CHEMICAL HERITAGE FOUNDATION

GEORGE ROSENKRANZ

Transcript of an Interview
Conducted by

James G. Traynham

at

New York City, New York

on

17 May 1997

(With Subsequent Corrections and Additions)

CHEMICAL HERITAGE FOUNDATION
Oral History Program
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GEORGE ROSENKRANZ

1916	Born in Budapest, Hungary, on 20 August

Education

1938	B.S., chemical engineering, Swiss Federal Institute of Technology
1939	Dr. Sci, Tech., Swiss Federal Institute of Technology

Professional Experience

	Swiss Federal Institute of Technology
1939-1941	Research Assistant
	Vieta Plasencia Lab
1941-1945	Director of Research
	Syntex Corporation
1945-1980	Scientific Director, Syntex, S. A.
1949-1956	Vice President and Director of Research, Syntex, S. A.
1957-1980	President and Chairman of the Board
1976-1982	Chairman of the Board and CEO
	Industria, Ciencia, Tecnologia [ICT]
1996-present	Founder

Honors

1949	Mexican Citizenship Award
1994	National Prize of Pharmaceutical Sicences "Dr. Leopold Rio de la Loza"

ABSTRACT

George Rosenkranz begins the interview with a discussion of his childhood years in Budapest, Hungary. After graduation from the German School, Rosenkranz attended the renowned Swiss Federal Institute of Technology. There, he received his B.S. in chemical engineering in 1938 and his Ph.D. in 1939. Rosenkranz studied under several luminaries in chemistry, most notably, Leopold Ruzicka. After receiving his Ph.D., Rosenkranz worked as a research assistant in Leopold Ruzicka's lab, where he headed a group researching triterpenes. In 1941, Rosenkranz had agreed to teach organic chemistry at the University of Quito, leaving in October 1941 to make the long trip to Ecuador. His three-week-long boat trip eventually stalled in Cuba. While waiting for the boat to Ecuador, Rosenkranz decided to remain in Havana. There he also met his future wife, Edith Stein. Rosenkranz soon landed a position as Director of Research at the Vieta Plasencia Lab. In 1945, Rosenkranz joined Syntex Corporation in Mexico as Scientific Director. His immediate work was on progesterone synthesis. Rosenkranz hired several up-and-coming scientists to work at Syntex, including Carl Djerassi and Alejandro Zaffaroni. Syntex's major successes were the synthesis of cortisone and Djerassi's synthesis of oral contraceptives, thus turning a little-known company into a major pharmaceutical powerhouse. In 1982, Rosenkranz retired as chairman of the board, president, and CEO of Syntex. Rosenkranz concludes the interview with a discussion of Syntex's growth, and thoughts on his family and future endeavors.

INTERVIEWER

James G. Traynham is a Professor of Chemistry at Louisiana State University, Baton Rouge. He holds a Ph.D. in organic chemistry from Northwestern University. He joined Louisiana State University in 1963 and served as chemistry department chairperson from 1968 to 1973. He was chairman of the American Chemical Society's Division of the History of Chemistry in 1988 and is currently councilor of the Baton Rouge section of the American Chemical Society. He was a member of the American Chemical Society's Joint-Board Council on Chemistry and Public Affairs, as well as a member of the Society's Committees on Science, Chemical Education, and Organic Chemistry Nomenclature. He has written over ninety publications, including a book on organic nomenclature and a book on the history of organic chemistry.

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INTERVIEWER: James G. Traynham

LOCATION: Carlisle Hotel
New York City, New York

DATE: 17 May 1997

TRAYNHAM: Dr. Rosenkranz, I know that you were born August 20, 1916, in Budapest. Please tell me about your parents and early childhood.

ROSENKRANZ: I was born into a middle-class family. My father Bernhardt—or Bernard—was a self-made man. He left his home in Györ, Hungary, when he was about thirteen to work in Vienna, Austria. Eventually he joined a company that made elastic belts and suspenders. Later on, he set up his own manufacturing company in Hungary in partnership with the people who had employed him in Austria.

My mother Ethel also came from a middle-class family. Her brothers, uncles, and other relatives were in the bakery business, but they were very intellectual. Several of my mother's cousins had strong interests in music, art, and languages. That was a very stimulating environment to grow up in.

As for education, I went to what was in those days one of the best academies in Hungary, the *Reichsdeutsche Schule* or German School. The European education system is different from the American: you go to the same school from elementary through twelfth grade, a total of twelve years.

TRAYNHAM: That was in Budapest?

ROSENKRANZ: Yes. I mention the school because apart from providing an excellent education, it was there my interest in chemistry got started. The director of the school was a chemist, and during my last two years, I learned so much chemistry that when I finally got into the Eidgenössische Technische Hochschule [ETH]—I'll tell you more about that in a moment—I practically didn't have to do anything in terms of learning for the first year.

I graduated from the German School in 1933, passing the *matura* exam. Next, of course, came higher education. My nightmare was that I would be accepted at the Hungarian University, as my parents hoped. I was their only child and they wanted me to stay close to home. But the political situation was such that I didn't want to remain in Hungary. We were a

Jewish family, and in those days, we had the so-called "numerus clausus." This meant that only 10 percent of a university's students could be Jewish. I was afraid that with my good grades, I would be admitted. My parents insisted that I apply, but I wanted to get away. As you know, Hitler came to power around that time.

There was another danger. I was a good scholar and I was awarded a fellowship to study chemistry at a university with one of the best faculties in this field—Charlottenburg, Hautenberg [Technical University] in Berlin. As I feared, I was accepted in Budapest. I didn't want to stay here; I didn't want to go there.

I pestered my parents so much that they finally let me apply to the ETH in Zurich. Before being accepted there, I had to take an examination in spatial geometry, which we were not taught at the German School. I passed and moved to Switzerland in 1933.

TRAYNHAM: You made the trip alone? Your family didn't relocate?

ROSENKRANZ: Sure, I went alone. For the first year, I lived with a Swiss family. That's when I learned Schwitzer-Deutsch, which is probably the only language in which I do not have an accent. [laughter] Schwitzer-Deutsch is very hard to learn because it's not really High German, and the accent is somewhat peculiar. I always loved languages and speak six. I grew up with Hungarian and German, learned French at eight, English at ten. Later I picked up Italian and Spanish.

TRAYNHAM: Tell me about your studies in Switzerland.

ROSENKRANZ: I stayed for eight years in Zurich attending the university, the normal process in those days. The first four years can be compared with undergraduate studies in the U.S. The ETH, which is the academic equivalent of MIT [Massachusetts Institute of Technology] or Caltech [California Institute of Technology], confers the degree *Diplom Ingenieur der Chemie*, which is not exactly the same thing as an American degree in chemical engineering, which emphasizes engineering. There, it's chemistry with some engineering.

I was very, very lucky because the professors I had were extraordinary. Several had already won the Nobel Prize and others received it later. In organic chemistry, I had Leopold Ruzicka; in physics, Paul Scherrer of the Debye-Scherrer diagram; and in analytical chemistry, William Treadwell, who is famous in the literature for his work on analytical methods. In inorganic technology and organic technology, I had two outstanding people: August Guyer and Hans Edward Fierz-David, who was sort of the father of the dyestuff industry.

In order to graduate from the ETH, you had to have focused by the end of your fourth year on four out of five major disciplines I did not select physical chemistry. Instead I chose

organic and inorganic chemistry, and organic and inorganic technology. Of all my teachers, Ruzicka was the most important. He inspired me to specialize in organic chemistry.

TRAYNHAM: What did you do when you weren't studying?

ROSENKRANZ: By the time I got to Switzerland, the economic situation had changed in Hungary—we were already in the Hitler years—and my parents couldn't support my studies any longer. The Swiss government did not allow foreigners to hold gainful employment. But I managed to support myself. In Hungary, I had been the junior table-tennis champion, and for a time in Switzerland, I made a living by freelance coaching a table-tennis team in the little town of Adliswil. The other thing that was open to me was theatre. I was assigned small roles, which gave me an indirect income. We weren't paid in cash—that was forbidden—but we had access to theatre tickets, which we could then convert into income. [laughter]

That wasn't all. At the end of the fourth year in order to graduate, you had to take both a written and oral exam and you had to write a mini-thesis, or *diplomarbeit*, in four of your five areas of special interest. One section of my mini-thesis was an assignment in organic chemistry in Ruzicka's lab. The assignment consisted of two parts. First, I had to do an organic analysis, then a small synthesis. For the organic analysis, I was given a sample mixture, from which I carefully picked some crystals to look at. I had about four weeks for this project. I quickly completed the analysis and wound up maybe ten to fourteen days ahead of the other students who each had a different compound to analyze and synthesize. So I told the teaching assistant who was a good friend of mine: "Let's start the synthesis." "No, you're too much ahead of the class to do that," he replied. "Just go and do what you want."

Well, I love to play tennis. So, one nice morning I'm coming down the Universitätstrasse dressed in my tennis outfit—you wore long pants in those days—when whom did I see but Ruzicka. I said hello to him. He didn't have too much contact with students, you know, except in classes. He looked at my bag and said, "Aren't you supposed to be in my class here? Aren't you supposed to be doing your diplomarbeit?" "Yes, Herr Professor." "Then how come you're here?" "Well—" and I told him the story. An hour went by, then my teaching assistant, Meldahl, called and said, "You idiot! What the hell did you do? Ruzicka came to me and said, 'What is this joke here with this guy, what's his name, Rosenkranz? He's wandering around the university with his tennis racket in hand when he's supposed to be in the laboratory. Give him some work to do.'" Meldahl continued, "You just made a big mistake. Now you can start your synthesis."

