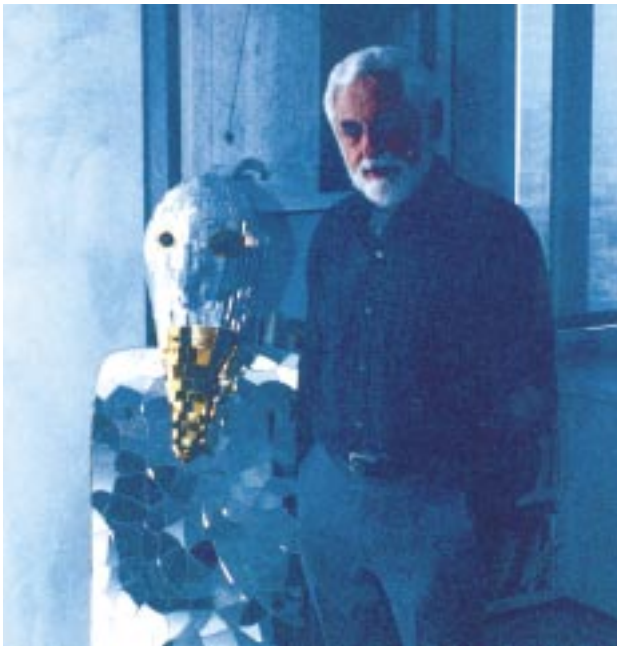


Carl Djerassi, pictured here with artwork from his collection. This sculpture, by artist Niki de Saint Phalle, is entitled "Wise Man."

Photograph by Walter van Schalkwijk.

Carl Djerassi: Renaissance Scientist Par Excellence

by Krishnan Rajeshwar and Walter van Schalkwijk

Carl Djerassi was born in Vienna, Austria, and received his education at Kenyon College (AB summa cum laude, 1942) and the University of Wisconsin (PhD, 1945). After four years as research chemist with CIBA Pharmaceutical Co. in Summit, New Jersey, he joined Syntex, S.A., in Mexico City in 1949 as associate director of chemical research. In 1952, he accepted a professorship at Wayne State University, and in 1959 his current position as professor of chemistry at Stanford University.

Concurrently with his academic positions, he also held various posts at Syntex during the period 1957-1972, including that of president of Syntex Research (1968-1972). In 1968, he helped found Zoecon Corporation, a company dedicated to developing novel approaches to insect control, serving as its chief executive officer until 1983. He continued until 1988 as chairman of the board of Zoecon (now a subsidiary of Novartis, Ltd.).

Djerassi has published over 1200 articles and seven monographs dealing with the chemistry of natural products (steroids, alkaloids, antibiotics, lipids, and terpenoids); with applications of physical measurements (notably optical rotatory dispersion, magnetic circular dichroism, and mass spectrometry); and computer artificial intelligence techniques to organic chemical problems. In medicinal chemistry, he was associated with the initial developments in the fields of oral contraceptives (Norethindrone), antihistamines (Pyribenzamine), and topical corticosteroids (Synalar).

For the first synthesis of a steroid contraceptive, Djerassi received the National Medal of Science (1973), the first Wolf Prize in Chemistry (1978), and was inducted into the National Inventors Hall of Fame (1978). He received the National Medal of Technology for his contributions in the insect control field (1991). The American Chemical Society honored him with its Award in Pure Chemistry (1958), Baekeland Medal (1959), Fritzsche Award (1960), Award for Creative Invention (1973), Award in the Chemistry of Contemporary Technological Problems (1983), Priestley Medal (1992), Willard Gibbs Medal (1997), and Othmer Gold Medal (2000).

Carl Djerassi is a member of the U.S. National Academy of Sciences and of its Institute of Medicine, as well as a member of the American Academy of Arts and Sciences, the Royal Swedish Academy of Sciences, and many other learned societies. He has received 18 honorary doctorate degrees from various academic institutions around the world.

