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Synthesizing a Life: An Interview with Carl Djerassi

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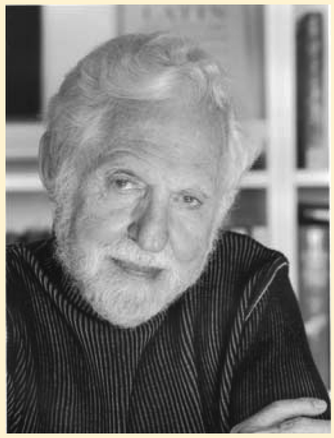
ABSTRACT: In this interview, Carl Djerassi recalls his first years, from his pleasant childhood, to how he escaped the Nazi persecutions, to his college education in America. He remembers how with his research group he won the race for synthesis of cortisone, and how they then synthesized norethindrone, the active ingredient in oral contraceptives. Djerassi also discusses the sometimes-difficult relationship of graduate students and postdoctoral fellows with professors. This is also the subject of two of his "science-in-fiction" books. Djerassi shares his views about the careers of women in academia, and the interactions and the problems that can arise when a university professor accepts a position in industry. Beyond discussing human reproductive advances and feminist positions, as well as recurring themes in his second life as a successful writer, Djerassi shares his personal experience with sorrow and death.



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A BRIEF BIOGRAPHICAL SKETCH

Carl Djerassi was born in Vienna, Austria, in 1923, to a Bulgarian father and a Viennese mother, both physicians. He lived in Bulgaria with his parents until he was five, when his parents divorced. He and his mother then moved to Vienna, and until age 14 Djerassi attended the *Realgymnasium* (the same school that Sigmund Freud had attended many years earlier), and spent summers in Bulgaria with his father. After the *Anschluss*, his father briefly remarried his mother to allow Carl and his mother to flee to Bulgaria to escape the Nazi regime. In 1938, he entered a private high school in Sofia, Bulgaria, The American College of Sofia, where most subjects were taught in English.

In December 1939, Djerassi arrived nearly penniless with his mother in New York City, and within a month he entered the Newark Junior College in Newark, New Jersey, as a premed major. Early in 1940, he wrote to Eleanor Roosevelt asking for help in securing a scholarship for tuition, room, and board to continue his college education. Fortunately, he was awarded a scholarship for the next semester at Tarkio College, in Tarkio, Missouri, the same college attended by Wallace Carothers, the inventor of nylon. He compressed his college career into five semesters: two in Newark, one semester in Tarkio College, and two semesters plus a summer at Kenyon College, in Ohio. He wrote: "what converted me into a chemist were a superb chemistry teacher at Newark Junior College, Nathan Washton ... the equally superb two-men Kenyon College Chemistry Department, consisting of Walter H. Coolidge and Bayes M. Norton, in classes ranging from two to four students; and my lack of financial resources for medical school" (ref 1, p 9).

Djerassi graduated in 1942 (A.B., summa cum laude), not yet 19, and then started working as a junior chemist at CIBA Pharmaceutical Company in Summit, New Jersey, where he codiscovered one of the first antihistamines, pyribenzamine (tripelennamine).[2] The success of this drug, used by millions of allergy suffers, and reading Fieser's book, *Natural Products Related to Phenanthrene*,[3] got Djerassi interested in steroids. After one year at CIBA, he married his first wife, Virginia, and started graduate work at the University of Wisconsin−Madison for his Ph.D. degree on the partial aromatization of androgenic steroids to estrogens, having as his advisor A. L. Wilds. In 1945, Djerassi earned his Ph.D. in organic chemistry and became an American citizen. He then returned to CIBA for another 4 years. In late 1949, he accepted a position at Syntex SA in Mexico City, Mexico, where he worked on a possible synthesis of cortisone with many collaborators and in a very well equipped laboratory. At that time, gas chromatography and high-performance liquid chromatography were still unknown; the products of organic reactions were separated using column chromatography and the only physical methods used by organic chemists were UV and IR.

In the two years Djerassi spent at Syntex, he coauthored about 60 papers, and developed a convenient three- or four-step synthesis of many estrogens.[4] In 1951, with the group at Syntex, he won the race for the synthesis of cortisone[5] from a plant-based raw material (diosgenin). Later that year, on October 15, the team completed the synthesis of the first synthetic oral contraceptive, "the Pill".[6] These accomplishments garnered an offer of an academic job, and in January 1952, Djerassi joined the faculty of Wayne State University in Detroit, moving there with his second wife, Norma. During the five years spent there—the last three as full professor—he and his students started a line of natural-product research in the area of antibiotics,[7] alkaloids,[8] and terpenoids.[9]

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Through the use of numerous optical rotatory dispersion (ORD) measurements, Djerassi laid the foundation for the use of this technique and, later, optical circular dichroism (OCD) in the determination of absolute configurations.[10] In 1957, he took a two-year leave of absence from Wayne State University to return to Mexico City as Vice President in charge of Research at Syntex, and to undergo a major operation: a permanent knee fusion, because of a skiing injury sustained during his teenage years on Mount Vitosha in Bulgaria. In the fall of 1959, he completed his first book, which summarized the ORD work,[11] and accepted a professorship in the Chemistry Department of Stanford University, where he spent 42 years, working on five new areas of research in addition to the lines started before.

Once again his scientific output was prodigious, with his 1000th publication being a review of his previous ORD and OCD work![12] In 25 years, starting in 1961, he coauthored 270 papers and four books[13−15] on the applications of mass spectrometry in organic chemistry. In 1967, Djerassi undertook a major collaborative program on the use of computer artificial intelligence techniques to structure elucidation in organic chemistry, working with Edward Feigenbaum and Joshua Lederberg in the DENDRAL (dendritic algorithm) project. This involvement produced a series of publications that culminated in his IUPAC lecture[16] in 1982.

These different studies might be sufficient for an ordinary researcher, but not for Carl Djerassi. ORD and circular dichroism require that the substrate be optically active. The idea has been to overcome this limitation by generating a magnetically induced rotation. In spite of some reported failure, the Djerassi group has been able to record satisfactory magnetic circular dichroism (MCD) spectra for all achiral carbonyl compounds.[17] Over a period of about 20 years, the group published about 70 papers on the MCD behavior of a variety of chromophores.[18]

A last topic of research that Djerassi has undertaken needs to be mentioned: marine natural products chemistry. Beyond the elucidation of novel marine sterol structures, this research theme deals with the biosynthesis of sponge sterols and phospholipids. The development of bioalkylation of the cholesterol side chain and the quite singular way Djerassi became interested in this research field is reported in a summary (ref 1, pp 114−138) of approximately 140 research publications.