TRAYNHAM: It was what you had wanted to do. What was the difficulty?

ROSENKRANZ: For a synthesis, you are generally assigned four steps. Meldahl said, "No, my friend, you have been given eighteen steps. You will never finish this, ergo you will never pass.

You will never get to the final exams." I started to work like a demon. But near the end of the academic year, when you were supposed to begin preparing for your exams, I still had done only nine or ten steps. I didn't finish. I thought I had blown it.

Then I received a special permit to take the oral exam before I finished the lab work. I got to my organic chemistry exam with Ruzicka. This exam usually took around half an hour. Ruzicka said, "Okay, well, let's see what you know, huh? Are you still playing tennis?" I replied, "Yes, but I have no time." [laughter] He said, "Okay, fine." Ruzicka pulled out Paul Karrer's *Lehrbuch der Orgnischen Chemie*, which was the bible of organic chemistry in those days (1). "In the Karrer, there are six errors. Name three of them," he said. I had read the book, and I could name three errors. "Okay. But let's see what else you know. Can you give me the synthesis of Vitamin B1?" This was completely new then, but I had read the recent publication. I wrote the synthesis on the blackboard. "B2." I wrote the synthesis for that one, too. He opened the Karrer book to the index, found the letter D, and began questioning me about the listed topics. He continued to the letter E, grilling me. Time passed. I'd been with Ruzicka one-and-a-half hours and was sure I had blown it when he arrived at F. I remember it as if it were today. He asked, "What is formose?" "Formose is a polymer of formaldehyde and a synthetic sugar, but if you write it with an A at the end, it's a peninsula in the Japanese Sea." (Nowadays, it's called Taiwan.) He looked at me and started grinning. He asked, "What are your future plans?" "Herr Professor, up to one-and-a-half hours ago, I was hoping to do my doctoral thesis with you; but now, since I obviously have blown it, I don't know what I'm going to do." He replied, "Okay, you can start working for me on Monday." That was it. I said, "But Herr Professor, I still haven't finished my synthesis." "Oh, that. Forget about it. You don't have to finish the synthesis." So, I am the only person in ETH history who got a degree for his work in organic chemistry without having to finish his diplomarbeit. [laughter]

TRAYNHAM: How did your relationship and work with Ruzicka go?

ROSENKRANZ: Eventually we became very, very good friends. When I started working with him, I focused on triterpenes. Ruzicka was famous for his work on steroids, which later had a certain impact on my life. What an understatement!

I still had financial problems, so in the evenings I went to the *Schauspielhaus* [theater] in Zurich, where I acted in several classic and modern plays. One night, we were doing a piece by [Luigi] Pirandello called *Jenny und der Herr in Frack*, which means, "Jenny and the gentleman in tails." I had a really wonderful part: I didn't have too much to do and I didn't have to wear makeup. When I was on stage, I looked down and saw Ruzicka in the third row. I wondered what would happen. Next morning, he telephoned me and said, "Rosenkranz, what on earth were you doing up on stage?" "Dear Professor, if you had my financial problems, you'd be up on the stage too." [laughter] He laughed, and then said, "Enough of this nonsense."

Within days, to supplement my fellowship, I was given a salary of eight hundred Swiss francs a month, which in those days was monumental, equivalent to about eight hundred dollars

per month. For a student and bachelor, it was fantastic. The only condition was that I quit the theatre.

TRAYNHAM: What was your work like?

ROSENKRANZ: I was heading a group that was working on triterpenes. My thesis had been on a triterpene called lupeol. This was an interesting project because lupeol turned out to be a pentacyclic triterpene. I proved that it has a five-membered ring—instead of the normal six-membered ring—with an isopropenyl group attached. That was new. Other researchers later confirmed my findings. More interestingly, this ties into my later history. I started speculating on how one could convert this compound into a steroid, which also has a five-membered ring. I became familiar with the work of Russell Marker, a brilliant organic chemist, and professor at the University of Pennsylvania who was working on steroidal sapogenins. When I wrote up my thesis, I left a sort of legacy by saying that this was something that should be investigated.

Ruzicka was also very interested in the biosynthesis of natural products, like terpenes. He had invented the isoprene rule. As I pointed out, the rule neatly tied in with the possible connection in the biogenesis between steroids and some of these terpenes.

TRAYNHAM: What was Ruzicka like?

ROSENKRANZ: He came into the lab early in the morning, at eight o'clock. He knew everything that was going on with every one of his doctoral students and postdoctoral fellows. Often he visited me while I was running a reaction, and he knew if I'd lost three milligrams of a compound. He would ask me, "Rosenkranz, what happened to those three milligrams of this derivative?" [laughter] He was a great leader. He would give us the results of the microanalysis check that had been run on the compounds we thought we had produced. If you made an oxime and you didn't get the right yield, he'd ask why. He remembered every detail, every compound.

Another episode that was typical of Ruzicka: selenium dioxide surfaced as a reagent about that time. The first application of selenium dioxide was in work with cholesterol derivatives; we knew about it. One day, I went to him and said, "Poldi—that's how we used to call him—I would like to use selenium dioxide with the triterpenes." He asked, "Why do you want to do that?" "I can introduce the double bond, and maybe I can put in a alpha-beta unsaturated ketone." "What's wrong with chromium trioxide?" "This is something new." "Okay, try it." After running the experiment, I went to him and said, "You see, I told you. What I got is very interesting." He replied, "*Nun ja, so kann man das ja auch machen*—Well, yes, you can make it that way too." [laughter] That was his answer to my great new invention.

His doctoral students were working in three fields: triterpenes, steroids, and fragrances. We, the foreigners, worked on triterpenes. The Swiss concentrated on steroids, because that

work was supported by Ciba [now Novartis]. The big secret was the third group. There were two outstanding chemists there. They were working in great secrecy on active ingredients of fragrances like irone and its derivatives, lactones and large rings.

Interestingly enough, and typical, as I later encountered when dealing with European industry, you were not allowed to know what the guy next to you was doing. This is sensible from one point of view but it's maybe not the most effective approach. I had many pleasant and brilliant colleagues. One was Leo [H.] Sternbach, who later invented Valium for Roche. He worked on the next bench to me, and headed another group working on diterpenes. Oscar Jeger, now a retired professor, was a little bit younger, and he was one of Sternbach's lab assistants. Thaddeus Reichstein, a later Nobel Prize winner, was working with Ruzicka as a TA [teaching assistant] in those days. Max Furter was the head of the microanalysis lab; he spearheaded applying the methods of physical chemistry to organic chemistry. I mention all these people because the Swiss school was excellent in teaching you how to work in the laboratory. Ruzicka instilled in you a great respect for physical methods of organic chemistry.

On the other hand, though, he didn't believe in the electronic interpretations of organic reactions and reaction mechanisms. This negative orientation played a crucial role in my work later, when I left Switzerland. When I came to the United States, I found that theoretical science had conquered many people, including Carl Djerassi, Gilbert Stork, and E. [Elias] J. Corey. Everybody was using electronic interpretations. I had to start learning all of this science from the very beginning just to be able to communicate with these guys.

TRAYNHAM: What was it like doing research in Europe during the War years?

ROSENKRANZ: The War started and I was still there working towards getting my advanced degree of a doctor of technical sciences. But I knew that once I finished my studies, I would have to leave Switzerland. With the help of Ruzicka, I postponed all of my exams while the Nazis were in power in Germany.

I would like to give you one episode of this phase. There were, of course, always Nazi sympathizers around. And nowadays, you hear so much about the connection between Swiss gold and the Germans, but not everybody was a sympathizer. Maybe the bankers were, but the Swiss people, I must point out in their defense, went with the Swiss military. They strongly believed in preserving the neutrality of Switzerland. Ruzicka was an interesting character. On the one hand, he was a Communist sympathizer, but on the other hand, he was a devout Catholic, and he had some sort of distinction from the Pope. And these two things seem really kind of contradictory.

TRAYNHAM: Unusual.

ROSENKRANZ: Yes, very unusual. He was protecting the Jews. One day, when there was a threat that the Nazis would march into Switzerland in the same way they had entered Belgium, Holland, and Poland, I went to the lab. There was nobody there; everyone had fled to the French border. Then Ruzicka came in wearing the uniform of a sergeant in the Swiss army chemical corps. Ruzicka said to me, "Rosenkranz—" excuse my interrupting for a moment, but in those days in Europe, if you were really intimate with someone, you called him by his family name, without mister, without doctor, not by his first name. "Rosenkranz, I'm not going to let these Germans have our lab books, the results of our research." We went outside the Zurich city limits, dug a hole, and put the notebooks into it.

TRAYNHAM: Did you wrap them to protect them?

ROSENKRANZ: Yes. Yet, as you know, nothing happened. Everybody came back and I went out with Ruzicka to dig up the notebooks. The notes weren't ready for publication then, as they were primarily ideas, charts, and so on. There were also many things that had not been written down. Ruzicka once told me that he had developed a total synthesis of quinine, long before Robert B. Woodward. Ruzicka said that he was going to leave it to posterity. I don't know what happened to it, though. I don't even know whether it was ever seen by someone else, or whether it was feasible, or just an idea, but whatever it was, those were his intentions. Later on, Woodward achieved the monumental task: the total synthesis of quinine.

