CENTER FOR HISTORY OF CHEMISTRY

VLADIMIR PRELOG

Transcript of an Interview
Conducted by

Tonja Koeppel

in

Zürich, Switzerland

on

17 January 1984

Vladimir
Prelog JH
3/18/96

TER FOR HISTORY OF CHEMISTRY ORAL HISTORY PROJECT

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V. Prelog
(Signature)

April 10, 1985
(Date)

Chemical Heritage Foundation
Oral History Program
315 Chestnut Street
Philadelphia, Pennsylvania 19106

ABSTRACT: In this interview Vladimir Prelog discusses his long and distinguished career as an organic chemist. He begins by recalling his early education in Yugoslavia, doctoral studies in Prague, and first job as a chemist. He returned to Yugoslavia in 1935 to teach at the Technical Faculty of the University of Zagreb. The interview continues with Prelog describing how he finessed the problems of war and foreign occupation by emigrating to Switzerland, where he began a thirty-five year long affiliation with the Swiss Federal Institute of Technology (ETH). The central portion of the interview contains Prelog's reflections on his research at the ETH. This includes work with the chemistry of natural products and with stereochemistry, and his creation (with Cahn and Ingold) of the CIP system for defining absolute configuration. The interview concludes with Prelog speaking about the growing complexity and expense of chemical research, his relationships with American chemists, his current research, and the future of chemistry and chemical education.

INTERVIEWER: Dr. Tonja A. Koeppel received a master's degree in chemistry from the Swiss Federal Institute of Technology in 1944. Since then she has written about, researched, and taught college chemistry. Dr. Koeppel is also an historian of chemistry. In 1973 she earned a Ph.D. degree in the history and sociology of science from the University of Pennsylvania. She is especially interested in the development of organic chemistry in the nineteenth and early twentieth centuries.

NOTE: The following table correlates the tapes of the Prelog interview with the pages of this transcript.

VLADIMIR PRELOG

1906 Born in Sarajevo, Yugoslavia, 23 July

Education

1929 D.Sc., Chemistry, Prague Institute of Technology

Professional Experience

1929-1935 Head, Laboratory of G.J. Dríza (Prague)
1935-1941 Lecturer and Associate Professor, Technical Faculty of Zagreb University
Swiss Federal Institute of Technology, Zürich
1942-1950 Lecturer and Associate Professor
1950-1976 Professor
1957-1965 Head, Laboratory of Organic Chemistry

Honors

1946 Werner Medal and Prize, Swiss Chemical Society
1962 Stas Medal, Belgian Chemical Society
1962 Medal of Honor, Rice University
1965 Marcel Benoist Prize, Switzerland
1966 Hanus Medal, Czechoslovakian Chemical Society
1967 A.W. von Hofmann Memorial Medal, German Chemical Society
1968 Davy Medal, Royal Society of London
1969 Roger Adams Award, American Chemical Society
1974 Paul Karrer Award, University of Zürich
1975 Nobel Prize for Chemistry
1976 Paracelsus Medal
1977 Order of the Yugoslavian Star
1977 Order of the Rising Sun, Japan
1978 Emil Votocek Medal, Chemical-Technical University, Prague

TABLE OF CONTENTS

INTERVIEW: Vladimir Prelog

INTERVIEWED BY: Tonja Koeppel

PLACE: Swiss Federal Institute of Technology
Zürich, Switzerland

DATE: 17 January 1984

KOEPPEL: Professor Prelog, you were born in Sarajevo on July, 23, 1906. To what country did Sarajevo belong at that time?

PRELOG: It was part of the Austro-Hungarian monarchy. My life has been affected in many ways because Sarajevo has such a bad reputation. As you may know, Archduke Franz Ferdinand and his wife were assassinated there in 1914 and that action is considered to be the proximate cause of the first World War.

KOEPPEL: Yes.

PRELOG: I realized how Sarajevo's reputation affected me when I had to acquire a sailing permit in 1950 in the United States. While doing so, an agent of the Internal Revenue Service interviewed me. He asked me, "Professor, where are you from?"

I said, "Zürich."

He responded, "Zürich, Sweden?"

I said, "No, Zürich, Switzerland."

He was a little irritated and said to me, "You were not born, of course, in Zürich."

I answered, "No."

He asked, "Where?"

I answered, "Sarajevo."

He then said, "Oh, that's the place where all this mess started."

I was very proud that while he didn't know that Zürich is in Switzerland, he did know that Sarajevo exists.

KOEPPEL: He didn't hold it against you, did he?

PRELOG: No.