Djerassi has pursued a distinguished career as an organic chemist, publishing over 1200 scientific papers, eight books, and attracting to his laboratory more than 300 pre- and postdoctoral colleagues from 52 countries. It should also be mentioned that the Prelog-Djerassi lactone, a product of chemical degradation of narbomycin and methymycin, might be used as a template for the synthesis of macrolide analogs.[19]

Djerassi serves as a most successful model of the scientist and entrepreneur who knows how to turn his discoveries into commercially useful and profitable enterprises without jeopardizing his academic standing. While teaching and researching in Stanford University, he also led a productive research career in industry. He served as president of Syntex Research, and helped to found several spin-off companies, including SYVA, a joint venture between Syntex and Varian, and Zoecon. In 1972, he left the presidency of Syntex and became CEO of Zoecon, a company focused on the development of biorational approaches to insect control with a minimal impact on the environment; see "How Do You Get a Cockroach To Take the Pill?",[20] for which he won the National Medal of Technology in 1991. Zoecon developed methoprene, an insect-growth regulator that mimics a hormone found only in insects; exposure to methoprene prevents juvenile insects from developing into reproducing adults. This work led naturally to the establishment of the International Centre for Insect Physiology and Ecology (ICIPE), which was founded in Nairobi, Kenya in 1970 with the support of over a dozen international academies through his initiative with Thomas Odhiambo, ICIPE's first director.

Working in industry made Carl Djerassi a wealthy man. His research into steroids and new physical techniques for organic analysis made Carl Djerassi into a famous scientist without peer. Yet, a bout with cancer reoriented his life in a quite unexpected direction, as will be clear from the following interview. At age 62, he decided to pursue a very different intellectual life: he became a writer. He is known as the initiator of "science-in-fiction" and "not-so-fiction" novels, in which he illustrates the human side of real scientists and the conflicts they face in their quest for scientific knowledge, personal recognition, and reward, with the aim of talking about the problem rather than the personalities. He is the author of five novels, two autobiographies, a poetry chapbook, a collection of short stories, a memoir, and nine plays—the majority in the form of "science-in-theatre". His first poetry volume, *The Clock Runs Backward*,[21] was published in 1991; his first novel, *Cantor's Dilemma*[22] was published in 1989, *The Bourbaki Gambit* followed in 1994,[23] and *Menachem's Seed* was published in 1996.[24] Among other plays, he is the author with Roald Hoffmann of the play *Oxygen*,[25] which premiered in the United States at the San Diego Repertory Theatre in 2001 and has since been translated into 16 languages. For more information, I recommend taking a short journey into Carl Djerassi's Web site.[26]

This interview took place in Sondrio, Italy, in April 2008. Carl Djerassi begins by alerting readers to his three published autobiographies for more extensive information and background.

EARLY INFLUENCES AND ACCOMPLISHMENTS

Let's start with an introduction for any reader. You are not the first one who has asked these questions, though not everybody asks the same ones in one single interview. I've really put them, not only into one but two autobiographies and a memoir—in fact, I may be the only person in chemistry who has written what amounts to three autobiographies. You'd think one is enough. Two is overkill, but three? I've not only put many things in there, but as a fiction author, I've put much of myself into my fiction. So, the real as well as more subtle answers will actually be found in my fiction, rather than my autobiography.

My first autobiography was an entirely chemical one in the famous 22-volume series of autobiographies of organic chemists that Jeff Seeman edited for the American Chemical Society in the 1990s.[1] The second one, *The Pill, Pygmy Chimps, and Degas' Horse*[20] was addressed in 1992 to the general public, but in 2001 I published a third one—a memoir—*This Man's Pill: Reflections on the 50th Birthday of the Pill*.[27] I wrote this because a lot of things had happened in the intervening decade of my life which I had not covered before. During that time, I had really changed from chemist to literary author. In addition, I reflected in that memoir on the societal, political, and cultural consequences of the Pill. I feel that at the outset, I must refer to those publications, because otherwise, I'll be talking for hours on end about topics that I have already covered in great detail in these three autobiographical writings.

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Liberato Cardellini: In "The Quest for Alfred E. Neuman"[28] you described your trouble as a Hitler refugee. How much did this persecution influence your life?

Most Americans, though few foreigners, will understand this reference to Alfred E. Neuman, because the former all know about *MAD Magazine* and its caption featuring an imaginary character by that name. This chapter from my big autobiography is a psychologically interesting one because it describes how I, a Jewish refugee from Nazi Austria, responded to the question of anti-Semitism even in cases where it did not exist—which is something that only refugees understand, quite different from let's say, American Jews, meaning Jews that are born in America. They display a degree of confidence because they feel at home, and while they may be considered a religious minority, they consider themselves Americans.

I was only 16 years old when I came via Bulgaria to the United States, originally from Austria, a few months after the Anschluss. You will remember that you've interviewed another refugee from Nazi Europe, Roald Hoffmann, but his case was very different because his father died in a concentration camp, and if he and his mother hadn't been hidden by decent Poles for a long time, he would have died too. When they eventually escaped, they went through all kinds of refugee camps before arriving in the United States. None of this applies to me. I came from a very small family. My father was a Bulgarian Sephardic Jew, who had met my mother, who was an Ashkenazi Jew born in Vienna, while they were both studying medicine at the University of Vienna. My parents had divorced when I was about four years old. So I had two homes: I was born in Vienna and lived with my mother and my grandmother in Vienna where I went to school. But I always spent summers in Bulgaria with a very large Bulgarian family on my father's side, and he visited us frequently in Vienna. So, it was a very pleasant childhood.