The political pressure the Germans exerted became greater and greater during the War. Ruzicka's right-hand man was a distinguished scientist named Moses Goldberg. By that time, Max Furter had become the president of Hoffmann-La Roche in the United States. The company was afraid the Germans were going to occupy Switzerland, so they had set up a U.S. subsidiary. Goldberg became the director of research, and he took many of his co-workers with him to the U.S. All these Jewish colleagues were saying that they couldn't stay in Switzerland because it was putting Poldi in jeopardy. I decided that I was also going to leave. Many years later I wanted Poldi to meet my family. I took my children to Zurich where he was sort of retired. He was in his home. I don't know whether you were at his home or not.

TRAYNHAM: No.

ROSENKRANZ: He had a beautiful rock garden and an outstanding collection of alpine flowers. Poldi liked plants, gardening, and he liked my children. We chatted about the olden days, and we talked about my life. Very, very often, as my colleagues tell me, Ruzicka used to quote that he had two students, who really made it good. One was Sternbach and the other one was myself. He always reminded me of that. He would say, "You know, you really must honor your ancestry because your chemical grandfather was [Richard Martin] Willstätter. Because I was Willstätter's student, you are his chemical grandson." We had such a wonderful relationship, Poldi and I. He was a tough guy when it came to the lab; otherwise he was very,

very sweet.

TRAYNHAM: I know bridge played an important role in your career, specifically in getting you from Europe to the New World. Can you tell me about it?

ROSENKRANZ: I learned to play contract bridge in Budapest, when I was eleven years old. My parents took classes. With my schoolmate, Albin Salton, who sat next to me in class, we learned as our parents learned. We ordered Culbertson's Blue Book from the United States and eagerly learned all his methods, soon beating our parents. These victories supplemented our allowances. I continued to play a little bridge in Switzerland. This was another source of income because I played in a club for money. But it is very difficult to play bridge for money when you have no capital to begin with.

I'm mentioning this because bridge allowed me to enter into the higher echelon of Swiss society, where I met a different circle of people. One influential person I met was the wife of the consul of Ecuador. She said to me, "I'll talk to my husband, and maybe he can get you a visa for Ecuador." I knew that if I had an academic post waiting, it would be much easier. I talked to Ruzicka about this possibility, and he got me a chair to teach organic chemistry at the University of Quito. So, I got a visa for Ecuador, and left in October 1941.

I had a very interesting voyage from Zurich through Nazi Germany, through occupied France, to Spain. There, I was supposed to take a boat to Cuba, with an onward connection to Ecuador. I traveled with my good friend Steve Kaufmann, who was also Hungarian and had worked with Ruzicka. He also got a visa, but wanted to go to the States. We boarded the same boat, along with someone we had met on the train, Nick Judovics, a co-worker of Professor Verzar in Basel. We became good friends during the voyage. Verzar was the inventor of the metrazol shock. First came the insulin shock in schizophrenia, and then they did it with metrazol. Nick Judovics, who later changed his name to Nick Young, was doing the main lab work. The three of us boarded the ship out of Bilbao. It took about three weeks to reach Cuba. By that time, I'd learned some Spanish. When we reached Cuba, I began waiting for the boat to Ecuador.

TRAYNHAM: During this nearly month-long trip, did you talk chemistry all the way, or did you play bridge, or did you just talk in Spanish?

ROSENKRANZ: [laughter] Now you are asking me a difficult question. No, we didn't talk chemistry. We were too worried about the War. As a matter of fact, we were stopped once by a German submarine and later by a British submarine. Apparently there was a German spy on our boat, who had hidden maps of mines. The British took the boat apart, finally finding the maps. We stopped in Bermuda too; it was all very scary.

Actually, when the German submarine stopped us, and we didn't know what was going to happen, I asked myself, "What if this is the end of your life. How do you feel about what you have done? Are you happy? Are you sorry? Or what?" I answered myself that I wasn't sorry about anything I had done, and that I had lived a good life. If this were the end, I knew I would have done it all over again the same way.

Needless to say, my parents were very disappointed with my decision to leave Europe. Slowly communication between us stopped. I couldn't reach them because of the situation in Hungary and they couldn't reach me. As it transpired, I was in Cuba four years and I never heard from them. Of course, it vindicated my decision to leave Hungary, painful though it had been to leave my parents behind. Soon after I arrived in Cuba, Pearl Harbor was bombed. My first thought was to go to the American Embassy and say, "Here I am. I want to enlist. I want to fight against the Japanese and the Nazis." But my friends discouraged me, telling me the Americans wouldn't take anybody in Havana. After Pearl Harbor, many, many friends arrived. There was a large group of refugees in Havana.

TRAYNHAM: You never made it to Ecuador. What happened?

ROSENKRANZ: The boat to Ecuador still hadn't arrived when Fulgencio Batista, who was then the president of Cuba, decreed that all refugees could remain and work in Cuba and have the same rights as citizens, except that they couldn't vote. Also, friends were telling me that I was crazy to want to go to Ecuador, that Quito was terrible, and that I would never earn enough money to buy a ticket back to Europe. I said, "Who the heck wants to go back to Europe? I certainly don't." I was being pressured to go to the United States. But instead, I decided to start work in Cuba. I went to the university and introduced myself. Despite all my qualifications, I was told they weren't interested.

I must tell you, almost in parentheses, that in those days something very interesting happened in Havana. There were a couple of hundred refugees, many of them Belgian and Dutch. These were people who were familiar with and employed in the diamond industry. In wartime, all diamonds went for industrial purposes, not to make jewelry. These refugees decided to build up a little business, and it was incredible. They were earning thousands and thousands of dollars a week. They were practicing all three phases of diamond production: cleavage, cutting, and polishing.

Incidentally, I met my future wife, Edith Stein, in Havana. She was also working in the diamond business as an accountant, literally. She was counting the diamonds, handing them out to people, and doing various other tasks.

TRAYNHAM: Is Edith also from Europe?

ROSENKRANZ: Yes, she was born in Vienna. By now almost everybody who was from Europe was in the diamond business. The five who were not were two friends of mine who are medical doctors, Claire and Robert Norton, who also came from Zurich. They live now in the States. Steve Kaufmann was number three, and Nick Judovics number four. We refused to give up our professions. Later on, though, Robert did start to work in the diamond industry.

Since the university wasn't interested, I went looking for work in private companies. There were a couple of pharmaceutical firms in Cuba, and one large laboratory called Vieta Plasencia. One of the owners was Dr. Angel Vieta, who was a brilliant person. He was the dean of the medical faculty at the university and also the director of the Hospital Calixto García, Havana's biggest hospital. Vieta had several honorary degrees from Columbia University and goodness knows where else. I went there to interview. I told Dr. Vieta that I would like to work for him. He looked at me and said, "You see this laboratory? It's now fifteen years old. It's the largest in Havana. For fifteen years I haven't had a single chemist in my organization. Why should I hire one now?" I replied, "Dr. Vieta, I won't convince you and you won't convince me. I am telling you that you need a chemist. You're telling me that you don't need a chemist. Well, give me a chance and I'll show you." Luckily, he liked me and I started to work for him for the glorious salary of twenty-five dollars per week.

TRAYNHAM: What did you do there?

ROSENKRANZ: I asked Dr. Vieta what he would like me to do for his pharmaceutical firm. If he didn't have anything specific in mind, I told him, I would think of something. He answered that that there was a lot of venereal disease in Cuba and that there were few good treatments available. Salvarsan was passé and penicillin hadn't been discovered yet. A Hungarian firm had produced an oil-soluble bismuth preparation. Dr. Vieta said, "I would like to have for my laboratory an oil-soluble bismuth salt. Can you make one for me?" "Yeah, sure," I replied cockily. Now I had to come up with something, a new compound. I knew what to do for the basic structure, I thought that maybe one end of the molecule should be the active site for the bismuth salt. The other end should make the compound fat-soluble. I decided to take an isoamyl malonic acid, hexyl half-ester, and prepare its bismuth salt. It was lot of fun.

Now, rapidly, I was learning about pharmacology, toxicology and biochemistry. [laughter] After I had synthesized the compound, we tested it on patients at the hospital, Calixto García. The product turned out to be fantastic. Vieta was happy. After a couple of months, my salary rose to fifteen hundred dollars per month. I also began to receive 15 percent of the profits on the products I developed for Vieta. I came up with a number of other compounds. One was a potent analgesic cocktail. It's still being used in Cuba as a non-habit forming substitute for morphine.

Word of what I was doing got back to the university, and its officials approached me, "Would you like to work with us?" "You didn't want me before." "That was a mistake. Would you like to have a teaching position?" "No. I don't want to give classes. But I'll tell you what

I'm willing to do. If you will send me a couple of people for their doctoral thesis, they can work with me and learn how to do research in the lab. That I will accept." I became an assistant professor without any lecturing duties. About twenty students came to work with me. Two of them became very famous. The first was Ernesto Eliel, who became professor of chemistry at the University of North Carolina at Chapel Hill, and eventually president of the American Chemical Society [ACS]. The second was a brilliant Cuban chemist, Fausto Ramirez. He also became a professor at Columbia University, but was killed in an automobile accident. For many years, Eliel and Ramirez would send postcards to me at Syntex signed: "Happy Holidays from your favorite dishwashers." [laughter]

TRAYNHAM: What happened to the colleagues you traveled with from Spain?