KOEPPEL: That was in l950?

PRELOG: In l950. Sarajevo is now famous because the Winter Olympics will be held there this year.

KOEPPEL: Yes. Well, you must have been a student in Sarajevo when the assassination occurred. Were you eight years old?

PRELOG: I was a student in elementary school at the time and

I was standing very near to the place of assassination. As a pupil I was assigned to throw flowers at the Archduke's procession. I was in the first row.

KOEPPEL: Oh, you were there!

PRELOG: The assassination occurred about two hundred meters from the place where I was standing. I didn't see it, however, because it happened around the corner.

KOEPPEL: It must have been terrible.

PRELOG: Yes, it was very bad.

KOEPPEL: There was much confusion, I guess.

PRELOG: I was, as in many other cases, a spectator of very important events.

KOEPPEL: Oh, yes, you were indeed! Two world wars. We'll get to that later. So, you went to grade school in Sarajevo.

PRELOG: Yes. We then moved to another place, Zagreb. During most of my stay in Yugoslavia I resided in the city of Zagreb, the capital of Croatia, the northern part of Yugoslavia.

KOEPPEL: What year did you move to Zagreb?

PRELOG: In l9l5.

KOEPPEL: So you were in about the third grade. You entered a different school and then...

PRELOG: I then attended Realgymnasium, a kind of high school, something between elementary school and university.

KOEPPEL: Oh, I see.

PRELOG: The system is practically the same in Switzerland.

KOEPPEL: Does it take you to the university level?

PRELOG: You attend Realgymnasium for eight years and then take what we call the maturity examination. After passing this examination you may be accepted by a university. This is more or less the middle European system.

KOEPPEL: Yes. You must have studied chemistry there because I noticed that you published a paper while still in this school.

PRELOG: For two years I attended school in a smaller town, Osijek, because my father was appointed director of a high school there. I had a very, very good teacher. I helped him

to build a small chemistry laboratory. As I have mentioned on several occasions, I proved that the level of chemical literature was not very high because my paper was accepted! It was published when I was about fifteen years old.

KOEPPEL: That's wonderful! What was the paper about?

PRELOG: It was about a titration apparatus.

KOEPPEL: You actually wrote it in German!

PRELOG: I wrote it in German and it was corrected by my teacher. It was accepted by the Chemiker Zeitung.*

KOEPPEL: You were bilingual?

PRELOG: No, I could only write German, not speak it. I had studied German at school. My mother tongue was Croatian and we didn't speak German at home.

KOEPPEL: I see.

PRELOG: We read German books at home. There were many German books at home, but we didn't speak German.

KOEPPEL: Yes, well, what was your father's name?

PRELOG: My father's name was Milan. It is a Yugoslav name. He was a professor at the Gymnasium. There were different branches of Gymnasia. One emphasized Greek and Latin for people who wanted to become lawyers or even study medicine. The other branch offered mathematics, natural sciences, and modern languages. It was called Realgymnasium.

KOEPPEL: I see.

PRELOG: I had taken the scientific education, not the humanistic one.

KOEPPEL: Your father was not a scientist?

PRELOG: My father was a historian at the Gymnasium. Very soon, however, he became professor of history at the University of Zagreb. We moved back therefore to Zagreb. The last years of my schooling at this level were in Zagreb.

KOEPPEL: Did your father's being an historian influence you? You seem to have an historical bent, at least in your latest work.

PRELOG: Yes. I come from a family of historians--even my

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*Vladimir Prelog, "Eine Titriervorrichtung," Chemiker Zeitung, 45 (1921): 736.

grandfather was a historian. I have a brother who is an historian, and my son is an historian. My son is now at the University of Marburg.

KOEPPEL: How did you become a chemist? Was your mother scientific in any way? Did she have a science education?

PRELOG: No, but I was always very much interested in science and I think perhaps I became a chemist as a kind of protest against my father.

KOEPPEL: Yes, that could very well be; it happens very often. So, you then moved to Prague to study chemical engineering.

PRELOG: Yes. At that time, you know, chemical engineering was very different from what it is understood to be today. It was really chemical technology. There was an institute of chemical technology in Prague. It was called a technical high school (technische Hochschule) as were many similar schools in Germany, but it had university status. It was not a high school in the American sense.

KOEPPEL: No.

PRELOG: Technische Hochschule is translated as institute of technology. For example, the Eidgenössische Technische Hochschule is the Swiss Federal Institute of Technology. It's somewhat like MIT. The school that I attended was called the School of Chemical Engineering. It was not engineering as it is taught today, which places very strong emphasis on apparatus and technical processes. It was partly pure science and partly descriptive technology. It was for a long time the same here in Zürich. It was not chemical engineering.

