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OBITUARY

Carl Djerassi (1923 – 2015): an Obituary for Chemists

"Research is not finished until it has been peer-reviewed and published"—Carl Djerassi

Carl Djerassi published a number of autobiographies. Perhaps the most interesting one for chemists to read is "Steroids Made It Possible" published by the American Chemical Society in 1990. Towards the end of this book, he writes "physical or analytical separation techniques have changed the conduct of organic chemical research more than any other development in the past three to four decades." Elsewhere in the book, he recounts that he views "steroids as both paint and canvas, and physical methods as the brush."

Djerassi (Figure 1) published nearly 1200 peer-reviewed, scientific research articles on natural-product structure and synthesis, fundamentals and applications of analytical tools—notably optical rotatory dispersion, magnetic circular dichroism, and mass spectrometry—and the early extension of artificial intelligence to structure elucidation. Three of his ten most cited papers are in mass spectrometry. His most cited paper (1275 times) is Mass Spectrometry in Structural and Stereochemical Problems XXXII. Pentacylic Triterpenes, by H. Budzikiewicz, J. Wilson and C. Djerassi, *Journal of the American Chemical Society* 85: 3688 (1963). Across twenty-five years, 266 of his research papers contributed to the development and application of organic mass spectrometry. Part I of this series appeared in 1962, and the last contribution, Part 266, appeared in 1986, both in *JACS*.

In recognition of his scientific discoveries, he was awarded both the National Medal of Science (1973) for the first synthesis of a steroid oral contraceptive agent and the National Medal of Technology (1991) for promoting new approaches to insect control. He also received the 1992 Priestley Medal (the highest award given by the ACS), the Thomson Medal from the International Mass Spectrometry Foundation (1994), the first Wolf Prize in Chemistry (1978), the ACS award in Pure Chemistry (1958), the Perkin Medal (1973), and many others. The American Society for Mass Spectrometry successfully nominated him for the 2000 Othmer Medal of the Chemical Heritage Foundation. That award recognizes outstanding contributions to chemistry in multiple areas, including innovation, entrepreneurship, research, education, public understanding, and philanthropy. Carl's credentials were strong across the board.

Carl came to the USA in 1939. With indirect assistance from Eleanor Roosevelt, he received a scholarship to attend Tarkio College in Tarkio, Missouri. He completed his A.B... at Kenyon College (Summa cum laude), Gambier, Ohio, in 1942 and received his Ph.D. at the University of Wisconsin in 1945. His thesis director was A.L. Wilds. As is well known, in 1949 at the age of 26, he joined Syntex, S.A. in Mexico City as an associate director of chemical research. In his first two years at Syntex, he and his team published more than 60 papers and filed numerous patents on steroid chemistry, in particular the synthesis of cortisone from a steroidal sapogenin obtained from Mexican yams. This work was followed quickly by the synthesis (October 15, 1951), patenting, and publication of norethindrone, the active steroid in two of the first oral contraceptives approved by the FDA. In 1952, Carl moved to Wayne University in Detroit and commenced his academic career. In Detroit, he opened new lines of natural products research and initiated his development of chiroptical methods with a large group of post-doctoral fellows and graduate students. In 1959/1960, he moved his laboratory to Stanford University, where he maintained an active research and training program until he closed his lab in 1992. He became Professor Emeritus at Stanford in 2002. All told, he trained more than 300 graduate students and post-doctoral fellows from 51 countries.

Figure 1. Professor Djerassi in his office in the Stauffer Chemistry Building at Stanford in September, 1963. Courtesy of Masazumi Ikeda and Yuzo Nakagawa

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At the time he started working in mass spectrometry at Stanford, he also brought thin layer chromatography and gas chromatography into his laboratory. With these new techniques, he was able to reduce significantly the quantities of material required for purification and characterization of new natural products. Mass spectrometry provided molecular masses and structurally characteristic fragmentation profiles on far less material than had previously been required just for a mixed melting point determination. Carl wrote that his attention was drawn to mass spectrometry and its potential for analysis of natural products by publications from Ivor Reed in Glasgow, the Stenhagens in Sweden, and Klaus Biemann at MIT. Carl acquired a CEC 21-103 mass spectrometer from the Consolidated Electrodynamics Co. in Southern California, and several post-doctoral fellows came from Europe to help initiate his studies. Herbert Budzikiewicz arrived in December 1960 from the University of Vienna and John Wilson soon thereafter, from Ivor Reed's lab. Dudley Williams joined the team in 1961, and work began on the series of books that was to shape globally the interpretation of organic mass spectra for the next 25 years.

Many organic mass spectrometrists believe that Djerassi's key contribution to the field of mass spectrometry is the use of isotope labels to define and refine fragmentation mechanisms. He was always very precise with words, and he taught his students that ions have abundances, while peaks have intensities. He instituted the use of fishhooks to indicate homolytic bond cleavage and arrows to indicate heterolytic bond cleavage and two-electron movement. All four of his books on fragmentation mechanisms emphasize the importance of this kind of electron bookkeeping. Although much of his own research appeared in *JACS*, the mass spectrometry field expanded very rapidly, and soon *JACS* and the natural product journals could not hold all the papers. Djerassi was influential in the introduction of two specialized journals by the British publisher Heyden and Son: *Organic Mass Spectrometry* and *Biological Mass Spectrometry*. These were combined in 1995 to form the present day *Journal of Mass Spectrometry* published by John Wiley.