ROSENKRANZ: Steve Kaufmann and I started to do some extraordinary things in Cuba, apart from my work at the pharmaceutical firm. First, we organized a collection of seashells for export to the United States in order to make necklaces. Then I began making vitamin A by molecular distillation. Steve and I organized the shark fishermen to collect shark livers for producing vitamin A. Then Steve began isolating caffeine from the roasting of coffee beans. We scraped the sublimates off the chimney walls and recrystallized it, obtaining practically pure caffeine.

I did a number of other odd things. Before the War, Cuba had packaged cigars in nice aluminum casings. However, aluminum was needed for the war effort, so I developed a wood wrapping for the cigars. I had to figure out the curve of water loss in cigars in order to create an adequate wrapping. I also designed a dehydration plant to process guava fruit, which was shipped to American servicemen as part of their meal packs. I did a lot of odd chemical testing, too. One time, I was called by a large insurance company that was stuck with crocodile hides from Argentina that had spoiled in transit by ship. The question was: had the hides spoiled because poor packaging had allowed salt water to seep in, or had some other type of damage occurred during the ship journey? It occurred to me that if ocean salt were the culprit, the hides should contain iodine. I had set up an analytical lab in Vieta Plasencia, and I carried out an iodine analysis and found iodine. It was salt-water damage. A side result was that Edith got a beautiful crocodile-hide handbag from my expertise. [laughter]

In another very funny incident, a man came to me and said, "My wife is killing me!" "How come?" "Well, with voodoo, my wife is killing me. She is putting a substance under my pillow every night, could you analyze it for me?" " Do you have it?" "Yes. Here it is." It was sodium bicarbonate. [laughter] I said, "Listen, my good friend. She is not poisoning you with voodoo or anything else. Go back and sleep."

TRAYNHAM: What else was going on in your laboratory?

ROSENKRANZ: I started a program looking at Cuba's natural products. I knew about hormones and I knew about yams, of which there are many on the island. I was trying to find the raw material for producing hormones using the method of Russell Marker. It turned out that all these yams were edible, and obviously didn't contain the necessary saponins or sapogenins. They only contained sitosterols. That was no good for manufacturing hormones, but we had a nice survey for publication.

Then I ordered some zarzaparrilla root from Mexico. I carried out the extraction, isolated the saponin and sapogenin, and tried to repeat Marker's making of progesterone and testosterone, with more or less success. Working in Cuba was hard because it was wartime, and there were no raw materials for synthesis. We only had benzene, sulfuric acid, and hydrochloric acid. Imagine, I had to make my own ether from alcohol! I trained the eight or ten thesis students I had, and I learned how to work with my employees. This was a great experience for me, but it was frustrating not to have the right compounds available.

By this time, I was corresponding with Ruzicka, and I was telling him how difficult it was to work in Cuba, and that my education at the ETH wasn't good for this type of life. I tried to perform large-scale chemical production, but I didn't know how to handle it. I didn't know enough about production equipment and I complained that the Poly hadn't prepared me well for this kind of life. He replied that no one told me to have this type of life. [laughter] Things were a bit frustrating on the personal front too about then. As I mentioned, I met my wife, Edith, in Cuba. It was love at first sight, and I asked her to marry me. However, some three years later, she still hadn't decided.

TRAYNHAM: You eventually left Cuba. How did that come about?

ROSENKRANZ: One day in 1945, I got a call from some Hungarians who were visiting in Cuba and were connected with a Mexican pharmaceutical firm, Hormona. They wondered whether I would like to go to Mexico for an interview. Being an adventurous soul, I accepted. However, I couldn't fly directly there on Pan Am, as I was classified as an enemy alien. I had to take Taca Airlines through Central America first, and then fly to Mexico from there.

On the first day of my visit, I was taken to Syntex, an affiliate of Hormona that had been set up in 1944 by Hormona's owner, Emeric Somlo, and Russell Marker, the organic chemist from the University of Pennsylvania, to synthesize sex hormones. The people there gave me a lab coat and said, "Look, we're making hormones; we're making progesterone. We are stuck because we can't run the oxidation from pregnenolone to progesterone." It turned out that Marker had left to form his own company. "Can you run the Oppenauer oxidation?" I shrugged my shoulders; any organic chemist worth his salt can do the Oppenauer oxidation. Then they told me that they couldn't make the catalyst, aluminum isopropylate. I couldn't understand why. They explained that Marker had painted all the windows white so nobody could see what he was doing. He'd also labeled all the reagents with code names, and nobody knew the code. They were confused. Moreover, there's a trick to making aluminum isopropylate that they

weren't aware of. To create the reaction, you have to first amalgamate the aluminum strips with mercuric chloride before putting them into the isopropyl alcohol. I did that; I ran the oxidation and I turned pregnenolone into progesterone. People were looking at me like I was Houdini. Immediately, they made me an offer to come to Mexico and work for Syntex.

I should give you some background here. Syntex was one of several Hormona-affiliated companies that Dr. Somlo, a Hungarian, had started. (Another was Triarsan, which produced arsenicals against syphilis, and which had as its chief chemist Professor Francisco Giral, the son of the former president of the Spanish Republic.) In Mexico in those days, if you started a new company, you could get a complete tax exemption for ten years.

Within months of setting up Syntex, however, Somlo and Marker had a fight, and Marker left. This wasn't really out of character for Marker, because he had had several fights before. He was a brilliant chemist, but a very difficult person. He had a sort of persecution complex, and couldn't get along with anybody. At the time of my interview, Syntex was about three hundred thousand dollars in the red. But if the company could produce progesterone efficiently, it was sure to turn a profit. The hormone was then selling for around a hundred eight dollars per gram.

Syntex's offer came at the right time. I had had enough of Cuba. There was no big future there, because there were no raw materials, nothing to build on. Also, living on an island, you get this island complex. You can't go anywhere because there is water all around. It is a well-known factor. You find it in people who live in the Bahamas or Bermuda, and so on. I negotiated a deal with Syntex in which I would get the same kind of salary that I was getting in Cuba, which was by that time about seventy thousand dollars a year plus 15 percent of the profits on the products that I developed.

I called Edith, who was still my "potential" fiancée. I told her, "I have accepted a job here. Will you marry me, or not? [laughter] Because I am going." Well, she finally said yes. I got back to Havana and told Vieta I was leaving. He tried to dissuade me, saying. "Don't leave, George. The Mexican offer is useless. I'll give you half the laboratory to stay here with me." He continued for quite some time, but I said, "No, thank you very much. I cannot do that." This was my adventurous soul talking. There was no big future in Cuba, so I left. [Fidel] Castro wasn't even on the horizon in those days, so he didn't figure into my decision.

In 1945, Edith and I were married, we moved to Mexico, and I started to work for Syntex.

TRAYNHAM: What did you do first at Syntex?

ROSENKRANZ: First of all, I did the progesterone synthesis. As I said, the workers knew what to do, but they didn't have the reagents. I started with twelve people: one chemist, eight lab assistants—all women—and three men to do the heavy job of carrying around things. After

progesterone, I began work on other sex hormones. We had to. By the time I arrived in Mexico about six months after my interview, the price of progesterone had dropped to eighty dollars per gram. Two months after I began working at Syntex, it was down to eighteen dollars per gram.

TRAYNHAM: What brought about that drop in price? Was it the production in Syntex, or was it other production?

ROSENKRANZ: No, it wasn't the production at Syntex. It had been so scarce at the beginning, but bigger quantities were now becoming available. For one thing, Marker had opened another company, literally across from Syntex, that made progesterone, too. Instead of dealing in single grams, progesterone could be produced in tens, or even hundreds of grams, so the price dropped. The price of testosterone, which Marker never made at Syntex, was around thirty-three dollars per gram. That price held up better because there was no efficient method of making big quantities of testosterone.

Testosterone synthesis is interesting because it seemed that it was impossible to make this hormone from yams. I developed the first industrially significant synthesis from the diosgenin derived from the yam, because I recognized that there's a suitable intermediate during the degradation of the sapogenin side chain. We started by producing diosgenin from dioscine, which is the saponin that occurs in the barbasco, the wild yam of Mexico. During the degradation of the spiroketal side chain, you get 16-dehydro-pregnenolone. Now, in this compound you selectively hydrogenate the double bond at 16, then you oxidize the –OH group at 3. The final product is progesterone. Eventually I worked out a method, preparing the oxime of the alpha-beta unsaturated ketone at 20, to carry out a Beckman rearrangement. In this way, you obtain the19 ketone, taking off the side chain in the process.

We worked very hard and for a long time on this approach. The problem was achieving reasonable yields. I got really disappointed and upset but eventually we succeeded. After we had finally made the first ton of dehydro-isoandrosterone [dehydroepi-androsterone] DHEA, one of my coworkers, Dr. Juan Berlin, who unfortunately died many years ago, presented me with a diploma. It read: "Famous words of a great scientist: The Beckman rearrangement is not a steroid reaction." [laughter] Next I started to work out different methods for the large-scale production of the other sex hormones.

TRAYNHAM: What were some of the difficulties you encountered and how did you solve them?

ROSENKRANZ: The biggest problem came with synthesizing estrogens from our intermediate. Progesterone and all the derivatives could be made easily from this compound, but estrone was different.