A few months after the Nazi *Anschluss* in March 1938—in other words months before *Kristallnacht* and the really vicious things, including deportation of thousands of Jews—my father came to Vienna and quickly remarried my mother so she would acquire a Bulgarian passport, and we could leave immediately. So I was not directly touched by the horrors of the Holocaust. That doesn't mean I wasn't traumatized, but that's a very different question. In September 1938, I entered the American College of Sofia, a boarding school where I learned English in Bulgaria, from American and English teachers. This was an enormous advantage, because in contrast to many of the refugees from Germany and Austria, when I arrived in the United States in December 1939, I spoke good English. I had an accent, but I spoke fluent English and thus had no language problems. Nevertheless I saw anti-Semitic questions that frequently really weren't meant that way and I was always very, very suspicious. In contrast to many of the other Jewish refugees, thousands and thousands of them, who stayed in the East Coast, around New York with its huge American Jewish population, I spent most of the time in the Midwest: at the beginning in Tarkio, Missouri, a place where there wasn't a single Jew. I attended Tarkio College where there wasn't a single European. Most of the people didn't even know where Bulgaria was. So it was a totally different experience from that of most other Jewish refugees of my generation. When I was confronted by questions that seemed to me as intrusive questions about being Jewish, they weren't actually meant that way. To a large extent they were questions stemming from curiosity and based on ignorance. Thus, most of the time I responded in a very evasive way as I related in detail in that chapter of my autobiography by relating the cover of *MAD Magazine* to images I had seen in Nazi Vienna.

You also need to remember that during the time when I grew up, acquired a Ph.D. in chemistry, and entered industry, there were many places where Jews were excluded. That was very typical at that time in the United States. There were many companies that had no Jews. There were many clubs that excluded Jews. Columbia University, right in Jewish New York, had a *numerus clausus* for Jewish students wishing to enter medical school. I was a professor in two universities, first at Wayne State University in Detroit, and then at Stanford University. At Stanford I was the first Jewish faculty member in the Chemistry Department. I do not mean to imply that Stanford in 1959 was anti-Semitic, because there were Jewish faculty members in other departments. But until then, the Chemistry Department had not had a single Jew, which now is not at all the case anymore. And at Wayne State University there had been only one Jew before me, Herbert C. Brown, who later on won the Nobel Prize for his work on borohydrides. He was born in London and came to the United States as an immigrant.

How did your group win the race for synthesizing cortisone?

Between 1949 and 1951, the question of how to synthesize cortisone from a plant material was perhaps the hottest topic in organic chemistry at that time. Cortisone had been synthesized once before by Lewis Sarett in a monumental synthesis in some 40 steps. It was really a masterpiece, but it didn't appear to solve the problem of the (limited) availability of cortisone, which, at the time, was thought to be a magic bullet for the treatment of rheumatoid arthritis and other inflammatory diseases. I had been working at that time already for four years after my Ph.D. at CIBA, the Swiss pharmaceutical company in New Jersey, but almost all of my interest in steroid chemistry had already been acquired during my Ph.D. work (1943−1945) at the University of Wisconsin where I had worked on the partial synthesis of the estrogens from androgens. So I became very interested in this problem, but it wasn't possible to work on it at CIBA. But a small Mexican company, Syntex, invited me in 1949—I was almost 26—to become associate director of chemical research, which was a wonderful opportunity, although most people thought I was completely crazy to go to Mexico where no chemical research work had seemingly been done before. But this was a wonderful opportunity: Syntex was very small, there was an outstanding Hungarian chemist, George Rosenkranz, educated in Switzerland who had also fled the Nazis, who was the technical director. He had invited me—I really mean seduced me—with a wonderful opportunity. He said "you will have a number of assistants" (compared to the one assistant I had at CIBA) "and this is the problem we want to work on: cortisone." Syntex also agreed that we would publish results very quickly, which was the clincher for me, because I ultimately wanted to get an academic position in a university and this might be a way to do it, to have worked on one of the hottest problems in organic chemistry. The aim was to do it from a Mexican plant starting material, diosgenin, which was really the reason Syntex existed, because this steroidal sapogenin, though existing also in other plants as well, was at that time easily extractable from Mexican *Dioscoreae* species. In fact, already in the early 1940s, the American Russell Marker had developed a simple, cheap synthesis of progesterone from diosgenin. Anyway, we started on devising a synthesis of cortisone from diosgenin; essentially no one knew that we were members of the competition consisting of people like Fieser and Woodward at Harvard, as well as chemists at the ETH in Zurich, at Oxford, and at companies like Merck, and Glaxo, and so on.

To everyone's surprise, we were the first ones to accomplish a synthesis of cortisone from a plant raw material. And that was really quite sensational. No wonder we got an enormous amount of attention not only in the chemical literature, but in the popular press as well. It really put Syntex on the scientific map. In retrospect, it is quite amazing that we did all this work in two years, namely not just the first synthesis of cortisone from a plant material but also the first synthesis of an oral contraceptive. I would say that these were the most productive two years of my life. And that's what got me my first academic job: a tenured associate professorship at Wayne State University in Detroit, which led to a full professorship a year later around my 30th birthday.

How was "the Pill" created?

I've written about this in such detail in all three autobiographies that it's not worthwhile to recount again in specifics, so I'll make it very quick and just refer people to the literature sources, because I've really published material documenting each step in very great detail. There was essentially no competition, meaning that we were working on the problem of creating an orally effective progestin when virtually no one else was working on this. Actually there was another company that became interested in that area although about a year later than we, and that was G. D. Searle, which, just as Syntex, doesn't exist anymore—both were eventually acquired by larger companies. At that time, G. D. Searle was a medium-sized, well-established pharmaceutical company near Chicago. In any event, we at Syntex were interested in developing new drugs so that Syntex could sell under its own name, rather than just manufacture known steroid hormones. Syntex at that time was only a bulk manufacturer of steroids like progesterone and testosterone, which were sold to other pharmaceutical companies. Progesterone had already interested me theoretically in graduate school because at that time one believed that any modification of the progesterone molecule would diminish or destroy its biological activity in contrast to the estrogens. There were many different nonsteroidal compounds, as different as diethylstilbesterol from estradiol, which were potent estrogens, so there were many structural modifications that were possible that would not diminish estrogenic activity. By contrast, it was assumed that progesterone was very structure specific. At that time (we're talking about 1950), progesterone was used in medicine for two indications. It was useful in the treatment of menstrual disorders and it was useful in the treatment of certain cases of infertility, because women who do not produce sufficient progesterone during pregnancy cannot maintain the viability of the fetus. But it was also known that progesterone was nature's contraceptive: women do not get pregnant during pregnancy because they produce progesterone all the time, which prevents further ovulation. What was not generally known, and it's very embarrassing in my opinion, is that an Austrian physiologist named Ludwig Haberlandt had already (in the 1920s) predicted the contraceptive potential of progesterone, and worked on converting this into reality. Even though progesterone had not yet been isolated in pure state, it had been used as placental or corpus luteum extracts, with which Haberlandt worked. He showed that such extracts prevented ovulation in rabbits and mice, and asked, "Why not use this as a contraceptive in humans?" And why not as a pill, which he called a pill "for the temporary sterilization of women". It got a lot of newspapers publicity in the late 1920s. All of this seems to be forgotten or ignored, and especially shamefully so by later American reproductive biologists. Haberlandt, supported by the Rockefeller Foundation, published an awful lot on this subject, including a small book, and then he committed suicide in 1932 because of all the opposition that he had encountered at that time in Catholic Austria. He was only in his forties when he died. Later on other biologists continued this work when progesterone became available in the 1930s as a pure synthetic compound, through the work of Butenandt and Slotta and other German chemists. But progesterone was active only by injection. For it to work as a contraceptive, it would have had to involve daily injections, which would have been unrealistic. Besides, contraception was not a high priority item during the war, and certainly not after the war when people were interested in the reverse: millions of people had died and survivors wanted children, resulting in the famous baby boom.