Djerassi has embarked on a second career in writing including five "science-in-fiction" novels: *Cantor's Dilemma; The Bourbaki Gambit; Marx, Deceased; Menachem's Seed;* and *NO*. He has also published a scientific autobiography, *Steroids Made it Possible*; and his collected memoirs, *The Pill, Pygmy Chimps, and Degas' Horse*. He has also embarked on a trilogy of "science-in-theater" plays, of which "An Immaculate Misconception" is the first installment (broadcast by the BBC as the "Play of the Week" in May 2000). His second play, "Oxygen" (co-authored with Roald Hoffmann) made its debut in May 2000 with a series of workshop performances at the Eureka Theater in San Francisco. His intent is to use both types of media as "an effective way of smuggling serious topics of scientific endeavor into the consciousness of the scientifically illiterate."

At the invitation of Prof. Djerassi, Krishnan Rajeshwar, Editor of *Interface* and Walt van Schalkwijk, Chair of the New Technology Subcommittee, attended one of the "Oxygen" performances on May 6. They also availed themselves of this opportunity to conduct a wide-ranging interview with this scientist/author extraordinaire the next day in Prof. Djerassi's residence overlooking San Francisco Bay. Following are excerpts from this interview.

Interface: *Let's talk about your early days in chemistry and the race for the discovery of the Pill and the synthesis of cortisone.*

Djerassi: Interestingly, there was not much of a race in the former case! But let me first start with the steroid story. The late 1940s were exciting days in steroid chemistry, especially since the anti-arthritic properties of cortisone had just been discovered. I was anxious to work on an improved synthesis of cortisone but I could not do that work at CIBA. Thus, when a chemist friend, Martin Rubin from Schering, proposed me for an opening as associate director of research at Syntex in Mexico City, I did not reject the possibility. The team there was comprised of George Rosenkranz and myself as the leaders; Gilbert Stork of Harvard as the consultant; two Mexican PhD scientists, O. Mancera and J. Romo; and Juan Pataki, a Hungarian like Rosenkranz, trained in Switzerland.

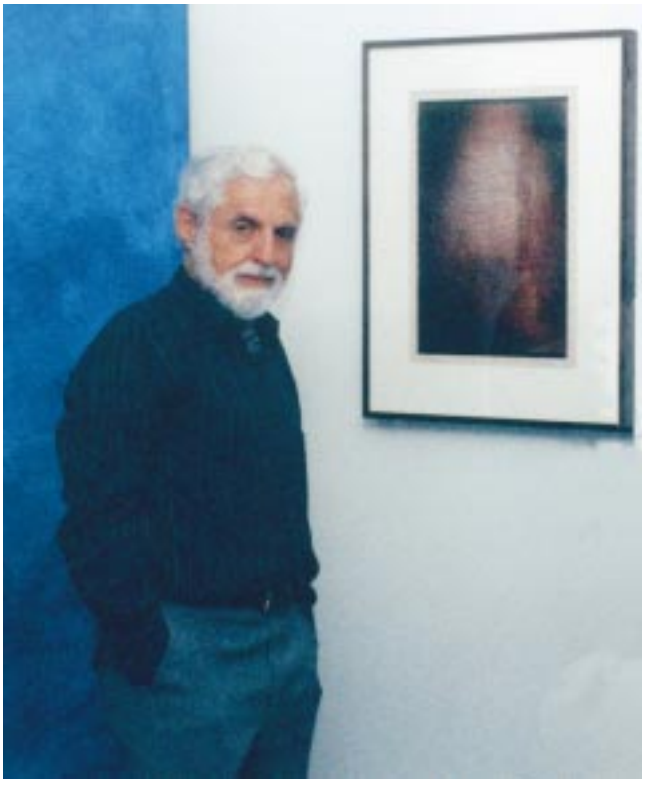
The starting material our team chose, as a more widely available alternative to the expensive bile acid employed by Merck & Co. in Rahway, NJ, was diosgenin. This naturally occurring plant steroid had been utilized by Syntex for the large-scale manufacture of progesterone and testosterone. In the end, no fewer than four communications to the editor, dealing with different synthetic approaches to cortisone, appeared in the August 1951 issue of the *Journal of the American Chemical Society*. Other than the Syntex group, the race involved two different Harvard University groups, headed by professors Woodward and Fieser, and another team in Merck headed by Max Tishler. The Syntex manuscript was received on June 22 and the other three papers arrived in July. *Life* magazine featured this victory of ours in a picture with the headline "Cortisone from Giant Yam" with the subsidiary headline "Scientists with average age of 27 find big supply in Mexican root." *(Ed. Note: see photo on page 26.)*