Djerassi initiated training in mass spectrometry of a first generation of graduate students, including Lazlo Tokes, Bob Shapiro, Sheila Sample, and Catherine Fenselau. The Stanford Ph.D.s and a crop of graduate students nurtured simultaneously at MIT constituted the first group of American chemical scientists who were formally trained in organic mass spectrometry. We were told to go forth and multiply.

At Stanford, Djerassi regularly held group parties at his home or at his ranch. At home, the tiles on the bottom of his swimming pool read "Built by ORD" referring to his book on optical rotatory dispersion. At one point in his career, he was publishing almost one paper a week, and many of these papers were written by hand beside the pool (see Figure 2). At his ranch in the hills above what is now Silicon Valley, the sign reads "SMIP" or Syntex Made It Possible." Later, the sign reads "Sic *manebimus in pace*." Eventually, Carl reconstituted the ranch as an artists' colony under the auspices of the Djerassi Resident Artists Program in memory of his daughter Pamela.

Figure 2. Carl Djerassi in the pool at a research group party in 1963. Courtesy of John Joule

Djerassi exercised great ingenuity in the classroom training he provided to both graduate students and Stanford undergraduates. In one of his early graduate classes, the students collectively wrote a book on steroid chemistry. The book was published by Holden Day and sold well. The profit was used to help erect a small round building for graduate seminars. He offered $100 for the best title for the book, ("Steroid Reactions: An Outline for Organic Chemists") which Catherine Fenselau won. He repeatedly offered well-subscribed undergraduate classes that addressed issues in scientific ethics and later incorporated the arts into a curriculum of science, ethics, and writing.

He thought and wrote about many of the issues associated with his science. In the 1960s, he was both half-time Professor at Stanford directing about 30 young scientists in his lab and also vice president (and then president) of Syntex Research, which had relocated its large facility to the nearby Stanford Industrial Park. For this situation, he developed a very early and ethically appropriate model to handle conflict of interest and the appearance thereof. On another front, he taught and wrote extensively about the tension between reliable birth control and the need to maintain procreation. This sense of social responsibility is apparent in his 1970 paper on "Birth Control after 1984" and his 1979 book "The Politics of Contraception."

One belief Carl held strongly during the years of the Cold War was that chemical education should be available at a high level in all the countries of the world. Through the 1960s and 1970s, his lab ran like a little UN, with post-doctoral fellows and graduate students from places like Brazil, Mexico, Japan, Canada, and China as well as most of the countries in Eastern and Western Europe. He supported the development of successful natural products centers in Brazil and Mexico by training local scientists and by supporting long-term appointments for foreign scientists who spoke the local language (see Figure 3).

Figure 3. Professor Djerassi talking in the laboratory with graduate student Hugo Monteiro (who joined the faculty at the Universidade de Brasilia) and post-doctoral fellow Dr. Keith S. Brown (who joined the faculty at the Universidade de Campinas). Photo credit: Chuck Painter/Stanford News Service

When Djerassi opened a second career 25 years ago as a writer of novels, poetry, and plays, he called his new art science-in-fiction and science-in-theater. Many of his fictional books and plays address ethical issues such as laboratory fraud ("Cantor's Dilemma") and scientific attribution ("The Bourbaki Gambit" and "Oxygen"). He has said that he sought to communicate to the broad public an understanding of the culture of science and to stimulate discussion about scientific ethics. He pursued this second career with characteristic intensity and vigor, traveling the globe to give readings and lectures. In 1990, he appeared at the 38th Annual Conference of the American Society for Mass Spectrometry in Tucson, Arizona, reading from one of his books and commenting on the relationship between science and the arts. On that morning, a one-of-a-kind picture was taken (see Figure 4) of three of the fathers of organic mass spectrometry—Klaus Biemann, Carl Djerassi, and Fred McLafferty.

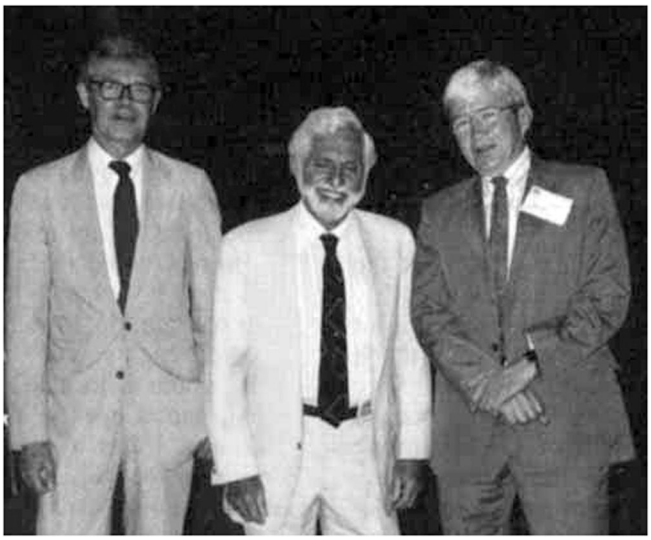

Figure 4. Klaus Biemann, Carl Djerassi and Fred McLafferty in a rare confluence at the 38th Annual Conference of the American Society for Mass Spectrometry, 1990. Reprinted by permission form John Wiley & Sons, LTD., *Organic Mass Spectrometry*, Steroids Made It Possible, Carl Djerassi, Vol. 27, 1341–1347

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