At the time we started working on progestins at Syntex, we were interested in the question of whether chemical modification of progesterone would retain biological activity. The manner in which we did this is too long a story and you can really read it in detail in my autobiographies, but we were able to make a compound, 19-nor 17α-ethynyltestosterone (commonly called "norethindrone") that was orally active and also more potent than progesterone, which was quite a breakthrough. The rest of the story—the biological work led by Gregory Pincus of the Worcester Foundation for Experimental Biology; the clinical studies started by John Rock of Harvard; the competition between Syntex and Searle—are covered in excruciating detail in a chapter entitled "Genealogy and Birth of the Pill" in my memoir, *This Man's Pill: Reflections on the 50th Birthday of the Pill*.[27] To this day, norethindrone is still used by millions of women and the seven other active ingredients of the hundreds of contraceptive formulations sold all over the world that were synthesized over the years following our work in 1951 are (with one exception) still only minor chemical modifications of the norethindrone structure. Let me end by making a comment about my use of the plural "we" in this greatly condensed account. This is not meant as the royal "we" but essentially involved a minute group consisting of the late Luis Miramontes (a very young Mexican chemist then in his early 20s who was doing his thesis work for a bachelor's degree at the University of Mexico under my direction at Syntex), George Rosenkranz, and myself.

Your achievements in chemistry have been recognized with a long list of honors and awards. What are the organic reactions you are most proud of?

I would say, no particular organic reaction, even though I'm an organic chemist who also did a lot of synthesis. But I really was not working on organic synthetic methodology. What I'm most proud of in terms of my chemical contributions is the application of physical methods in organic chemistry. There I think my academic group made some very major contributions for many years and this is true particular of chiroptical methods (ORD, OCD, and MCD) and mass spectrometry, and we've published hundreds of papers and several monographs in those particular fields. So I would say in the context of being proud of chemical contributions these are the ones that are the most lasting ones.

NAVIGATING CAREERS IN BOTH ACADEMIA AND INDUSTRY

You held leading positions in industry and academics. What are your views on their interaction?

These are actually views that I have expressed many times, and will be expressing interestingly enough this year in a couple of major lectures. One of them will be at the Austrian Academy of Sciences, just about a few days before my 85th birthday. And the title of it will be (I'm translating it because I'm giving that lecture in German) "Professional Bigamy, Virtue or Sin?" I'm talking exactly about your question, which describes a situation that is occurring more and more, particularly in the United States. At one time that was also true in Germany, before the war. If you think of people like Fritz Haber or Adolf Butendandt in Germany or Leopold Ruzicka, in Switzerland, they were really all involved both in industry and in academia. That was common there, but not in the United States. Later on, it became common in the United States, and professors would be consultants, but it was really only when the biotechnology industry flourished that this bigamous relationship would occur more frequently. But much earlier, already in the early 1960s, I may well have been one of the first ones who had concurrent formal positions as a vice president and then president in a company as well as being a professor of organic chemistry. This was possible at Stanford, a private university that permitted that. You could not have done this for instance next door at the University of California, which was a state university. I was encouraged at Stanford at that time by Provost Fred Terman, who many consider the founder of Silicon Valley. That's why he was so interested in bringing me to Stanford, because he already knew that I came from industry. At that time, the Stanford Industrial Park was predominantly focused on electronics and physics, and there was no chemistry or biology, although Stanford had already a powerful medical school. Hence they wanted to attract someone who could also bring that sort of industry there. Syntex was one of the first, eventually one of the biggest biomedical industrial concerns in Silicon Valley. So, I am a believer in this type of bigamy, but one has to be very careful, and I think it has to be an open bigamy, it has to be very transparent: you need to know exactly what is going on. I was able to indulge in this luxury in a way most people cannot, because I completely separated my work in the two fields. What I did in industry, at Syntex, at Zoecon and some other companies that I've helped found, had nothing to do with my academic research. I've patented nothing in my academic research. There was no conflict of interest, because what I did at Stanford—let's say mass spectrometry, chiroptical methods, other natural product research—had nothing to do with what Syntex and Zoecon were doing. That is a luxury most people cannot afford. Most people are in both areas, because they are using their expertise as well as what they discovered at university, and then try to translate it to industry. And I think that is, within limits, okay. But one has to be very careful, especially as it affects one's academic co-workers. And certain institutions do it much better than others, and I think Stanford does it very well.

In 1991 you won the National Medal of Technology and closed your laboratory in Stanford. For what reasons would a successful chemist close his lab?

First of all, the timing of the two events was completely coincidental; they had nothing to do with each other. I actually closed my lab a year later in 1992. I had already decided to close it in 1985; but you can't do that in one year with a large research group, because if you make such a decision you can't just go and say to the others "I'll close my lab". What are you going to do with the 20 or so people that work with you? Are you going to kick them out, students working on a Ph.D.? That was not realistic. So, the two events were quite unrelated.

