Satoru Masamune

July 24, 1928 - November 9, 2003

Satoru Masamune, Editor-in-Chief of Volume 55 of *Organic Syntheses*, passed away on November 9, 2003. He was 75 years old.

Sat Masamune was born in Fukuoka, Japan, and received his undergraduate education at Tohoku University. In Sendai, he carried out undergraduate research in the laboratory of his future father-in-law, Professor Tetsuo Nozoe. After receiving his bachelor's degree in 1952, he moved to the United States to pursue graduate studies at the University of California, Berkeley as one of the first Fulbright Fellows. He received his Ph.D. in 1957, working under the direction of Henry Rapoport.

Masamune spent the period 1956 to 1961 at the University of Wisconsin, Madison, first as a postdoctoral fellow in the laboratory of Eugene Van Tamelen, and then as a lecturer. In 1961, he received an appointment as a Fellow of the Mellon Institute in Pittsburgh, where he was to stay for the next three years.

Masamune's syntheses of the diterpene kaurene and the diterpene alkaloids atisine and garryine catapulted him to the first rank of synthetic organic chemists upon their publication in four back-to-back-to-back-to-back communications in the *Journal of the American Chemical Society* in 1964. These diterpene alkaloids possess exceedingly complex hexacyclic structures consisting of an intricate network of six interconnected rings, and their structures appear formidable and intimidating even to a synthetic organic chemist today! Perhaps most astonishing is the fact that Sat accomplished this tour de force singlehandedly, that is, literally with only his own hands, thus beating out more than 20 competing research laboratories around the world who were in hot pursuit of the same target molecules. This boded well for what Sat might accomplish were he to have the benefit of a group of coworkers!

In 1964, Masamune joined the faculty of the University of Alberta in Edmonton where he was promoted to full professor in 1967. He was recruited to join the faculty of MIT in 1978, and was named the Arthur C. Cope Professor of Chemistry in 1991. He became an emeritus professor at MIT in 2000, but remained actively interested in research, visiting his office nearly every day until his death.

Sat was a great friend, an extraordinary scientist, and an inspiration as a colleague. His creativity, high standard of excellence, and his incredible work ethic were an inspiration to his coworkers and colleagues alike. Among the many remarkable features of Sat's scientific career, two qualities particularly stand out in my mind as characterizing his great body of work: breadth and depth.

The breadth of Sat's interests and accomplishments was extraordinary. His selection of research projects was guided, always, by what he identified as *the* most important problems of the day, regardless of whether that might require him to foray out of his current comfortable and familiar sphere of research, thereby abandoning an area in which he might recently have established pre-eminence. As a result, his program spanned an astonishingly broad range of problems, bordering on one hand research in physics, as in his collaboration with the late Professor Tanaka of MIT, and bordering, at the other end of the chemistry spectrum, the interface where chemistry meets biology, as exemplified in his research on enzymatic reactions and on catalytic antibodies.

With regard to depth, I allude to the way in which, with every scientific problem that attracted his interest, Sat attacked the problem with a thoroughness and intensity unsurpassed by any chemist in my personal experience. These characteristics, together with his uncompromisingly high standards of scientific rigor, served him well as on more than one occasion he entered a research area rife with controversial results and competing claims, and time and again in short order carried out the definitive experiments that solved the key problems of the field and clarified the vexing ambiguities from earlier research.

In addition to his pioneering work on the synthesis of the diterpene alkaloids, Masamune made monumental contributions in a number of other areas of organic chemistry. Sat had a lifelong fascination with unusual cyclic structures possessing arrays of conjugated pi bonds. The origins of this passion no doubt has its roots in his undergraduate studies on the chemistry of tropones and tropolones, research he performed as an undergraduate at Tohoku University in the laboratory of Professor Tetsuo Nozoe. The theoretically interesting molecules which attracted Sat's attention, and the attention of many, many other scientists in the 1960s, 70s, and 80s, included a variety of fascinating structures predicted to possess imposing instability, instability derived from the fashion in which their structures were expected to be twisted, warped, distorted, stretched, and compressed, or destabilized by effects such as anti-aromaticity. Sat's contributions in this area are too many to enumerate, but include, most notably, the synthesis and investigation of members of the [4] and [10] annulene families. Thus, Masamune and his students were the first to prepare the simple [10] annulenes, which they achieved by an inspired choice of a synthetic route involving the photochemical generation of these exquisitely delicate and unstable structures at low temperature in the absence of other potentially reactive species. This work was a true tour de force, both intellectually and experimentally.