KOEPPEL: Yes, I was a student at the ETH and I remember that. So, you started to study chemistry in Prague. You described this in one of your recent publications--or actually I think it was a lecture, "Thoughts After 118 Semesters of Chemistry."*

PRELOG: Yes. I don't think, however, that American schools use the semester.

KOEPPEL: Yes, they do. In a way, though, you're right; many universities go on trimesters. The conventional way, however, is still the semester.

PRELOG: It is fifty-nine years now since I started at the Institute of Technology in Prague.

KOEPPEL: What you want to say is that you were always a

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*Vladimir Prelog, "Gedanken nach 118 Semestern Chemiestudium," Chemie und Gesellschaft, G. Boche ed., (Stuttgart: Wissenschaftliche Verlagsgesellschaft, 1984).

student as well as a teacher.

PRELOG: Yes, I have always been a student. I was also a teacher, but I feel more like a student.

KOEPPEL: That's the best philosophy. You mentioned in this lecture that you were not too happy with your first year of chemistry because your work lacked philosophical depth.

PRELOG: Yes. I thought that that first year would be very exciting and very deep, but the daily work was rather dull. I really knew all about these things. I found it dull, for example, to determine the amount of iron in a mixture of iron and cobalt in qualitative or quantitative analysis. It was something which I didn't think I would have to learn at a university.

I found a young mentor who helped me, or rather who showed me how to do science. This happened in organic chemistry, which I considered initially to be very empirical. At the time, I liked to generalize. I thought that I should first learn very general things and then go into details. Later, I learned that it's better to start with specific things and then to develop something more general. That's what I learned from Rudolf Lukes, at that time, a graduate assistant and not much older than myself, but much more advanced in his knowledge of organic chemistry. His advice strongly influenced my development as a chemist. He taught me how wonderful organic chemistry really is. He showed me how well organized it is and how easy it is to start scientific work in organic chemistry. It is relatively simple to go from the known to the unknown. If you like to make generalizations in the beginning it is, of course, extremely difficult. To do that successfully you must be knowledgeable and talented.

KOEPPEL: So, you took the conventional courses. I assume that you started with general chemistry and, what else did you take, physics?

PRELOG: We had quite a lot of technology. I did it successfully, but very superficially. I was interested only in organic chemistry once I became acquainted with it. I did all of the other things very routinely.

KOEPPEL: Reluctantly?

PRELOG: I couldn't do it reluctantly because I had very little money. So, I had to do it very quickly.

KOEPPEL: I see.

PRELOG: I finished my studies in the shortest legally possible time.

KOEPPEL: Which was how many semesters?

PRELOG: Eight semesters. In that time I had practically finished my doctoral thesis. According to the law at that time, I could not take my doctoral examination until two semesters after I had received my diploma. Therefore, I had to wait a year. I was already employed when I took my doctoral examination. I more or less finished my studies in nine semesters. I had to get the engineer's diploma first and then earn the doctorate.

KOEPPEL: What was the topic of your dissertation?

PRELOG: It was about the constitution of a natural product which was called rhamnoconvolvulinoic acid.* It was an aglycone of a glycoside. My sponsor was Emil Votocek, a well-known sugar chemist. He was a pupil of the famous German sugar chemist Bernhard Tollens.

KOEPPEL: Oh, yes, I see! The Tollens test!

PRELOG: But I didn't like sugar chemistry.

KOEPPEL: Why not?

PRELOG: At that time, in some way, sugar chemistry reached a stage where it didn't develop significantly. Only routine work was being done. So, I asked for a natural compound, but not a sugar. I more or less investigated a by-product, a hydrolytic product, an aglycone, of a glycoside. I had the structure in a short time. It was a small, but good, piece of work.

KOEPPEL: Well, it seems to have brought you into one of your main fields, natural products.

PRELOG: I became an addict of natural products and I have stayed one all of my life. Other things that I have done well have had a connection with natural products. Natural product chemistry has always been the starting point.

KOEPPEL: Did your work with natural products also get you into sterochemistry?

PRELOG: Yes, because if you deal with natural products you learn that you need stereochemistry. It is not a special science. It is a way of looking at things. So, if you work on natural products, you always find that they present stereo-

chemical problems. To understand what happens, to understand the reaction mechanisms, you have to consider the stereochemistry. All of my stereochemical problems were more or less the result of my work on natural products.