I chose to close my lab in 1985 when I was diagnosed with a very serious case of colon cancer. Before learning about the postoperative prognosis, I was very depressed, and for the first time thought about mortality. Strangely enough I had not thought about death before, not that I didn't believe I would die. But I assumed that it was still a long way off. I was then 62 and had been very healthy, other than my skiing accident involving my leg and resulting knee fusion. So I did not think of death. I didn't think I would die tomorrow, next year, next decade. My father died at age 96 in an accident. My maternal grandmother was 101. Even my mother only died at 91, so, you know, I didn't think I was ready to die yet. And then suddenly I realized that who knows how long I would live? In cancer they always talk about five years: if one can survive five years then presumably the cancer had been extirpated. And I thought: gee, had I known five years earlier that I would come down with cancer, would I have led a different life during these five last years? And my answer to myself was yes. I said, well, Carl Djerassi, now you know it. Maybe you only have five or less years to live. What are you going to do about it? I decided I wanted to live another intellectual life: a very different one. And decided, therefore, to stop research, but I was not going to tell it to anyone, because that would be very demoralizing to my students. So I simply decided I would take no more doctoral students, and the ones who were working with me, the maximum amount of time that would stay with me would be about five years to get their Ph.D. And then I would still accept some postdoctoral fellows during that time, because they only come for one or two years. And then you know it's finished. So, by 1989, when I really started reducing the size of my research group on a substantial scale I wrote the first autobiography. I wrote my first novel, *Cantor's Dilemma*,[22] which, incidentally, was published three years ago in Italian by Di Renzo Editore in Rome, this house then also published the Italian translations of all my other novels. In 1992, my last two graduate students got their Ph.D. and I closed my lab. Not that I retired from Stanford. I just decided not to do anymore research because that took an enormous amount of creative time, and I was going to spend it as an author rather than as a chemist.

SEEING CHEMISTRY IN ART

As an art collector and artists' supporter, you like the beautiful. There is chemistry in art: is there art in chemistry?

Well, there's chemistry in art, but I don't think you mean in terms of the chemistry of paints, for instance. So let me answer it in a round about way. In my newest book, called *Four Jews on Parnassus—A Conversation*,[29] which was recently published by Columbia University Press, I talk there about the process of canonization: when does a person become famous, when does the work of art become famous? A work of art will really only become famous because of its aesthetic and technical components, but particularly the aesthetic ones, or perhaps also the metaphoric ones, and I don't know where that comes in with respect to chemistry. I mean, to a chemist certain chemical structures are aesthetically very beautiful, but there aren't that many, I mean not thousands upon thousands among the millions of chemicals. Most of them, aesthetically speaking, look pretty dull. Aside from some personal favorites you can come up with some very intriguing three-dimensional protein structures or with the fullerenes, which may appeal to the general public, but these are the minorities. To me, the chemistry in art is a technical component. When it comes to aesthetics, it may apply to chemists, but not to the general public and I don't think to most of the artists. Now when you say "is there art in chemistry?" you can make a case for. It is interesting that Escher, the Dutch artist, is one of the favorites of chemists, in particular of stereochemists, because in Escher's artistic work, you see certain elements of that. I'll give you another example: I had in my office in Stanford a very large oil painting by a very well known and respected Swiss artist, Lenz Klotz. I saw it once on the wall of the Guggenheim Museum in New York in 1960, and I was very struck by that abstract artist. To me, it looked like a cloud chamber explosion. I have another work at home, a large oil painting by a Californian artist, Lee Mullican, which I saw once in the Museum of Modern Art in San Francisco. In Mullican's work I saw all kinds of chemical symbols but he never saw them. He didn't know they were in there. So, here I'm saying the chemist Carl Djerassi saw really scientific images in these paintings. One of Paul Klee's drawings I own looks to me very chemical. Perhaps I missed your question in the metaphoric sense by responding too specifically. I myself don't see that much relation between chemistry and art, which is strange since I'm very much of a collector of art and very much involved with it.

POLITICAL AND CULTURAL ASPECTS OF CHEMISTRY ACHIEVEMENTS

Among your many honors, you received the National Medal of Science from President Nixon. Why were you named in Nixon's enemies list in the same year?

Not just in the same year but within two weeks of the time that I received the National Medal of Science—that was very amusing. I was on the "White House enemies' list" for a simple reason: I was very much against the Vietnam War. And I was very open about this, and apparently there was this White House enemies' list, during the paranoid days of Nixon who collected names of opponents of his policies. And it was a distinguished list, I remember Alexander Calder being one of the names on it. But, of course I didn't know I was on that list. That was a sort of secret list and presumably the list makers were going to try to do something beyond gathering names, perhaps examining the income tax records of people, and trying to show that they may have done something inappropriate, and so forth.

So that was all theoretical. But then when I got the National Medal of Science in 1973, it was on the same day that Vice President Agnew resigned, which was a sensational day in the United States. And it was actually quite amazing that Nixon must have known that his whole house of cards was about to collapse. Nevertheless there he smiled, giving the National Medal of Science to people at the White House and I remember him asking me an idiotic question. I was promising myself not to smile at him, but I couldn't help in view of our conversation. In all the photographs I was grinning because he asked me how Stanford was going to do in its football game with the University of California. But American football leaves me completely cold. That is still my European youth: to me, football was soccer, while American football seemed just a dull game of huge people, where most of the time nothing happens. I just said, "I don't know". And we both laughed. And then the newspapers of course discovered that there was a White House enemies' list and it so happened because of the timing, there I was just getting the National Medal of Science from Nixon, and he probably didn't know I was on his list of enemies. But in the newspapers in San Francisco, there was a wonderful headline "Nixon Gives Medal to Enemy", which was very amusing.

You have written "We are seeing a gradual separation of sex and fertilization",[30] and we are in an age of mechanical reproduction. What role did the Pill play in the promotion of reproductive rights?

