Carl Djerassi

Carl Djerassi (1923–2015)

Carl Djerassi died at the age of 91 on January 30, 2015 at his home in San Francisco after a long bout with cancer. He is best known for synthesizing the sex hormone norethindrone and thus helping to give women control over their fertility. He patented it shortly after its synthesis in 1951, and it is used to the present day in the oral contraceptive commonly known as The Pill. He was recognized with the US National Medal of Science, the US National Medal of Technology, the Wolf Prize in Chemistry, the Priestley Medal of the American Chemical Society, and was awarded with more than 20 honorary doctorates from universities all over the world. In later life he became a celebrated author of plays, poems, short stories, and a new writing genre he called "science in fiction". Best known to chemists is his play *Oxygen*, which was written together with Chemistry Nobel Laureate Roald Hoffmann. Few can rival Djerassi's combined accomplishments in chemistry and the arts.

As one of his colleagues in the Chemistry Department at Stanford University, I had the opportunity to get to know him well and observe his multifaceted life. Space prevents me from offering a fuller description, but I can recommend most enthusiastically his many autobiographical writings (for further information see his website http://djerassi.com/), in particular, his last autobiography *In Retrospect: From the Pill to the Pen* (Imperial College Press, London, **2014**). Short of meeting him in person, nothing conveys the force, character, charm, wit, and brutal honesty of Carl Djerassi than three particular videos. The first, made in 2009, celebrates Stanford pioneers in science and has a superb introduction to Djerassi's work by our colleague, Paul Wender. The second, made in 2011, is an interview with Chemistry Nobel Laureate Roger Kornberg. The third, made in 2014, is a departmental celebration of Djerassi as a nonagenarian, with introductions by my colleague, Chemistry Nobel Laureate W. E. Moerner, and myself (see http://web.stanford.edu/group/Zarelab/Djerassi.html).

Djerassi, who was born in Vienna to Jewish parents, left Austria with his mother in 1939 to escape the Nazi regime and came to the USA almost penniless. In 1945, at the young age of 22, he completed his doctoral studies at the University of Wisconsin in only two and one-half years and earned his PhD in organic chemistry. His thesis was on the transformation of testosterone to estradiol, which is a form of estrogen, a female sex hormone produced by the ovaries. This would mark the beginning of his long-term interest in steroidal compounds. In 1949, after working at the Swiss company Ciba in Summit, New Jersey, and synthesizing the first antihistamine, Djerassi accepted a position to head a research team at Syntex in Mexico City. This group worked on developing a practical synthesis of cortisone. Syntex was using Mexican yams as a rich source of diosgenin, the starting material for the synthesis of testosterone and progesterone, the latter of which is involved in regulating the menstrual cycle, pregnancy, and embryogenesis of humans and other species. Progesterone was known to be degraded in the stomach and gut. Syntex was seeking to find a form of progesterone that could be orally administered. In 1951, Syntex filed a patent based on the work of Djerassi's group for the compound 19-nor-17α-ethynyltestosterone, known as norethindrone ("nor" stands for the absence of a methyl group), which could enter the blood stream unaltered and was several times more potent than naturally occurring progesterone. Through subsequent clinical trials by Min Chueh Chang, Gregory Pincus, and John Rock, this compound was shown to be an effective contraceptive agent, giving rise to the birth of The Pill.

Djerassi was a prolific scientific author, with more than 1200 publications to his name. It would be folly to imagine that anyone could summarize this work in one paragraph, but I will try. His best scientific work might be his development and application of new methods for determining the structures of organic compounds. Like in so many other similar cases, these methods are used extensively by others, but their origins are often forgotten. During the 1950s and 1960s, Djerassi conducted extensive research on the structure elucidation of antibiotics. His group was the very first to determine the structure of a macrolide antibiotic (this group contains many clinically important compounds such as erythromycin). Djerassi pioneered the use of optical rotatory dispersion and circular dichroism in organic chemistry through research that spanned three decades into the mid-1980s. He then moved to the study of magnetically induced optical activity (magnetic circular dichroism), which does not require intrinsic chirality. Djerassi's group along with those of Biemann and McLafferty brought mass spectrometry to organic chemistry in the early 1960s. Over a period of 30 years, Djerassi's group introduced mechanistic interpretations of mass spectra that enormously expanded the use of the technique in structure elucidation. In the 1960s, in a series of investigations (initially in collaboration with Joshua Lederberg and Edward Feigenbaum of Stanford University), his group was the first to carry out research on applications of computer-aided artificial intelligence techniques to chemical structure elucidation. In 1972, Djerassi initiated his last major research project, which was concerned with the structure elucidation, biosynthesis, and possible biological

function of marine natural products. This work involved the isolation and structure determination of around 150 marine steroids. He certainly must be regarded as among the greatest chemists ever to have been associated with the Chemistry Department at Stanford.

Djerassi's work has significantly benefitted chemistry and will continue to do so for generations to come. This fact is all the more remarkable when one remembers that throughout his career at Stanford he only held a part-time appointment and continued to be quite active in industry. He was one of the founders of such companies as Zoecon, which uses steroids for insect growth regulation, and Affymax and Affymetrics, which make arrays for sequencing DNA.

Djerassi's contributions to chemistry have been monumental, but so far this recitation of his achievements fails to capture the complex nature of this individual, a person who in 1973 received from President Nixon the National Medal of Science and was also named on Nixon's black list of enemies, which Djerassi attributed to his opposition to the Vietnam war. As a person, he was a visionary and his style was self-assured, self-possessed, and unyielding, which brought more than one chemistry department faculty meeting to an abrupt close. Although he was a polarizing figure in the department, I count myself among his devoted admirers. In many ways Djerassi was a driven person. He always felt a longing for a home and for acceptance among his peers, a topic that Jeff Seeman has written poignantly about, see *Chem. Eng. News* **2013**, *91* (42), 10–14 and *Angew. Chem. Int. Ed.* **2014**, *53*, 3268–3279. Carl Djerassi's legacy to chemistry has been truly immense. It is difficult to expect to see the likes of such a giant of an individual, such a towering forceful intellect, ever again.

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Obituary

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Carl Djerassi died at the age of 91 on January 30, 2015. He is best known for developing the synthetic hormone used to the present day in the oral contraceptive commonly known as The Pill. Djerassi's other achievements include the use of mass spectrometry in organic chemistry, and extensive research on antibiotics and marine natural products. He was also an author of plays, poems, and short stories, including *Oxygen*, written together with Roald Hoffmann.