I was scanning the literature all the time of course, and in 1948, I came across the name

of Carl Djerassi. He was working in Wisconsin, doing dienone-phenol rearrangements in unsaturated steroids. I felt that maybe I should hire this guy. I telephoned him, inviting him to Mexico. You will find in Djerassi's book, *The Pill, Pygmy Chimps and Degas Horse*, a description of our first encounter (2). When he visited, he saw on the patio where we had a big stack of extraction vats, a small machine that kept shaking, performing a catalytic hydrogenation in the sunshine. Djerassi wrote that he was most impressed by operation's simplicity. Also, he liked what we were doing and how we were doing it. Last but not least, he liked me. So, he accepted a position, becoming the first of my imported stars.

TRAYNHAM: You've attracted other stars as well.

ROSENKRANZ: My next crucial hire was Alex [Alejandro] Zaffaroni. We had been corresponding since 1949 when Alex requested some of our steroid for his brilliant research in paper chromatography. We met finally at the Laurentian Hormone Conferences in 1950. It was incredible empathy and chemistry at first sight, and we developed a deep friendship that has continued through our lives. In fact, all of us at Syntex acted as if we were a big family. We mixed science with movies and parties.

In the lab we tackled the estrogen synthesis. It was known that during the War the Germans had made estrogen synthetically. Basically, you have to get rid of the angular methyl group between ring A and ring B, and aromatize the A ring. Alejandro Zaffaroni monitored the pyrolysis of the precursor using a method we worked out together. A year or two after I left Cuba, I brought Steve Kaufmann—who had taken my place at Vieta Plasencia—to Mexico to join us at Syntex.

Here we come to a very important point. I found in Mexico the same kind of situation that we had experienced in Havana. There were no really good laboratory or research scientists in Mexico because there was no chemical industry except for petroleum. University students who were taught chemistry were trained to become teachers. Nobody had any laboratory experience. I started a Ph.D. program. Later, Carl Djerassi joined me and we continued training people in lab work and doing research. Strangely, Mexicans with only a high-school education have a knack for laboratory work. Our staff learned to do with ease chromatography, then more difficult chemical techniques; it was incredible. They just picked it up. We developed a method of "working with few heads and many hands," as Djerassi called it.

Also, I was hiring more chemists. There was one Mexican chemist, Octavio Mancera, who had been working with Sir Robert Robinson in England for his post-doctorate. I brought in José Iriarte, also from Mexico, who was a student of Henry Gilman, a famous Iowa professor who was working on catalytic reactions. Jesús Romo, Enrique Batres, Luis Miramontes, and Juan Pataki were others who made important contributions as well as Rosa Jashin, Mercedes Velasco, Irma Schroeder, and Tere Cárdenas. Slowly we built a great team.

TRAYNHAM: Tell us about one of Syntex's stellar successes, the synthesis of cortisone.

ROSENKRANZ: Right smack as I was building the company and finishing the industrial synthesis of all the hormones, the big corticoid race started. Every institution—European pharmaceutical companies, U.S. chemical companies, and universities like Harvard—was very involved. Everybody was trying to achieve the industrial synthesis of cortisone because cortisone promised to be a wonder drug. It was even featured in a movie: a girl who couldn't walk because she had arthritis took a couple of milligrams of cortisone and suddenly could stand up and dance.

Using outstanding Mexican and foreign chemists and with the help of brilliant outside consultants like Gilbert Stork, our research efforts were crowned with immense success. Our wining performance in the cortisone race and in the subsequent development of the "Pill" were noticed worldwide and became the talking point of several prestigious magazines like *Fortune, Time*, and others. Our scientific efforts suddenly brought Mexico universal interest and recognition.

This is not the place to discuss details of the race to produce cortisone or the subsequent development of the Pill, many of which can be found in Carl Djerassi's autobiography, *Steroids Made It Possible* (3). The dedication he inscribed on my copy of his book reads: "GRMIP (the true title) for one of my oldest friends, George, with deep affection." If you haven't guessed, GRMIP stands for: George Rosenkranz Made It Possible. Thanks, Carl, for your friendship and the many unforgettable years of shared experience and reciprocal inspiration.

One event that isn't well known occurred one Sunday morning when Carl and I went to the laboratory. By that time in the cortisone race, we had made dihydroallocortisone from diosgenin. That Sunday we brominated this compound and we got the 2-4 dibromoderivative. I cooked this up with collidine to get rid of the bromine. We thought we'd get cortisone, the delta 4-3 ketone. Actually, what we got was a mix of prednisone and cortisone. Thus Carl and I invented prednisone, and there was a patent issued on this later. Schering Plough filed a patent interference, but we won. Because of this invention of ours, Schering had to pay a royalty to Syntex for years on the sale of prednisone.

Carl was a great theoretical chemist, but he wasn't as good in the laboratory as maybe many of my colleagues were. Perhaps this was the result of our different background in schools. The Zurich school was famous. As you have been there, you know how well those people worked in the lab. I don't know how it is now. Nowadays, there seems to be a lot of theoretical chemistry that is being done there.

TRAYNHAM: What was the life like during those years?

ROSENKRANZ: Those were the glorious days of science and top-level chemistry. We went to

many symposia: the Laurentian, the Gordon conferences. In the evenings at the Gordon meetings, there was always a social gathering. Bill Johnson and I used to play the piano fourhanded, mostly boogie-woogie. Bob Woodward came along, he grabbed me and I sat on his shoulders. He was a big tall guy and I said to him, "You know, Bob I rode many, many things in my life. I rode mules, I rode horses, I rode buses, I rode cars, I rode bikes, but I never rode a genius." [laughter]

TRAYNHAM: There was a crucial turning point in Syntex's history when the company became a pharmaceutical firm. How did that come about?

ROSENKRANZ: Syntex was a firm that was doing original chemistry research and making chemical intermediates for others like Squibb [Bristol-Myers Squibb], Upjohn [Pharmacia-Upjohn], Pfizer, etc. We were in the pharmaceutical business but we weren't selling the pharmaceuticals ourselves.

How did Syntex become a pharmaceutical firm? It's a complicated story. One of the indirect factors that led to the change was an antitrust suit. U.S. pharmaceutical firms wanted to import huge quantities of barbasco root in order to manufacture steroids domestically. Through our efforts steroids had become Mexico's fifth-largest export, and naturally the government didn't like this idea. They put an export ban on the root, whereupon a couple of American pharmaceutical companies filed an antitrust suit against Syntex. Although Syntex was a Mexican company, it had a small subsidiary in New York, which was a chemical-specialties company exporting some minor stuff. The American government claimed jurisdiction over Syntex through the subsidiary. While we were dealing with the antitrust suit Charles Allen came along.

He was a very famous investment banker with an excellent nose for everything. Eventually, the Allen interests bought Syntex under the condition that I become the president and CEO and Alejandro Zaffaroni, vice-president. Djerassi had already moved on to Wayne State University. Together with Alex, I made the biggest decision in the history of Syntex. We recognized that we were heavily involved in research. Our people were working and turning out new compounds, but we were selling intermediates to pharmaceutical companies. We opted to switch the focus of the company from making steroid intermediates to manufacturing pharmaceuticals. I must add that the prices of hormones were declining further. All kinds of manufacturing technologies were being developed and making steroid intermediates wasn't a big business any longer. So, either we had to vegetate and not do any significant research, or we had to keep the research and become a pharmaceutical company. Both Alex and I were lovers of research. By now we had many accomplished scientists working for us, including many Mexicans. Carl was sending us a number of his postdocs as well. We had chemists like Howard J. Ringold, Franz Sondheimer, Bert Bowers, Ricardo Villotti, John Edwards, John Zderic, and a number of other excellent scientists turning out very important research.

Once the decision was made to become a pharmaceutical firm, I brought Carl back to

Syntex. The collaboration between the three of us was an absolutely unique constellation. It was such a powerful driving force. Each of us assumed a role that wasn't his original one. In this triumvirate, everybody had ideas, and very often, conflicting ideas, of what to do. Carl was wishing the research to go in one direction, then in another. Alex was quiet, but firm; he already had some business and technology knowledge, and he was always receptive to new technologies and ideas. I was the same, but I became the moderator and coordinator in all these matters. In my opinion, this was the most powerful combination that existed in this industry at that time. Later on, other things happened, and I'll talk about them.

TRAYNHAM: With your new and heavier responsibilities, did you have time to do any laboratory research yourself?

ROSENKRANZ: At that time I was so involved with the other aspects of the business that I was forced to turn away from working in the laboratory, yet I still followed what was happening. You know, I believe that in the life of a chemist there are two major turning points: one, when he decides to leave academia's pure, pristine research and go into industry; the second, when he is in industry and must decide whether to become an executive or stay with research. These can be very difficult decisions. The first wasn't difficult for me because I was thrown into industry. But the second was a hard challenge.

I haven't mentioned to you that I was always very interested in psychology. I love people. Professor Carl G. Jung was in Zurich while I was there. For three years, I attended his lectures. Much of his time was spent analyzing a single dream. He said, "The dream is a little hidden door in the innermost secret recesses of the soul." His talks and his entire way of looking at events and human interactions had a deep impact on me. I remember his saying, "Knowledge rests not on truth alone but on error also." He made me think about what research is. Is it a quest for truth? Or is it solving problems? For me, problem solving was always the most important thing. One type of problem solving is resolving conflicts. That's where the human element comes in. Partly because I was already in the role, and partly because I had absorbed so much of Jung's theory, and partly because I have a deep fascination for human relationships, I took the road to be an executive. I had knowledge of managerial sciences and setting up productive interpersonal frameworks. If someone came to me with a good idea, I'd usually say, fine, let's do it. I was known for having an open-door policy. Anybody could come to me and complain. I remember when one of my dear friends and chemists dashed into my office, pounded on my desk, and said, "Boss, you're completely wet! This is absolute idiocy what's going on here." [laughter] I laughed and replied, "Now, what's the matter, John. Tell me, what's the problem?" I didn't get upset. That is not the way most executives would react, but when you really love what you do, it is easier to stay calm.