The birth of the Pill began with the new steroid, norethindrone that we synthesized at Syntex on October 15, 1951. Not in our wildest dreams did we imagine that this substance would eventually become the active progestational ingredient of nearly half the oral contraceptives used worldwide. The patent application was filed on November 22, 1951, and it is the first patent for a drug listed in the National Inventors Hall of Fame in Akron, Ohio. *(Ed. Note: A fascinating historical account of these discoveries can be found in:* Steroids*, Vol. 57, p. 631 (1992). See also* The New York Times *science segment on Tuesday, May 9, 2000 for a story on the discovery of the Pill by two other pioneers in this field, Gregory Pincus of the Worcester Foundation for Experimental Biology in Shewsbury, MA and John Rock of Harvard Medical School).*

Interface: *You were one of the trailblazers in the now common trend of academic professors being actively involved in technology start-ups. Can you comment on this?*

Djerassi: This really started with my move to Stanford from Wayne (now Wayne State) University, Detroit. The legendary Fred Terman, then Stanford's provost and the man generally recognized as the creator of the Stanford Industrial Park and of Silicon Valley, and a professor from my graduate school days, William S. Johnson, had a lot to do with my move to California. While many academics over the years had been suspicious of my "bigamous" professional life, Terman was not. Terman felt that the presence of a first-class medical school (Stanford's medical school had moved two years earlier from San Francisco to the Palo Alto campus) and an upgraded chemistry department would encourage biomedically or chemically oriented industrial enterprises to join the electronic and computer companies in the Stanford Industrial Park. In his eyes, my industrial connection with Syntex made me attractive, not suspect.

I call this situation, "intellectual polygamy." Namely, if an academic wants to shepherd his or her scientific baby along the road to practical maturity (and indeed, financial gains), why should such a person have to abandon the academic laboratory? Monogamy is great for stable marriages, but what is the evidence against the benefits of intellectual bigamy in academia and ultimately to society? A few years ago I gave a commencement address at the University of South Carolina on precisely this topic, which I titled: "In Praise of Polygamy." While this title undoubtedly raised a few eyebrows, I do hope that the pedagogical importance of this concept was not lost. I strongly feel that a professor with active participation in the extremely complicated, multi-disciplinary approach to practical realization of laboratory discoveries, is likely to be a much better mentor. By the same token, an academic serving in some part-time directorial or managerial position in industry, will offer a perspective rare in conventional businesses. *(Ed. Note: A fuller discussion is contained in: "Basic Research: The Gray Zone,"* Science*, Vol. 261, p. 972, August 20, 1993. A status report of this trend may also be found in an intriguing article titled: "Who Wants to be an Academic Millionaire?" that appeared in the* Chronicle of Higher Education*, March 3, 2000.)*



Djerassi, with "Hero Mother," by artist Paul Klee. Photograph by Walter van Schalkwijk.

A photo of the press conference announcing the first synthesis of cortisone from a plant source at Syntex in Mexico City in 1951. Life *magazine featured this achievement with the headline "Cortisone from Giant Yam."*

Interface: *This brings us to a very serious "pipeline" problem in science. That is, increasingly, the bright minds of the next generation appear to be drawn to careers in medicine, law, and even, business rather than to basic sciences.*

Djerassi: I think the problem can be partly traced to the very poor job we have done in projecting science to the general public. Frankenstein, Strangelove, the nerd—these are the "scientist role models" generally found in the media. Let me cite you another example, Steven Poliakoff's "Blinded by the Sun," a British play that received much publicity even in the scientific press. While illuminating in many respects, it nonetheless failed in its presentation of the actual science; the science in the play was depicted through meaningless gobbledygook that is unlikely to enlighten an audience equipped with more curiosity than knowledge about science. I have chosen the rarely used genre of "science-in-fiction" and "science-in-theater" to illustrate the human side of real scientists, and the conflicts they face in their quest for scientific knowledge, personal recognition, and financial rewards.