The separation of sex and fertilization is the main topic of my current scientific lectures as well as of some of my plays. "An Immaculate Misconception"[31] is the first play I have ever written that by now has been translated into a dozen languages. But my last play, "Taboos", which deals with the fear of people about this impending separation, had its American premiere in September 2008 in New York at the SoHo Playhouse and a month later in as distant a place as Bulgaria (it actually had its world premiere in London in 2006). Taboos are also the subject of a book that was published in July 2008 by the University of Wisconsin Press under the title *Sex in an Age of Mechanical Reproduction*.[32] You ask, "what was the role of the Pill on the promotion of reproductive rights?" In term of reproductive rights it is quite obvious, because it permitted fertile women to separate sexual intercourse from contraception. Until then sex and reproduction were always connected and this separation is only true of the Pill and of intrauterine devices, which unfortunately are not very popular in the United States although they are widely used in other countries, particularly China. Putting it another way, the Pill enabled couples to have sex without reproductive consequences. But the reverse, reproducing without sex, was only made possible in 1977 by the invention of in vitro fertilization by Edwards and Steptoe in England. Numerically this means that about one hundred million women are on the Pill at any one time, while in the case of in vitro fertilization, since 1977 at least three million individuals have been born who were conceived without sexual intercourse. So these are very dramatic illustrations. But the real separation of sex and fertilization has been demonstrated unequivocally in the country where we are sitting, Italy. Because Italy has one of the lowest family sizes, about 1.2−1.3 children per family, with Spain about the same. One common denominator between Spain and Italy is that they are both officially Catholic countries. I said "officially". How is it possible to have 1.2 children per family without the total separation of sex and fertilization? Suggesting that people in Italy practice no more sexual intercourse after they had their 1.1 children is of course preposterous. So my answer to your question is really, "Ask any Italian and Spaniard how they do this." The separation of sex and fertilization is more dramatically illustrated in these two countries than any other country with the exception of China, which officially has a one-child-per-family policy. Clearly, the Pill has had an enormous effect, but not an exclusive one. And I think that in vitro fertilization is another very important component.

MENTORING THE MENTORS

In your writings you showed that scientists have the same limits as all other human beings. Some of us share the misfortune of being exploited during the first years of our university career by our supervisors. How can the "tribal culture" of scientists be improved? What about a code of conduct for professors?

Well, here you really talk about the relationship of graduate students and postdoctoral fellows with professors. That's a very complicated issue—an issue that unfortunately is not addressed in our scientific teaching, certainly not in chemistry. People learn it only by human experience, sometimes in a positive way or even more frequently in a negative way when the damage has already been done. That has been one of the main reasons for writing my "science-in-fiction" tetralogy, particularly my first novel, *Cantor's Dilemma*,[22] and to a certain extent also some of the components of the second one, *The Bourbaki Gambit*.[23] To my pleasure, *Cantor's Dilemma* has become a textbook or recommended reading in many universities and colleges, in a few places even in the last year of high schools because it really is a very realistic description of both the positive and negative aspects of this mentor−disciple relationship. The latter is a very important component of scientific culture, and in quite a number of aspects differs fundamentally from that of the humanities, yet we talk very little about it. I had the following very personal example in my own family. I was married three times; my third wife, Diane Middlebrook, to whom I was married for 20 years before she died recently, was a professor of English literature at Stanford. So she was in the humanities, whereas I was in chemistry. She had never had anything to do with chemists before, and while she also had a lot of graduate students, she was actually amazed that my name appeared on the publications of my graduate students. She said: "I don't do this, my students publish their thesis work themselves." We debated the pros and cons of this practice, and the reasons behind that difference between the two academic disciplines I described in realistic detail in *Cantor's Dilemma*. It's a novel that has been reprinted at least once every year. It came out in paperback in 1991 and is now in its 24th print run.

And now to your question about a code of conduct from professors. In theory I'm a great believer in codes of conduct, in the same way that every physician is supposed to subscribe to the Hippocratic oath. But my own feeling is that such codes don't have much of an impact. An intrinsically ethical person is going to behave ethically not because there's a written code of conduct, but because they've been taught the basis of ethical behavior and they practice it all the time. The Hippocratic oath or a code of conduct for professors is not going to prevent unethical behavior by the violators. At best, they offer some guidelines to people who, on their own, have not paid much attention to ethical behavioral questions. A code of conduct for scientists has been published by the National Academy of Sciences, and the American Chemical Society did something like this for chemists, but I would say that 99% of all graduate students haven't read them and thus will not know what is in them. It is like giving someone one lecture on human reproduction at the age of 10, or 12, or 14, and that this is the entire sex education they get for the rest of their life, rather than a continuous, logical, gradual explanation of human reproduction and human sexuality. I once published in *Chemical & Engineering News*[33] a very serious proposal on the topic "Who will mentor the mentors?" In other words, who will examine the professors in the context of their mentoring ability, which is really what you are talking about here, the code of conduct for professors. And that's what we don't do. At Stanford University, we have continuous student course evaluations. Every semester the students get special forms and they evaluate the entire course content, lecturing ability of the professor, the fairness of the grading, the breadth and depth of the course, and so on. And the professors don't see that, because it is anonymously submitted to the Dean office. The professors get the summarizing results, and sometimes they are quite devastating—and quite appropriately so. In our departmental promotion procedures, we take these student evaluations into consideration. Yet we do none of this about the mentoring ability of professors with graduate students. In part because we are worried that the professors will try to guess who the graduate students are who completed the questionnaire, as we are now dealing with much smaller numbers. I would welcome more evaluation because once again we don't teach the professors how to be good mentors. They are supposed to acquire this on their own. It's really basically like expecting first-time parents to just learn how to become good parents, without giving them advice on how to do this. That is an extremely serious problem that is not addressed in many countries and most institutions. So, I would say read my novels for that.

■ SEX, REPRODUCTION, AND FEMINISM

Sex is another recurring topic in your writing, and eroticism fills the existential void in many of us in industrialized societies. As it was for the Roman Empire, is this a sign of the decline of the western civilization?