TRAYNHAM: What steps did you have to take to transform Syntex into a pharmaceutical powerhouse?

ROSENKRANZ: The first phase was what I called Operation Fence-Mending. I had to repair the damage done by Somlo, who was a very strange person. He never made a decision, and people got frustrated and offended. "You can't work with Syntex," was the byword. I had to go round the whole industry and convince them otherwise. The next step was to peddle the contraceptive we had developed. I offered it to Parke-Davis, but officials said, "We won't touch the thing. There are religious problems and so on. No, we won't touch it with a ten-foot pole." Then I went to Upjohn, which we had been supplying with progesterone. I got another, "No." This time it was the so-called NIH syndrome: not invented here syndrome. [laughter] "We have it, we have it. We have our own synthesis of progesterone derivatives. We are not interested." I went to Pfizer. In those days, Pfizer had a president and an executive vice-president whose names I won't mention, but they were important and successful executives. The executive vice-president said, "Contraceptives? Progesterone? The market for this is only one million dollars per year. We are not going to bother with this kind of market." Eventually, Ortho came along and we did it together.

Then I had to establish collaborations with Ciba, with Organon. We had a number of new compounds, including many new steroids. Still, we couldn't sell them, because of FDA [Food and Drug Administration] regulations and other factors. Alex and I came up with a concept, which was the biggest hit for Syntex. We would go to a large pharmaceutical firm and offer it the compound. We would tell the company that we could manufacture the compound, that we had proof of concept and clinical evidence to back up what the drug could do. The company would have to do only some phase-three testing and maybe some clinical and pharmacological research. We offered to be a partner. We would not sell the drug to them on a licensing basis. Instead, we asked what markup they would like to have—one to three, one to four—on our products? We didn't give them a selling price because it's against the law in some places in the world. And after all, they were the marketers. Syntex would get 30 percent of sales on average.

This was a completely new concept in the pharmaceutical industry. Alex and I became famous for this no-royalty and no-fixed-price approach. I went around making deals in each country with the largest pharmaceutical firms: in England with ICI [Imperial Chemical Industries PLC], in France with Roussel [Aventis, Inc.] or a subsidiary of Roussel, in Germany with Grunenthal, in Italy with Recordati. We built up a whole rainbow, a whole spectrum of distributors, with whom we had these relations. My only condition was that the labels state "a Syntex-ICI product" or a "Syntex-Recordati product," and so on. Overnight, without one cent of investment, we built up worldwide distribution of our pharmaceutical specialties. We also had a hook: our partners got first refusal on the results of our new research. Why would they find this attractive? Because we were successful in basic research.

Then, of course, Syntex grew. Carl Djerassi went back to the U.S., this time to Stanford [University], becoming a full professor. I forgot to tell you that Syntex from the very beginning was registered as a Panamanian corporation. Even in Somlo's time, there were some tax conveniences. Later on, this became a very profitable device. Once we had built up a worldwide distribution network, we went to establish ourselves in the U.S, in the San Francisco

Bay area. We founded Syntex Laboratories as an American corporation. As a consequence, we had to have someone go to the United States—either Alex or myself. We were getting close to flipping a coin, but then I said, "Alex, you go." [laughter] Alex went, becoming the president of Syntex Laboratories in the United States. He was there for a number of years and our company grew. One day we started to think that maybe we should expand beyond steroids into other fields.

TRAYNHAM: How did you accomplish this?

ROSENKRANZ: As usual, we went around getting the best people. We brought in Joshua Lederberg, the Nobel Prize winner, and later on, E. J. Corey, followed by other Nobel Prize winners in the medical areas. So, now we had chemical, clinical and microbiological research, everything a pharmaceutical firm needs. We started to become an integrated pharmaceutical company. Bert Bowers, a chemist of first order, had joined us earlier, and I started to groom him as my possible successor in the organization. Then Alex brought in Alex Cross, who was working with Derek Barton in England. We had lots of English chemists coming in.

Alex Zaffaroni realized that the system of delivering drugs wasn't right. He said, "We have all these new compounds. They are all so active. They get into the body, and only about one-hundredth of the active compound reaches the target, because in the meantime the liver is metabolizing it. There has to be a better way of doing things. We have to work on the delivery system." I said, "Bravo, Alex! Go for it! That's what you should do." One day Alex came to me and said, "No, George, I cannot continue, because the people don't believe in my ideas about the delivery system." I replied, "Come on now, what nonsense is this? You're the president of research; you're the president of our company in the United States. What is this? "I cannot make people work on something that they don't believe in. I am going to leave Syntex and set up my own company." "Alex, don't do it." "Yes, I will have to do it." Well, we worked out a formula. We got 20 percent of Alza Corporation, which was the company he started. This was done to avoid possible suits from Syntex stockholders. Later on, the Alza stock was distributed to our shareholders. Then I had to find a successor to Alex; I chose Bert Bowers. Carl Djerassi became head of all research. I was still president.

TRAYNHAM: Did any other expansions occur?

ROSENKRANZ: We got involved in ventures like Syva, a collaboration with Varian, to develop organic molecules to act as superconductors. We set up Zoecon, with Carl as President, to develop compounds to interrupt insect growth. When Syntex's research director, Ralph Dorfman died, I hired John Fried. Research under him produced all these wonderful compounds: Naprosyn, Ticlid, Cytovene, Toradol.

This was the pay-off of my basic philosophy of getting the best people and not being too concerned about what they cost. Give them the freedom to work, to think. Get them the best

coworkers and let them be happy! I believe in participatory management. I don't believe in telling everyone the way it has to go. This, of course, was not the European, Swiss, or English way, where management directs from the top down to the bottom. As a matter of fact, even before the Japanese, I invented the bottom-up-to-the-top approach. Later on, the Japanese were surprised to find that we had this operating process, though ours wasn't as elaborate as theirs.

In a very friendly way, I made the final decision, but it came from calm consultation and discussions. In the early days, Alex, Carl, and I hammered out ideas with violent discussions at high decibels. Once in those days, my wife, Edith, came down from upstairs in our home and wanted to see if there were any survivors left. [laughter] Finally, we all laughed our heads off at the way we had been behaving. It was a slow but continuous transition from cocky, brilliant amateurs to competent professionals. We were such brilliant amateurs, we had a saying: "Why do it the normal way if we can do it differently?" I mean, we were accused of thinking that way. We seemed to want to reinvent everything from A to Z. Then later on, we were doing the clinical research, finances, everything. Then, even later, I started slowly to gather a couple of specialists in each section, and organized the business, as it should be.

TRAYNHAM: It became more conventional?

ROSENKRANZ: No, it did not become more conventional, in one sense at least. But first let me finish the story of how Syntex was sold to Roche, and then we can talk about that. Syntex became the outstanding company in the Bay area, and we were different. Everybody characterized Syntex as a "nice" company. We kept our word, we were good partners, we worked quickly, we did good research, and we had brilliant people. We achieved something, becoming a "somebody" in the pharmaceutical industry from a "complete unknown" or "south-of-the-border" nobody. I think we became the eleventh-largest pharmaceutical company. This was all based on a philosophy of excellence and easing human relations. Give people what they want; let them have peace of mind; let them concentrate on their work; try to take away all their outside stress. Of course, sometimes a researcher came to me and said, "Upjohn published before me. Here I am in the middle of some research, but look at the *Journal of the American Chemical Society*." I would say, "That is life," this happens, but that next time he would be first.

Incidentally, I am a rather modest person. I am not interested in the limelight or publicity. One thing however, of which I am proud is that together with my colleagues, we advanced steroid chemistry in the 1950s by ten years, just by our publication policy. We had a very simple policy: patent and publish. By that, we gave the stockholders what they were entitled to, and our researchers what they needed—publication and peer recognition. The other pharmaceutical companies——particularly the European ones, where secrecy is such an important thing, and U.S. companies also—eventually were forced into this position of allowing their scientists to publish because if they didn't, there would have been a palace revolution by their own people. They would have pointed to us: "Look at Syntex, all the research they are doing, and they're publishing the results. Here we are doing the same thing, and we have to

keep it in our drawers?" They had to publish, and this was to the benefit of both the whole scientific community and the field of chemistry. I am proud of that achievement. Cortisone, the Pill, and other things that I did in my life were okay, but the human contribution that I made to the growth of science and Syntex were more important to me.

TRAYNHAM: What caused Syntex to fall from the heights it achieved?

ROSENKRANZ: In 1982, I retired as chairman of the board and president and CEO, and Bert Bowers, whom I had picked as my successor, took my place. I remained on the board as founding chairman. My policy was never to second-guess my executives during my time as CEO, and I didn't want to do that as a board member. I told Bert, "Okay, this is now your game, and I'm going to give you absolute support as long as your policies coincide with my conscience and philosophies. It will be easy for me because, having been on one side of the fence, now I'm on the other side. I think it will be good for the company, good for the stockholders, good for you, good for the employees, and I hope also good for me."