Interface: *You have become interested in the important issue of the role of women in science and technology. Of course, this aspect has also been the subject of much recent discussion within the narrower context of chemistry. Any comments?*

Djerassi: This is an interesting and important issue. For example, in countries such as Argentina and the Phillipines, women comprise the majority of the faculty population in several universities. Why is this so? Perhaps the answer lies in the fact that the men are viewed as the bread-winners in their culture. Thus the women migrate to the "less time-consuming" and more flexible schedules typical of an academic career. In my recent book "NO" *(Ed. Note: This novel will be available at the ECS fall meeting in Phoenix in conjunction with Prof. Djerassi"s Plenary Lecture),* I have turned to two gender issues: the historic marginalization of women in the male-dominated scientific universe and the attempts of women, as well as some men, to change this state of affairs. Most of my female characters (including Renu Krishnan in "NO") are portrayed as "independent"—a pejorative term to some but the ultimate compliment in my own eyes. In particular, Asian women in American science are triply marginalized: as women in a male-dominated glass-ceilinged field, as foreigners of color, and finally, coming as they do from a culture in which a woman's role is clearly defined, by the process of eventually losing part of their native culture without gaining an acceptable new one. Renu Krishnan represents a distillation of the complicated conflicts faced by such women. *(Ed. Note: For a discussion of the role of women scientists in the narrower context of analytical chemistry, see the article by E. Zubritsky titled "Women in Analytical Chemistry Speak" in:* Anal. Chem., *April 1, 2000, p. 272A. A more general article on women faculty in MIT appeared in the* Chronicle of Higher Education, *Dec. 3, 1999. The full text of the MIT report is available at: http://chronicle.com/documents.)*

Interface: *A word that has been bandied about lately is "globalization." Of course this has also been a lightning rod for a segment of the population with agendas of their own, e.g., trade unionists and environmental activists. What is your take on the globalization trend in science?*

Djerassi: A striking phenomenon of the contemporary science scene is the remarkable Asianiztion of the American academic research enterprise: Asians represent in certain disciplines, such as chemistry and engineering, the majority of graduate students

Phoenix Plenary Preview

As a preview of the plenary talk that Prof. Djerassi is scheduled to give at the 198th ECS meeting in Phoenix on October 23, 2000, he had the following to offer via e-mail from London:

"Science-in-fiction" implies that everything dealing with science and scientific behavior is depicted accurately and plausibly, whereas no such restriction needs to apply to science fiction. That requirement for accuracy is one reason why "science-in-fiction" can have important pedagogic applications, for instance by smuggling scientific facts into the mind of a reader who had only expected to be entertained.

But why is "science-in-fiction" so rare? Is it because so few authors are trained to write in that genre? Is it because any mention of "didactic" or "pedagogic" in literature is automatically suspect or criticized? Or is the above definition of "science-in-fiction" so self-limiting that neither many authors nor readers are attracted to it? As the author of a tetralogy of science-in-fiction novels and of a prospective trilogy of "science-in-theater" plays, these restrictions have clearly not deterred me.

The final volume of my tetralogy, *"NO,"* deals with the biotech industry, the interaction of academic scientists with entrepreneurs and Wall Street, and most appropriately to this occasion with some novel aspects of electrochemistry—aspects with which most participants of this meeting are likely to be unfamiliar. Hence, I will attempt through science-in-fiction rather than slides to both instruct and entertain.

in many American universities. In many of these institutions, more than half the postdoctoral fellows have received the bulk of their college or university education in Asia. Initially overwhelmingly Indian and Japanese, since the 1970s, they have become outnumbered by Chinese and Korean visiting scientists and immigrants. At a recent Berkeley commencement of about 2,000 students, I happened to scan the list of graduating students: nearly half of the students bore Asian names! Is this good or bad for American science? I happen to think that this cross-fertilization is a very healthy portent.

A few years ago I served on a review panel for the Swedish National Research Council. One of the major concerns that arose out of this review exercise was the extreme homogeneity of the scientific personnel and the consequent proliferation of scientific inbreeding—a situation that encompasses both personnel training and fertilization of ideas. American science is fortunate in this respect.

A related aspect of globalization is "appropriate technology." For example, it hardly makes sense for an African country to develop a tertiary education/training program in an area such as ultra-fast spectroscopy. On the other hand, it makes eminent sense to establish centers of excellence in areas such as insect control. I was involved with one such center in Nairobi. Again a "top-down" approach in training personnel in super-specialized and appropriate areas such as insect control can be very effective. The revolution that is quietly taking place in information technology in a country like India is another good example of the concept of appropriate technology.

