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PROFESSOR SUMIO UMEZAWA

With the dedication of this issue of *Carbohydrate Research* to Professor Sumio Umezawa, we are honoring a distinguished scientist, scholar, teacher, and administrator who has greatly contributed to development of the chemistry of antibiotics, especially the field of sugar-containing antibiotics.

Sumio Umezawa was born in the midtown (Nihonbashi) of Tokyo on November 22, 1909, being the eldest son of Dr. Junichi and Mrs. Takako Umezawa. His father was a medical doctor who served as director of various government hospitals. Sumio became interested in chemistry as a boy through his father's work on biochemistry. In 1930, he entered the Faculty of Science, Hokkaido Imperial University (Sapporo), and carried out his thesis work for graduation in the organic chemistry laboratory of Professor H. Suginome, who had just returned from study abroad in Sir Robert Robinson's laboratory in Oxford. After his postgraduate course, supported by a foundation, he was appointed as an assistant, and, in 1940, as Associate Professor of Organic Chemistry of his alma mater. In 1942, he moved to the Department of Applied Chemistry, Faculty of Engineering (formerly called Fujiwara Institute of Technology), Keio University (Tokyo), where he remained until his retirement in 1975. He was appointed Professor of Organic Chemistry there in 1944, and served as the Chairman of the Department of Applied Chemistry, and as the Dean of the Faculty of Engineering from 1964 to 1969. He was granted the title of Professor Emeritus of

Keio University in 1975, and, since 1974, has served as Director of the Institute of Bioorganic Chemistry established at that time by the Microbial Chemistry Research Foundation, where he remains active and productive.

Umezawa did not begin his career as a carbohydrate chemist. His first series of papers (1936–1939) described the synthesis and substitution reactions of selenophene and the first synthesis of selenophthenes by the reaction of acetylene with heated selenium, for which work he received the Ph.D. (Doctor of Science) degree in 1942 at his alma mater. Umezawa became interested in the chemistry of natural products when he joined Professor Suginome's team, which was concerned with isolation and structural studies of Aconitum alkaloids (1941).

Umezawa's first research at Keio University concerned processes for penicillin production, conducted at the request of the government during the war. He succeeded in the first isolation of penicillin in Japan, working in cooperation with Professor Hamao Umezawa, his younger brother. Thus he began a life-long work on the chemistry of antibiotics.

Umezawa's interest in the field of aminoglycoside antibiotics dates back to his studies on processes for production of streptomycin in about 1945 and to his structural studies on kanamycin, which was discovered by Professor Hamao Umezawa in 1957. Aminoglycoside antibiotics are composed essentially of carbohydrates, and the remarkably successful clinical application of this group of antibiotics aroused widespread interest and stimulated intensive investigation of them by organic chemists. Umezawa accomplished the first total syntheses of a number of aminoglycoside antibiotics, including paromamine (1966), neamine, trehalosamine (1967), kanamycins A, B, and C (1968), butirosin B (1972), tobramycin (1973), streptomycin, dihydrostreptomycin (1974), and neomycin C (1979). Furthermore, extension of his synthetic work, combined with H. Umezawa's pioneering work on the mechanism of resistance of resistant bacteria, opened a rational way to the chemical modification of aminoglycoside antibiotics to overcome inactivating enzymes.

Antibiotic resistance is a serious concern in present chemotherapy. S. Umezawa's initial approach involved the total synthesis of the 3′-*O*-methyl and 3′-deoxy derivatives of kanamycin A (1971). It was found that the synthetic 3′-deoxykanamycin A exhibited remarkable antibacterial activity against resistant bacteria as well as against common bacteria, whereas 3′-*O*-methylkanamycin A was almost devoid of activity. This experiment by S. Umezawa was of great importance in that it substantiated the proposed biochemical mechanism of resistance of resistant bacteria. Subsequently, he and his coworkers extensively studied regioselective deoxygenation of various natural aminoglycoside antibiotics, and furthermore studied deoxygenation not only at C-3′ but also at other positions. One of these semisynthetic antibiotics, assigned the generic name Dibekacin, is 3′,4′-dideoxykanamycin B, and it has been commercialized as a useful drug for resistant infections. In the industrial processes for preparing Dibekacin, the Tipson–Cohen procedure for introducing unsaturation, which was developed by Professor D. Horton into a novel, intracyclic

unsaturation procedure for sugars, was successfully applied to the regiospecific unsaturation of the pseudotrisaccharide.