Syntex kept on growing. Bert Bowers did an outstanding job. He was different from me because my orientation was more internal. I was trying to grow the company from the inside by constantly adding excellent people. Bert was very much interested in getting outside recognition for Syntex. He became president of the Pharmaceutical Manufacturers Association. We went through a period of acquisitions, some good, and some bad. Well, that's the name of the game. Research was blooming; new products were coming forth. We became a major marketing force. Unfortunately, Bert wasn't well. I remember during his early years in Mexico, I had to rush him to a hospital because he had some bleeding and needed a blood transfusion. Later on, it turned out that he had a very serious disease. He knew it all the time. I guess that is one explanation for some of the things he did in his life. He knew that he had about ten years left, and he had to compress everything, what he wanted to achieve and what could be done, into that decade. We didn't know anything about it until near the end. One of the big problems was that, while I had spent a considerable amount of time training my successor after I had identified and chosen him, Bert didn't have time for this; he was so involved in managing the growth of Syntex. And unfortunately, when he passed away, we didn't have a well-planned succession. Bert recommended Paul Freiman, who was an excellent person. But this was new for Syntex, because he came from the marketing side of the company.

Now, I always believed that to run a complex pharmaceutical company, you have to have a scientific background. It doesn't matter whether it's engineering, research or production, but you have to understand the science. I've always been proud of knowing about a lot of different things, maybe not in depth, but in general. If somebody came to me and would tell me a story about some new great discovery or invention I'd look at him, smile, and say, "Don't snow me. I don't accept that." Now, that's very difficult to do for a person who comes, let's say, from the accounting or financial or marketing side. He cannot easily distinguish between the alternatives. If you are in such a position, you must have a confidant who knows about all the things you do not and whom you can trust 100 percent. That's difficult, because human nature is not like that.

Everybody has axes to grind; everybody has his own line and agenda.

Bert and I, we were organic chemists. As such, we were proud that we could do everything. Maybe not as well as other people, but [laughter] at least we thought we could. In Freiman, Syntex had a CEO who was faced with learning everything in a couple of years when we had spent decades learning it all. Here was a big pharmaceutical company, with brilliant people in all domains, and he was to run it.

At the same time, pressure from Wall Street was mounting. At the beginning of Syntex, we had had a price/earning multiple of infinity because we didn't have any income; we had only assets. Later on, when the money started coming in, the P became increasingly important. Syntex stock did an incredible job. It went up and up, and it split so many times. The mentality of Wall Street started to change simultaneously with our growth. Financial analysts became concerned about the performance of companies by quarter. I told them a hundred times, and Bert told them a hundred times, that you can't measure a pharmaceutical company on a quarter-by-quarter basis. But they were portfolio managers who gave reports on a quarterly basis. This was a conflict that didn't do Syntex any good. Somehow the word went around Wall Street that Syntex's pipeline of new research wasn't as rich as before. It was absolute baloney. The stock came under pressure; the price went down. Unfortunately, Charles Allen, who believed in us, and who supported us to the last moment, died. We didn't have the support of the Allen group to weather these things. Also, the Allen group got concerned that as the stock went down, it would go down further. There was a continuous pressure on us to sell the company.

Roche had courted Syntex for about fifteen years, but Bert and I had never wanted to sell the company. But watching the stock price come down, the chief stockholders and their friends became nervous, and didn't believe in the promise of our new products. Finally Roche made an offer, which was at that time sensational for the stockholders, and the company was sold for 5.3 billion dollars in 1995. If you remember, when I joined Syntex, it was three hundred thousand dollars in the hole. I was able to take the company from that to a value of 5.3 billion dollars. For the stockholders, it was marvelous. For the employees, it wasn't so good, unfortunately, although we had all the provisions for compensation and benefits. The philosophies of a European company—or, for that matter, maybe for all large pharmaceutical companies—are quite different from the philosophies I believe in and built on. Roche integrated Syntex into their way of doing things, their way of thinking, their way of managing. As a consequence, Roche lost a tremendously large percentage of the excellent people I had gathered over the years, because Roche couldn't give them the kind of security that they had felt at Syntex.

This is a very interesting phenomenon, because if you look at the people who were formerly my stars, they are now CEOs or presidents or presidents of research of Bay-area biotech companies. It is like a university with its alumni. They are all around, and we get together. I heard something recently that nearly brought tears to my eyes. Two of my former people were reminiscing about the good old days at Syntex. They agreed, "Syntex was like Camelot." That was our way. We were a really nice company, giving everybody a possibility for self-realization and harmonizing personal goals with achievements for the company, for the stockholders, for the whole health field, for humanity. I think this was the greatest thing. Now,

I'm not saying that my way was better than other ways. Who am I to say that? One person has one philosophy, and that's it.

Syntex continues within Roche. In research, they have made some interesting achievements in transplants, which were based on our earlier findings. The drug Cellcept, which we developed, is on the market. There are other products, which have been developed further and launched. A splinter group remains in Palo Alto, which is now called Roche Bioscience. They are doing research; they are working very well. I would say about half of the people who were present originally dispersed in the Bay Area and elsewhere in the world, in Europe, and are making a contribution.

TRAYNHAM: The remarkable story of Syntex took place in Mexico. Do you think there was something unique about the situation there that enabled this to occur? Or could it have occurred at the same time elsewhere?

ROSENKRANZ: Well, I have often been asked that question. My answer has always been that you need luck. And what is luck? You have to be at the right place at the right moment, with the right people—that is luck. We were in Mexico, we had the raw material, and there we got this fantastic constellation of people. There was the idea behind it. There was the motive behind it. Maybe it could have taken place somewhere else. Certainly the question of the raw material was very important. I think Syntex would have taken a completely different track if it had been in the United States. We would have worked under different circumstances, and maybe would have gone in a different direction.

TRAYNHAM: Now tell me about your family. How did you balance work with family?

ROSENKRANZ: Well, in my life the family stands in first place. It comes before work and before science. I have a wonderful wife. We are now married for more than fifty years. We have three outstanding children. We raised them to be the best. I have always thought that education comes first. Having gone through so many upheavals in my life, I told them that the only important thing is what you have in your head; you don't know what's going to happen tomorrow. Money doesn't mean anything. Money can be here today, disappearing tomorrow. I have seen that happen again and again. What does money buy you? "The only thing of value that I can give to you, my children, is the best education." They all went through the best schools in Mexico, they all went to Stanford, they all graduated from Stanford, and they are all different.

Our oldest son, Roberto, received his Ph.D. in pharmacology and toxicology at the University of California, Davis. Then he took a postdoctoral fellowship in the Department of Medicine at Stanford University under the direction of Dr. Kenneth Melmon, Dean of the Medical School. Then in 1982, John Fried hired him behind my back and against my will to

work in Syntex Research in pharmacology. While working in research he completed an MBA at the University of Santa Clara. After nine years in Syntex research, he took on different positions of increasing responsibility in management occupying senior positions in new product development, marketing, sales strategy and business development. As the health care system in the U.S. changed, Roberto moved into managed care to find novel strategies for marketing and selling pharmaceutical products to the different health care organizations. He has been innovative and successful in his approaches. Finally, when Roche took over, Roberto was the most senior person from Syntex Laboratories who remained with them, accepting the position of Business Unit Director for Northern California/Nevada. Roche has, I think, twenty directors in the country. Roberto had over fifty people reporting to him, and was managing about a hundred twenty million dollars in sales, among other things. In November 1996, he became President and Chief Operating Officer of a biotechnology firm in the Bay area. He is a fantastic sportsman, like his whole family. He is married to a lovely American girl, Heather. They have three children, Tamara, Adrian, and Monica. They are a wonderful, loving family.

Our second son is Gerardo—Jerry. He attended Stanford University where he earned an undergraduate degree in electrical engineering and graduate degrees in a joint program between the Department of Electrical Engineering and the School of Business Administration. Upon graduating from Stanford, Jerry joined a start-up company, Telenet, which went public, was acquired by GTE, and ultimately became Sprint International. During his ten years with the company, Jerry held senior-executive positions in management, global business development, and international sales. Jerry was always fascinated by new technological innovations and ultimately founded his own company, Ventech International. Ventech was established to provide business development services to venture capital backed, early stage technology companies. He also married a very nice American girl, Lauren, and has two sweet children, Lily and Tommy.

Our youngest son is Ricardo. He graduated from Stanford University and the Cornell Medical School. He is married to a wonderful Mexican girl, Laura, the daughter of an illustrious Mexican doctor's family, and they have one child, Alejandro. They live in Chicago where Ricardo is a neonatologist at Northwestern University Hospital. He is taking courses in public health policy, and also, as with all my family, he is very interested in music. He plays the piano, he composes, and he has even produced a record.

Edith and I are very happy with how our children have developed. We hope that they will lead very happy family lives. There's nothing to complain about there, and I'm looking forward to the future.

As for myself, during my time in Syntex and after my retirement I have developed a number of other interests. One of them is music; I play the piano. I am also interested in art. Of course, bridge is a large part of my life. I have written eleven books on bridge (4). I have won eleven U.S. national championships, and probably over a hundred Mexican National championships. I have a column in the monthly magazine of the American Contract Bridge League. I also write for French bridge magazines, two English ones, one Italian, and one Swedish magazine. Bridge is very important to me. In sports, I play tennis and golf, and I used

to ski a lot.