Interface: *Returning to the image "crisis" that science faces, the situation is particularly bad for chemistry, in part fueled by the media where a certain degree of chemophobia pervades. A case in point concerns the recent movie: "Erin Brockovich," in which chemistry was cast in a rather bad, environment-damaging role. Is this justified and what can be done in terms of damage-control, both from an environment perspective and from a popular perception viewpoint?*

Diary Entry (11 August 1983)

We sit in Copenhagen,
Chemists from a dozen countries.
The talk is heavy; the words are long:

Male contraception,
Cures for cancer,
Morphine substitutes,
Drugs from the sea,
Medicines for the year 2000.

We've mouthed these words for many years,
Formulae hiding the chemists,
Who are these colleagues, students, strangers?
What do they do besides chemistry?

If this were the Holiday Inn,
Not the Royal Danish Academy,
Would I guess who they are?

A convention of grocers? Too serious.
Car salesmen? Too little polyester.
Bankers, Lawyers? No vests.
Clergymen? Wrong collars.
Poets? Nobody smokes.

How did they come to chemistry?
What do they do besides chemistry?
What do I do besides what I do
Besides chemistry?

—C. Djerassi, SANDS 1987, p. 10

Djerassi: The chemical industry has to shoulder at least some of the blame for this state of affairs. They were less than responsible in the 60s and 70s in the manner in which waste chemicals were released to the environment (Love Canal comes to mind here). On the other hand, we have to recognize the good that has come out of chemical and pesticide use. For example, typhoid in Naples, Italy, and malaria in Sri Lanka could not have been contained after World War II without extensive use of (the much-maligned) DDT.

I have a good perspective on environmental problems accumulated from my many years of involvement with Zoecon Corporation. (I had surprised everyone, including myself, by resigning as president of Syntex Research in 1972.) It taught me that unlike in the human drug market, where alleviation of pain and suffering in the affluent world is the target of most pharmaceutical companies, cost and price completely control the insecticide/pesticide marketplace. It makes no difference how environmentally harmless or how biodegradable a new insect control agent is: if it exceeds the highly constrained budget of the farmer, no market penetration accrues. The culmination of my involvement with Zoecon was the National Medal of Technology that I received from President Bush in recognition of this company's pioneering work on environmentally more benign insect control agents. This company, however, was acquired by Novartis, Ltd; so if the measure of success of a company lies in independent corporate existence, we didn't make it!

Unfortunately there are many examples of media hype and conspiracy theories that seriously undermine much of the unpublicized work toward environmental mitigation by the chemical/biochemical community. This is especially egregious when such hype is promulgated by Nobel Laureates! A case in point is "Dancing Naked in the Mind Field" by Kary Mullis. In this book, the author not only rejects fears of a reduction in the ozone layer as absurd, but proposes instead, that such claims constitute a clever manipulation by DuPont Co. to market a substitute for Freon whose patent has expired. *(Ed. Note: A more detailed critique of this particular book may be found in:* New Scientist, *November 21, 1998, p. 51.)*

Interface: *Who would be the guests at your fantasy dinner party and how would you like to be remembered?*

Djerassi: These are not easy questions to answer! Certainly I would not have any chemists (or even scientists) for that matter as the invitees! I find them too one-dimensional nowadays. I will probably have writers, playwrights, actors (not screen but stage), painters, and musicians as guests.

What legacy would I like to leave? Perhaps as a scientist who moved beyond traditional confines to an acute awareness of the societal impact of scientific research. My chemical contribution to the discovery of the Pill certainly reflects this transition. For example, it is gratifying yet humbling to be included by *The Times* (London) in the list of the 30 people who had most impact on life in the past millennium. Yet I don't take these things too seriously. How could I have had more impact than someone like Beethoven, for example, who's missing from this compilation? Clearly, my name as the only living person in that list is only there as a surrogate for a discovery (in this case the Pill), which otherwise would have been made by someone else—a fact that applies to all the other scientists on that list, from Newton to Einstein. But Shakespeare, for instance, is there in his personal capacity, because if he had not lived, *King Lear* or *Hamlet* would never have appeared! ■

To learn more about Carl Djerassi, visit his website at: www.djerassi.com.