During the course of his synthetic work, Umezawa developed several techniques for selective or specific protection of hydroxyl and amino groups in aminoglycosides, and these have been used to great advantage in his syntheses of aminoglycoside antibiotics. Furthermore, Umezawa (with Drs. T. Tsuchiya and K. Tatsuta, 1966) discovered a new reagent ("TACu reagent") for the determination of configuration in aminoglycosides and aminocyclitols. The reagent specifically forms a copper(II) chelate between a vicinal, diequatorial hydroxyl and amino group, but not between vicinal hydroxyl groups, and the reagent has been widely used for the structural determination of aminoglycosides.

In addition to extensive studies on the aminoglycosides, Umezawa has been broadly interested in the chemistry of sugar-containing antibiotics. Collaboration between the groups of H. and S. Umezawa (1972) led to elucidation of the structure of the disaccharide portion common to the bleomycins. Bleomycins are useful antitumour agents discovered by H. Umezawa and his coworkers in 1966, and are glycopeptides composed of a novel hexapeptide, a terminal amine, and a disaccharide. Furthermore, Umezawa (with Drs. T. Tsuchiya and T. Miyake) has recently synthesized the disaccharide (1981). Very recently, the outstanding collaboration of the groups of H. and S. Umezawa led to the first total synthesis of bleomycin A_2. In addition, Umezawa and his coworkers are engaged in extensive studies on chemical modifications of macrolide antibiotics containing one or more sugar residues, some of which may be amino sugars. This pioneering research has very recently afforded a number of semisynthetic, macrolide antibiotics that are remarkably active against Gram-negative bacteria, against which the usual macrolide antibiotics are inactive, being active only against Gram-positive bacteria. This work opens up an important new aspect for the macrolide antibiotics. Together with work already described, Umezawa has pursued many other topics, including synthetic studies on various groups of antibiotics and related compounds, isolation and structural elucidation of a number of new microbial metabolites, and new organic reactions. The researches of Professor S. Umezawa are described in some 270 scientific papers and reviews.

Professor Umezawa has served on many committees of the learned societies and the Ministry of Education (Japan). He has been President of the Chemical Society of Japan, and President of the Society of Organic Synthetic Chemistry (Japan). He has been Editor of the Journals of these two Societies, and recently he was accorded Honorary Memberships by both Societies. He is a member of the Editorial Advisory Board of *Carbohydrate Research*. He was an Expert Member of the Science Technology Council to the Cabinet, and Expert Member of the University Establishment Council at the Ministry of Education. Since 1971, he has been Vice-President of the Microbial Chemistry Research Foundation. He serves as Councilor of many societies, including the Japan Antibiotics Research Association (Tokyo) and the Japan Chemotherapy Research Association (Tokyo).

Keio University recognized his achievements by bestowing the "Gijuku Prize"

in 1949 and the "Fukuzawa Prize" in 1963. In 1964, he received the Award of the Chemical Society of Japan, and, in 1980, the Japan Academy Prize. In the autumn of the past year, he was highly decorated for his distinguished service.

Professor Umezawa has been invited to many international meetings to give special or plenary lectures. In 1971, he delivered a special lecture on "New Developments in the Synthesis of Aminoglycoside Antibiotics" at the Symposium on New Natural Product Syntheses, XXIIIrd IUPAC Congress in Boston. At that time, the chairman, Professor Karl Folkers, introduced Professor Umezawa by familiarly calling him "Mr. Antibiotic of Japan". Professor Umezawa's beaming smile at that time is still fresh in our memories.

Professor Umezawa lives in the city of Tokyo and often enjoys country life with his family at their resort house by Kawaguchi Lake at the base of Mt. Fuji. Professor Sumio and Mrs. Yoshiko Umezawa have two daughters, Miyoko and Asako, and a grandchild, Hiroki, who is the son of Asako and Dr. Miki Wadachi, Associate Professor of Physics, Tokyo University. Sumio belongs to an illustrious scientific family, including, besides Professor H. Umezawa, Kuniomi Umezawa (a geologist) a former Vice-Minister of the Science and Technology Agency, Dr. Tsutomu Umezawa, a physician, and Minoru and Hiroomi Umezawa, both of whom are professors of physics.

In conclusion, as a representative of his pupils, I offer my cordial congratulations to Professor Umezawa on the occasion of his seventy-third birthday and wish him and Mrs. Umezawa many more years of healthy life, hoping that he will continue to give us his valued guidance and encouragement.

TSUTOMU TSUCHIYA