pharmacy.

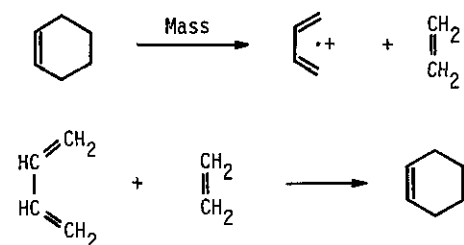
His first chemical work appeared in *J. Pharm. Soc., Japan*, 1950, 70, 258, entitled "Syntheses of Imidazoisoquinoline Derivatives, I. Synthesis of 9,10-Dimethoxy-3-(p-aminophenyl)-5,6-dihydro-benzoglyoxalocoline". One year later, Professor Kametani received a doctorate, his thesis being "Studies on the Synthese of Aminoisoquinoline Derivatives", from Tokyo Imperial University, in 1951.

At the early stage, Professor Kametani's works were subjected to syntheses of heterocyclic compounds containing a nitrogen atom, with somewhat complicated structures. However, his works were rapidly extended when he moved to Sendai, after about a ten years stay at Osaka University, where he became Professor of Pharmaceutical Institute, School of Medicine, Tohoku University in 1959. His energy towards the syntheses of isoquinoline-type alkaloids was amazing and a proverbial mountain of valuable, interesting and fruitful papers were published successively in a short period. Professor Kametani synthesized more than fifty alkaloids belonging to morphine- and morphinan-dienone-, protoaporphine- and aporphine-, coclaurine and biscoclaurine-type alkaloids, Erythrina

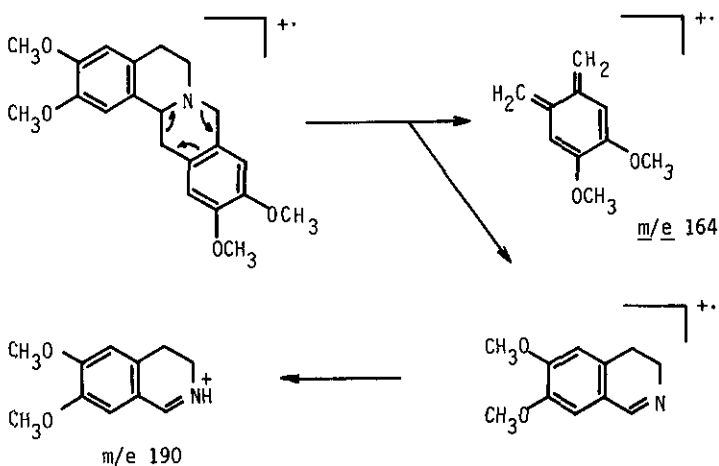
and Amaryllidaceae alkaloids etc. using many interesting and unique methods as for instance phenolic cyclization, photo-Pschorr, photolytic cyclodehydrobromination, biogenetic phenol oxidative coupling, etc., besides the commonly used methods such as Bischler-Napieralski, Pictet-Spengler, Pomeranz-Fritsch and Ullmann reaction, with very excellent results.

Professor Kametani also succeeded in the synthesis of "Pentazocine" and its derivatives, a very useful analgesic which is commonly used at present. Furthermore, syntheses of the naturally occurring biological active substances such as galanthamine, camptothecin, some sesqui- and di-terpenes and β -lactam type antibiotics were also achieved by Professor Kametani.

Although so many excellent synthetic works were published by Professor Kametani as mentioned above, his most brilliant and exciting work was the so-called "Retro Mass Spectral Synthesis". The first paper of this series was presented at the "19th Symposium on the Chemistry of Natural Products" in 1975. In this paper Professor Kametani suggested that synthesis of the subjected compound should be designed on the basis of mass spectral fragmentation of the target substance. For instance cyclohexene gave two fragments in mass spectra, as shown in the Figure, and so cyclohexene should be synthesized with ethylene and butadiene:



Firstly, he studied the mass spectral fragmentation of protoberberine-type isoquinoline alkaloid thoroughly and he obtained the following results:

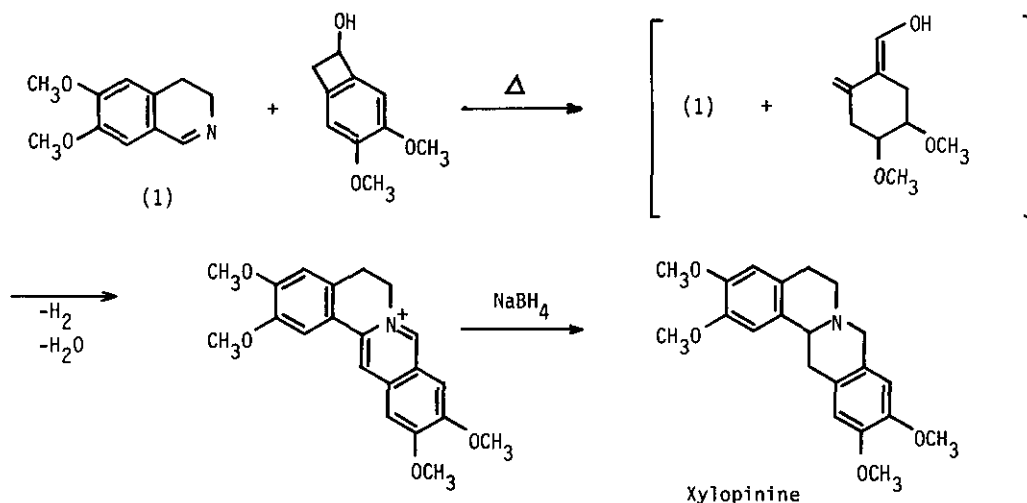


Professor Kametani chose two synthons (equivalent to each mass fragment), one is dihydroisoquinoline (1) and the other benzocyclobutene (2) corresponding to the mass fragment of m/e 164.



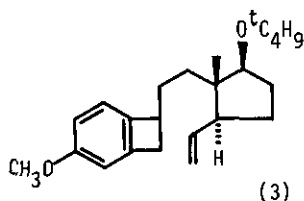
Furthermore, in order to give a high regioselectivity of the cyclobutene synthon, some suitable substituent was introduced on the cyclobutene ring and it was also clarified that its selectivity was greatly affected by the E-effect of the introduced substituent on the cyclobutene ring.

Xylopinine and berberine were synthesized by this method.



By analogy, emetine, corynantheine, yohimbine, reserpine and their derivatives, as well as the indoisoquinoline-type alkaloid, olivacine, and the fundamental skeleton of the very common antibiotics terramycin or adriamycin were also synthesized with very simple and effective procedures.

Recently Professor Kametani also applied of this retro mass spectral synthesis and was able to synthesize optical active estrogens using an optical active indane derivative which was condensed to the methoxybenzocyclobutene ring (3).



A very potent androgen, Δ^{14} -19-nortestosterone, having about 100-1000 times the activity when compared with testosterone, and some di- and triterpenes were also synthesized by the same idea. Thus retro mass spectral synthesis, developed by Professor Kametani, was highly evaluated and many fruitful contributions were made to the field of synthetic organic chemistry.

Professor Kametani also established publication of the International Journal "Heterocycles" in 1973. It seemed very difficult to establish the new journal, especially in the case of an international journal. However, Professor Kametani conquered many difficulties and at present this journal has become one of the most valuable and famous worldwide publications concerning heterocyclic chemistry.

Up to the year 1972, Professor Kametani's published papers totaled 500, and it is very easy to suppose that the number of his papers will reach the one thousand mark by the end of this year.

Professor Kametani likes alcohol very much and every evening after working hours he can be found in one of his favorite spots up to midnight drinking whisky with or without his friends. Therefore most all of his foreign as well as Japanese friends have a question "When does Professor Kametani find time to write a paper?". Really, Professor Kametani is a magician in the field of organic chemistry.

These very excellent and valuable contributions of his works, as mentioned above, to the synthetic organic chemical field brought him the following Awards:

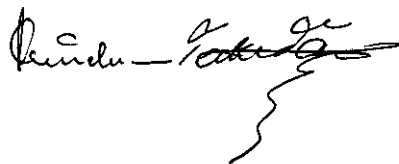
Academic Prize of the Pharmaceutical Society of Japan in 1969

Medal of Honor with Purple Ribbon in 1979

Award of Japan Academy in 1980

Fujihara Prize in 1980

Last and not least, it should also be mentioned that the help and cooperation of his charming and lovely wife, Mrs. Nobuko Kametani, contributes no small part in making Professor Kametani's work possible.

A handwritten signature in black ink, appearing to read 'Kametani', with a long, sweeping flourish extending downwards and to the right.