Similar tools were brought to bear as Masamune undertook pursuit of the Holy Grail of the field of theoretically interesting molecules, cyclobutadiene. This simple structure had defied the best efforts of numerous prominent chemists since the molecule was first discussed 100 years earlier. Masamune's keen theoretical analysis of the problem, and again, his extraordinary experimental acumen, enabled him to perform what is regarded as the most impressive and definitive work that was carried out in this very prominent area. Sat's research on the cyclobutadiene problem climaxed with his

instantly classic 1978 paper which he elegantly entitled "Cyclobutadiene Is Not Square", a paper in which he revealed unequivocal evidence for the correct ground state structure of this most famous of elusive Huckel ring systems. Space does not permit me to provide a full account of his many other triumphs in the field of strained and unusual "unnatural products", but let me call a roll of some of his many conquests in this area: basketene, the trishomocyclopropenium and pyramidal $(CH)_5$ cations, the aza and oxo [9] annulenes, the bridged 1,5-methano [10] annulene. In addition, in the 1980s and 90s the Masamune group also contributed to the chemistry of strained molecules composed of the Group 14 elements silicon, germanium, and tin. This is yet another case where Sat entered a totally new area and in remarkably short order performed definitive work, solving problems that had eluded the best efforts of the specialists of the field over a period of years.

Another area of significant contributions involves the chemical synthesis of the macrolide antibiotics, a field that first attracted Sat's interest in the late 1960s during his tenure at the University of Alberta. Why was Sat attracted to this problem? No doubt because it was universally regarded as the most formidable problem then confronting the science of organic synthesis. Just several years earlier, referring to one of the most well known and prototypical macrolides, R. B. Woodward had written that in spite of all the recent fabulous advances of the field of synthesis, the synthesis of these molecules "with all our advantages, looks at present quite hopelessly complex". Sat and his group are credited with what is now recognized as the first successful, total synthesis of a stereochemically complex, medicinally important polyoxo macrolide, specifically, the antibiotic methymycin. This monumental achievement was described in a series of three back-to-back-to-back JACS communications that appeared in 1975. I was a graduate student at Harvard at the time and I vividly remember the excitement, and envy, that the appearance of these publications engendered. The solution to this synthetic problem, from today's vantage point, would be described as "classical". However, we are only able to characterize it thus because of the revolution that was about to take place in synthetic organic chemistry, a revolution in which Sat was to be a key architect.

The term "revolution" is appropriate here, because it is no exaggeration to say that the strategy of "double asymmetric synthesis" has revolutionized the way chemists go about the synthesis of a very broad range of molecules, namely stereochemically complex, acyclic compounds. Landmark papers from the Masamune laboratory in the period 1979-1980 established the utility of this important concept in the context of the boron aldol reaction, a process for which Sat was one of the pioneers, and the power of this strategy was demonstrated convincingly by the Masamune group through the total synthesis of 6-deoxyerythronolide B in 1981. The conquest of this molecule was followed in rapid succession by successful ascents of a series of other synthetic Everests, including narbonolide and tylonolide in 1982, key components of rifamycin S and streptovaricin A also in 1982, amphotericin B in the period 1984 to 1988, bryostatin and pimaricin in 1990, and calyculin A in 1994.

Sat's contributions were recognized over the years with numerous honors and awards. In 1978 he received the ACS Award for Creative Work in Synthetic Organic Chemistry, and in 1987 he was the recipient of an Arthur C. Cope Scholar Award. He was a fellow of the Royal Society of Canada and of the American Academy of Arts and Sciences, and was named a Centenary Scholar of the Chemical Society of London in 1980. Sat received the prestigious Fujihara award in Japan in 1997.

Sat had a number of passions outside chemistry, most notably classical music, baseball, and sumo wrestling. A longtime resident of Newton, Massachusetts, he is survived by his wife, Takako (Nozoe), his daughter Hiroko, his son Tohoru, a sister, Michiko Hiyama of Hirosaki, Japan; and four brothers, Tadashi of Sapporo, Japan, Osamu of Akita, Japan, and Shinobu and Tsutomu, both of Tokyo. Sat Masamune is dearly missed by his family, former coworkers, and his colleagues.

Rick L. Danheiser
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