Then, of course, there is the computer, which came into my life about ten years ago. I am reasonably computer literate. Every morning on my computer, I get information about what's going on in the world, in the pharmaceutical and in the biotechnological areas. After my retirement, I became more profoundly interested in a number of scientific disciplines like immunology, genomics, and molecular biology. They are all far away from my original training as an organic chemist. As I told you before, I like to have a broad understanding of everything that is going on.

I'm still very active in the sense that I'm on the board of directors of Digital Gene Technology, which is in genomics. I am interested in venture capital, constantly looking for different new ideas. Also I have a company in Mexico, which is utterly my idea, and to describe fully would take much more time that you can afford here. Basically, I'm trying to bring academic research and industry together in Mexico. I call myself, vulgarly, a "broker of science." Other people say I'm a catalyst, but you know, it's just a question of nomenclature and semantics.

My company ICT [Industria, Ciencia, Tecnologia] is trying to identify needs and problems in industry and resolve them with help from academia. We try to find the academic people who can do this and match them with industry. We make a contract with A; we make a contract with B. The company makes a profit on this arrangement. We supervise, we monitor, and we try to solve their problems. The batting average? Who knows? It's too new! I began ICT in 1996, and luckily, most people feel it is a sensational idea. We are just trying to see how people respond, whether we can do all the work. I am the president, but I have no financial interest in the company. Any money we make that would be my share will go to philanthropic purposes, mainly in science to reverse the brain drain and try to bring Mexican scientists back to Mexico. I am the president of the science board, which includes such illustrious people as Alex Zaffaroni, Elias J. Corey, Kenneth Melmon, and Dr. Guillermo Soberon, the former minister of health and ex-dean of the UNAM [National Autonomous University of Mexico].

Other current interests apart from my family and our grandchildren include a lot of travel. Also, I follow soccer and basketball [laughter], which is the latest thing, as Ricardo lives in Chicago.

TRAYNHAM: Can you think of anything else that you want to add to make your story complete?

ROSENKRANZ: No, I think my story is complete. I'm very, very contented; I live a very happy life. I've gone through many, many crises in my life that I didn't mention. My life at Syntex wasn't all milk and honey. As usual, there were problems; there were ups and downs. With the help of my wife and family, I've been able to weather all these adversities, all the conflicts. Basically, I'm an optimist. I've an immense drive and thirst for everything that's

new, for new science, for new events, for new technologies. I wish I could live to see all the things that are coming, which I guess is a common aspiration of most, maybe all, people like me.

TRAYNHAM: Maybe you should return to scientific endeavor to prolong life.

ROSENKRANZ: No. That was a different phase of my life. It was a great phase; it was lovely to do that, but it is behind me. I think understanding science, using science, combining different things in life that are science-related, which are really maybe unusual and certainly innovative, that's more challenging. Innovation is the word, whether it's just breakthrough or combination, association.

TRAYNHAM: One question I would like to put to you is connected with *The New York Times Book Review*. Each year, the editor of *The New York Times Book Review* closes the year with a list of one hundred books that the editor believes to have been the most significant books published that year. Among those included in the list for 1996 was a book by the title, *The End of Science*, in which the author expresses a conviction that all of the great discoveries in science have been made, and that from now on science will just be diddling with details; that there's no more expectation of really significant discoveries (5). What's your reaction to that point of view?

ROSENKRANZ: My reaction is it's absurd. Your question reminds me of something I forgot to mention to you earlier. When I left Switzerland, and I said goodbye to Ruzicka, he told me, "Rosenkranz, I wish you all the best. I know you're going to do good things in your life. There is one thing, one bit of advice, that I would leave you, which is: don't touch steroids with a ten-foot pole, because everything that can be done has been done already." "Thank you, Herr Professor," I replied. Actually, he used the—do you speak German, or do you understand German?

TRAYNHAM: *Ein bisschen* [a little].

ROSENKRANZ: Actually, he told me, "*Rosenkranz, Lassen Sie die Steroide in Ruh, alles ist schon abgegrast.*" [Rosenkranz, leave the steroids alone, everything has already been grazed.] You know, like the cows that eat all the grass. [laughter] My response to this is I came to Mexico; I became involved in steroids, and look what happened. Cortisone appeared, and all the other drugs. However, eventually I said, "Okay, everything has been done in steroids." And nothing happened for ten years. What do I see now? The most startling thing is that steroids are coming back.

For instance, there is one derivative of a triterpene, with which I have been involved. It belongs to the family of triterpenes on which I did my thesis. It seems to be active against melanoma. Now, I mean, this is such an absurd thing. How is it possible? How can these compounds have all this biological activity? There is never an end. There is always something new that comes along. It's a different view, a different invention. Look at molecular biology, or cloning.

I'm particularly fascinated by genomics because I think that the future lies in this discipline. All the pharmaceutical firms have discovered this too. We're now mapping genes. Then we'll be looking more closely at molecular events, what switches the genes on, what turns them off; and what happens when you chop them off, put them together. It's a whole new science. That goes to your question, to your remark, that everything has been done. Never, will there be a moment when everything has been done. It's not a question of the details. Fundamental discoveries are going to come in the future and it will be just a wonder. I wish I could wander along and look at Wonderland! [laughter]

[END OF INTERVIEW]

ADDENDUM

A note to the reader:

After receiving the transcript of my interview, it became clear to me that considerable editing would be necessary in order to achieve fluidity of thought, chronological accuracy, and ease of readability. Fortunately the oral history editor of Chemical Heritage [Foundation] agreed with me, and I proceeded to take advantage of this license. As more than three years have passed since this interview was done, I decided to include a follow-up of the events of the last three years.

Much to my regret, Syntex under the Roche aegis has nearly disappeared. However, in Mexico, where everything originated, it continues to thrive (the name now is Roche Syntex), receiving the well-deserved recognition in scientific, governmental and public circles. In the U.S., the Syntex Alumni Association is thriving with hundred of members. Syntex alumni have spread and are working in many pharmaceutical companies as well as founding and consulting with start-up biotechnology and genomic companies. One of the topics that were repeatedly heard at their last meeting on February 5, 2000, was the importance of my managerial philosophies, the success that these principles had brought to them and their companies, and how they had imparted pieces of the Syntex culture all over the industry. It gives me great pleasure to know that I have had a positive impact on these people and that my philosophies that started fifty-five years ago are going strong and are being passed on to new generations of scientists and managers.

I have added three more enterprises in the pharmaceutical sector to my activities, acting as adviser to the CEOs. All in the United States, they do not conflict with each other; on the contrary, I found unusual synergisms to the benefit of the respective parties. Particularly exciting is my association with PHERIN, a California enterprise dealing with the therapeutic application of human pheromones. Interestingly all are sex specific steroids, active in picogram quantities, and they show remarkable physiological activities. As a matter of fact, their lead compound was first synthesized by Franz Sondheimer and me in the 1950s.

My prediction about genomics has been fulfilled; they're now the center of attention of the scientific and financial world

My interest in innovation continues, sometimes reflected in venture capital activities, often with my dear friend Alex Zaffaroni. The passing of time has only strengthened the bond between our families and us. My hobbies continue and recently I was inducted into The Hall of Fame of Bridge. Our eldest son Roberto is presently on the board of several companies, engages in venture capital, investments, and recently formed his own startup pharmaceutical company: Roxro Pharma LLC.

As a natural extension of Ventech's activities, Jerry began co-investing with several top venture capital funds and took an active role in helping the portfolio companies grow. In some instances his role has been that of an angel investor. For example, Jerry was the founding

investor of StarMedia Network, Inc., which became the first Internet Company targeting Latin America to complete a very successful IPO in the United States. Jerry remains a Director of StarMedia and sits on numerous other boards. He continues to invest in early-stage Internet, telecommunications, information technology, and new media companies.

In the past couple of years, our son Ricardo, the pediatrician/neonatologist, has taken a more serious interest in health services administration. He is the Founder and CEO of Inovamed, a company developing an integrated health care delivery system throughout Mexico that includes hospitals, outpatient clinics, diagnostic laboratories, drug stores and managed care services. His vision is to permit access to healthcare for as many Mexicans as possible. A new addition to his family is our seventh grandchild, Ana Cecilia.

On the female side, my daughters-in-law continue to be charming mainstays of their families. Our seven grandchildren Tamara, Adrian, Lili, Monica, Tommy, Alejandro and Ana Cecilia see to it that their parents have their hands full.

My darling wife, Edith, with her deep love and understanding is the inspiration of all of us. She is a tower of strength, making her presence felt with her dedication to our whole family. To her goes my endless love and gratitude.

NOTES

1. Paul Karrer. *Lehrbuch der organischen Chemie* (Leipzig: Thieme, 1933).

2. Carl Djerassi. *The Pill, Pygmy Chimps, and Degas' Horse : the Autobiography of Carl Djerassi* (New York: Basic Books, 1992).

3. Carl Djerassi. *Steroids Made It Possible* (Washington, DC: American Chemical Society, 1990).

4. See for example:

   George Rosenkranz. *The Romex System of Bidding; a Dynamic Approach to Bridge* (New York: World Publishing Company, 1970).

   George Rosenkranz. *Win with Romex: the Key to Accurate Bidding* (New York: Crown Publishers, 1975).

5. John Horgan. *The End of Science* (Reading, MA: Addison-Wesley Publishers, 1996).

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