I do not think so at all. Because if it were the decline of the rest of civilization then I would say that it assumes that sex has only one function, and that is reproduction. And of course I do not believe so at all. One of the things that separates us with few exceptions from millions of species, is that we humans could have sex 365 days a year. I don't mean that we do so every day, but we are biologically capable of doing this while most species are not. Most species can only have intercourse when photochemically or otherwise stimulated, and thus are ready for reproduction. Dogs are one of the very best examples. They basically copulate twice a year when the female is ready for copulation and the male then of course responds to that. So I think sexuality and sex, and pleasure in sex, are important. Naturally, it covers everything from exploitation to intimate loving relations. And one has to address it that way. You are right; it is a topic that I have addressed in many novels. In my last book, the *Four Jews on Parnassus—A Conversation*,[29] I do it perhaps in the most intellectual way, because it contains a chapter called "Pornography in an Age of Technical Reproduction". What I'm really talking about is the difference between pornography and erotica and that is of course the way you get a transition from the very positive aspects of intercourse of sexual attraction to the more negative aspects, in particular to the exploitative ones. So, I think, what you are really talking about here is exploitation. And I'm very careful to differentiate them. I think you are right: every one of my novels, almost every one of my plays, has an erotic component. But I challenge you to find a really exploitative one. Or if it is an exploitative one, it's usually used to illustrate what I want you not to be doing. So, it's a topic that I deliberately picked. It's interesting that quite a number of people have criticized me about this. I still remember how irritated one reviewer of *Cantor's Dilemma* was in *Nature* about some of my sexual allusions. And then one very distinguished scientist, whom I did not know personally, wrote such a cutting rebuttal that I had two totally different opinions on this topic in *Nature*, which pretty well settled the issue.

You support feminist positions: Do you have something to be forgiven for by women?

I don't believe so. I think it's just the other way around. I think I'm fundamentally a male-feminist. Not that I became that in any formal sense until probably fairly late in life when I married my third wife who was at that time the Chair of Feminist Studies at

Stanford. There's no question that you could almost say that I've gotten my academic exposure to the topic in bed. But if one asks, "what is the definition of feminism?" you will get many academic answers. My wife's definition was: it's a question of power relations. And she's absolutely right. The question of power relations between men and women is a subject that has become an overpowering component of every one of my novels. I actually said so specifically in the introduction to my third novel, *Menachem's Seed*,[24] where I address the patriarchal, phallocentric nature of much of our tribal behavior.

For instance, I denounce the glass ceiling for women. Can I also suggest how to improve the situation? Yes, I think it is not enough for just women to push for it. I think it is crucial that men do this as well. And that is why I was so interested in teaching in Stanford's feminist studies program although I didn't succeed in one regard: I wanted to get a lot of men into my class and I never did. It was always mostly women. And I think it's crucial that you have men. That is one of the reasons why I turned to fiction writing, because that is a topic that I address in many different ways, in every one of my novels and in a number of the plays. But I think the key to it is the exposure of men to these problems. I think one of the problems in male-dominated disciplines, with chemistry being a good example, is that they are tough fields that involve a lot of training. A woman is usually in her late 20s before she has earned her Ph.D., and then she would do some form of postdoctoral and other training when she is already in her early 30s before she can embark on a professional career and if she is ambitious, as ambitious as a male counterpart, then she really works 60–80 hours a week for six years, which are the years when she is considered for tenure. Before you know it, she is in her mid- or late 30s and during that time most women in experimental disciplines cannot afford to have children. They cannot do it financially or in terms of the time commitments imposed on them. Yet most societies still assume that the first few years of bonding and upbringing of infants and young children is a woman's charge. Of course that's where I disagree. I agree that the woman has to give birth to the child, and that it's best if she can nurse her baby for some time, which generally is better than bottle feeding. Some babies need to have a bottle very early, in which case you can enlist the man immediately. But after that, it can be very much a joint affair. It has become that in more and more modern couples, but there are still an awful lot of instances where this is not the case, and particularly not in traditional societies. And that I think is one of the sources of conflict. Not only that women have to make a decision between childbearing and professional advancement, but that there are many employers who consider potential pregnancies a negative factor in deciding to hire and promote women. Often, an employer makes this calculation: "If I hire her, and then she becomes pregnant, she's going to take maternity leave for a year; if she should have a second child, that's another year and we can't possibly afford such long maternity leaves." Some countries handle it much better and I would say the Scandinavian countries are a good example of how to do it better, whereas some other countries are doing it much less effectively.

MOTIVATIONS, PROJECTS, AND FUTURE PLANS

At 20, you and your co-workers developed a successful antihistamine, tripelennamine. Then, you were successful in so many fields, including sports, where you climbed mountains, including in the Himalayas to an altitude of 14,000 feet, notwithstanding your fused knee. Where do your motivations come from? Did you reach so many goals because of the studies you have done, because you are a workaholic, or because of the creative competition of the environment?

Ah, it's not because of the studies I've done. I worked in many different fields, because I was always an intellectually polygamously orientated person (Figure 1). But I think I also chose good topics. I was lucky in many cases and you need good luck and the right timing. Hard and intelligent work alone won't necessarily lead to success. But it's primarily the following two: I'm a workaholic and the competitive aspects of the scientific enterprise infected me. I'm glad we're ending the interview with that topic, because ambition and competition are two key components of scientific culture and they are not all positive. For me, I write about them because writing such novels and plays has become a form of auto-psychoanalysis. There is no question whatsoever that I have become much more reflective toward my own behavioral practices, which perhaps are a bit extreme, but they are typical of those of all my colleagues in the very "tribal culture" of science and in particular of chemistry. And I wrote about it in my fiction as a form of mea culpa, because I think such workaholism may be productive for science, but not for a full life. There are other things in life rather than just work. And a telling example is that for the past 10 years I haven't gone on vacation; the last time I went on a vacation was in the middle 1990s. It's ridiculous to say that to Europeans who annually go on four, five, or six weeks of vacation. I used to look at vacations in a macho sort of way: "ah, all they're doing is going on vacation". But in fact it's stupid of me to say that. I should be doing more of that myself. There's more to life than just working all the time because even if you work all the time you cannot accomplish everything that you want to do. So you might be more realistic and be selective and realize that it is not just your own personal life, but also your relationships with other people, whether it is your family, friends, or acquaintances, who are affected by your workaholism. I now completely accept that even though I don't practice it to any extent. I always hope that I'll improve the next year. But at least, I hope through my writing to influence other people, to say that there's more to life than just pure, continuous work. But there has to be a value judgment instituted by the institutions, in this case

Figure 1. The "intellectual polygamist" Carl Djerassi, in 2008. Photograph by Isabella Gregor; reproduced with permission.

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by the academic institutions, and they don't do that. We expect chemistry graduate students in the United States to work seven days a week and to be in the lab in the evening. Almost any professor in the top research universities who goes around in the evening and doesn't find his graduate students there has some form of negative feeling.

I'll give you a very pertinent illustration. In spite of what I've said, as a graduate student I never worked in the lab at night. I was already married, and at that time I felt, I'm not going to do this. Of course, that was a long time ago. But I was very well organized. So, during the time I spent in the lab, I did work long hours from eight to six. But I didn't come back at night and I didn't work weekends in the lab. I was working maybe 45 hours or 50 hours per week, but certainly not the usual 60 or 80. But even that is not completely correct, because I then worked also at home. "Work" doesn't just mean working in the lab; it may be reading scientific literature or writing papers.

I still remember a superb conference at Stanford that I chaired, with six outstanding speakers, one of them who was perhaps the best young organic chemist in the United States at that time (I won't mention his name, because he's so well known), and he gave a truly brilliant talk. His own former mentor, a more senior professor, was also one of the speakers. As we were standing around during intermission, I turned to the younger man and said:

> You know, this was such a good talk that you gave. If I were a beginning graduate student, age 22, I would really enjoy working with you. But I want to ask you a serious question. Not a joke. And I'm not flattering you. Suppose I came to you and said, my name is Carl Djerassi and through some magic you can convert me into a 22-year-old student but you'll know that I'll develop into the present Carl Djerassi (whom he also admired: he liked me and he respected my work), so you'd be proud to have had me as one of your students. And I come to you and say, professor, I'd like to work with you but I have to make something clear: I'll not work in the lab at night, I will not come on weekends, but I'll be in early in the morning. I don't go out for coffee, and take no lunch break. I commit one of the worst sins: I'll have a sandwich in the lab while I'm working; or if something is refluxing, I don't watch it reflux I do a second experiment at the same time, I'll be very well organized and productive but I'm only going to be in the lab 45 hours. So, will you take me?"

Before the young organic chemist even answered, his professor said, "Yes, I'll take you." I said, "I didn't ask you, I asked this man." Because this man was in his early 30s and he was famous for coming to the lab at six in the morning and leaving late in the evening. He had around 30 graduate students and postdocs, and he realized that I was testing him. He took some time before saying, "You know, I'm tempted, but the answer is no. I wouldn't take you because even if all you say is true, you can't get as much work done in your 45 hours as I can get from other students in 80, and I want that work from them." In other words he was using them as virtual pairs of hands in a form of voluntary slavery, which so many graduate students do these days and to which I object fundamentally. Even though I am a workaholic in my own way, I did not expect that from my students, but most of my colleagues do that. And that, I think, is one of the most serious problems, and the only way we can solve that is to change the current lab culture.

What other important achievements do you plan in the future?

I am working all the time, really seven days a week. I'm mostly writing now, but if in addition you look at my lecture schedule, you'll say it's one of the maddest ones you've ever seen: every couple of days another country, another city. But right now this is my form of therapy for the really tremendous loss of my wife in December 2007. I find that by working all the time and meeting new people during my travels, I don't sit around mourning about my personal problems. But, I'm a writer and of course I have a lot of other things that I really want to write about, which I already have in my head, so that is what I'm doing now. And my lectures are really presentations, because I use audio-visual material, I use music, I use dramatic readings, because I want to touch as many people as possible through my writing, and I want to encourage them to go and read what I'm writing. I'm not so concerned whether they buy the books, I don't care whether they read them in a library, or photocopy them, or steal them. But I have something to say in my books and plays and I want people to read the texts or see the plays, so that's what I do.

To pursue your distinguished career in organic chemistry you had to work so many hours a week. Do you think that working so many long hours led to a balanced life? If not, does this account for why so few women are chemists at the level you achieved?

As I already stated, the answer to the first part of your question is absolutely no. It does not lead to a balanced life. To some extent that may be one of the reasons why there still are relatively few women chemists at the very top levels. In the physical sciences, a larger proportion of women leave academia after earning their Ph.D., because they realize that they will be competing with young men who are totally involved in these 16-hour workdays, and many women don't want to do this. That is probably why more of these women work in industry, where the hours are fixed, and particularly in intelligently managed industries, where there's some real support structure, both in respect to mentoring within the organization and to offering compromises for women who do not wish to be penalized for becoming mothers. Some companies even have onsite childcare. If you provide a support structure and treat women fairly, then I think they will stay. But right now we don't do much of that in academic chemistry.

A personal and very delicate question: you founded the DRAP (Djerassi Resident Artists Program) inspired by two women: your daughter, and your wife, Diane Middlebrook. Is this a way to make sense of the deep sorrow coming from their deaths?

The answer is yes, but it depends what kind of death. And this is where there's a fundamental difference. I mean these are the two biggest tragedies of my life. My daughter's death 30 years ago when she was 28 was through suicide. Suicide is a very different death from illness or accident. In many respects long-lasting illness is a direct opposite, because then you expect death. This was the case with my wife where we both lived under a Damocles' sword, certainly during the last three years, when we knew she was dying. But that she would be dying before me turned out to be unexpected because she was so much younger than I. We coped with it well, in the way in which I had to cope with my daughter's suicide, which was the time when I had just met my third wife. A father does not expect to survive his children, it's almost anti-biblical, and particularly in this case because at that time I was so extremely close to my daughter. She was married, she lived on the same general property, our family ranch, she was an hour away on foot from my house, but it was our own property so it was very intimate. (My son also had a house on that property.) Her death was totally unexpected, because I'd spent some hours of the preceding day with her by my swimming pool when there was no indication whatsoever that she was on the brink of suicide. The next day I got a frantic phone call from my son in-law informing me that there was a suicide letter waiting when he came home. He was a physician and he didn't know what had happened to her or where she was. When we finally found her body several days later and I had to come to terms with the fact of her death, I absolutely buried myself in work. I could not have survived otherwise. But suicide is a death that has a purpose, and the person who commits suicide usually sends out a message, sometimes a written one, but even in its absence, the survivors ought to be able to figure out what had prompted this irrevocable step. I wanted to create something living out of my daughter's death, I didn't want to build some memorial or create a grave. Instead, we scattered her ashes in a waterfall on our property which she and I had discovered, and where I had said: when I die I would like to see my ashes distributed there. So, this was my answer in the context of my daughter's death and why I founded an artist's colony in her memory. When my wife died, it was expected, because she was suffering from an incurable form of cancer. We are now raising funds to build another building for more artists at DRAP, so that there will be further facilities to increase the capacity of the program by ~50%. In both cases, I wanted to create again something living out of death.

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