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*E. Votocek and V. Prelog, "Sur l'acide 3,12-dioxylpalmitique composant de l'acide rhamnoconvolvulique," Collection Czecho-slovak Chemical Communications, 1 (1929): 55.

KOEPPEL: I want to ask you many more questions about stereochemistry, but I will first ask you what you did next. You went into industry...

PRELOG: Yes, in 1929. I mentioned that in my talk here.* 1929 was a time of great economic crisis in the United States as well as in Europe. There were very many unemployed people in Czechoslovakia. I was a foreigner there and, consequently, there was no place for me at any institution at which I could do the kind of chemical research that I wanted to do.

I was very happy when a place was offered to me by a friend of my mentor, Lukes. Although a chemist, the friend was really a merchant. He had two shops with chemicals and chemical apparatus. Very often, he needed some compounds that were not available commercially. He wanted me to organize a small laboratory in which we could make those compounds--something like the beginning of the Aldrich or Fluka company on a very small, very modest scale. Well, we did that. He bought a small house that we rebuilt into a laboratory. We brought some apparatus there from his shops and started to prepare rare chemicals. One of our customers was a military research laboratory. I prepared a number of toxic compounds for them. We prepared many other compounds not commercially available, but of interest to somebody. We prepared, for example, great quantities of ammonium sulfite, which was used for permanent waves, and was not commercially available at that time, or at the least, was very expensive. We also prepared large quantities of chloroacetophenone for the police. That too was not commercially available at that time.

KOEPPEL: For the police! What was that used for?

PRELOG: It was used as a lachrimator. There were many other such things. We also had a small analytical laboratory, and in the evening I did some research. I was stimulated by my boss who wanted a doctor's degree, and who therefore worked in the evening as well as during the day.

KOEPPEL: You're talking about the friend of Lukes?

PRELOG: Yes, his name was Gothard Dríza. He had only an engineer's degree and was my first doctoral student. It was an unusual situation, to be an employee and the employer's mentor. But, he was a very nice person, so it worked very well. He was only about ten years older than I was, and passed his doctoral examination summa cum laude.

KOEPPEL: That was quite successful.

PRELOG: Yes. I was successful with my first doctoral student.

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*See Prelog, "Gedenken nach 118 Semestern..." (cited on p.4 above), p. 8

KOEPPEL: Were you careful with your toxic chemicals? So many great chemists were poisoned at an early age because they did not have sufficient ventilation in their laboratories.

PRELOG: When I think now of what we did then, I realize that the working conditions were terrible.

KOEPPEL: You didn't realize it at the time, but you seem to have survived it.

PRELOG: More or less. We worked under criminal conditions!

KOEPPEL: No fume hoods?

PRELOG: Oh, yes.

KOEPPEL: You did have fume hoods? You did get good ventilation?

PRELOG: Yes, but what we prepared were often strong carcinogens, such as nitroso urea. We didn't even use gloves. I remember that I prepared it myself. We filtered it on a big Buchner funnel. With bare hands, we prepared liters of ethereal diazomethane solutions that somebody wanted. We prepared all kinds of arsenicals and things like that. We prepared derivatives of tellurium, selenium...

KOEPPEL: It sounds dreadful.

PRELOG: It sounds dreadful, and yet I am now over seventy-seven years old. Carcinogenesis is a very special problem. I wouldn't recommend that anybody do what we did. I am now very, very careful that my coworkers don't do such things. At that time, however, we didn't know better. That was the time when the first carcinogens were really discovered. Before that time, carcinogenicity didn't exist in the terminology of chemistry. The first carcinogens were compounds like benzopyrene and similar compounds from coal tar that were discovered in England. Still, we didn't know anything about the carcinogenicity of other chemicals.

KOEPPEL: You did publish several papers during your industrial period.

PRELOG: Well, not so many, but I wanted to do some work besides the daily work that I had to do. Also, I wanted to do something socially relevant; I wanted to eradicate malaria. So, I picked the synthesis of cinchona alkaloids, like quinine and similar compounds, as a subject of inquiry.*

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*Vladimir Prelog, Rativoj Seiwerth, Viktor Hahn, and Eugen Cerkovnikov, "Synthetische Versuche in der Reihe der Chinaalkaloide I," Berichte der Deutschen Chemischen Gesellschaft, 72B (1939): 1325-33.

At that time the constitution of quinine was known, but not its configuration. There was no synthesis of quinine itself, only of dihydroquinine. The starting material was not easily available, so it was necessary to find a cheap new method, which could be used on a large scale, to produce the nonaromatic half of the quinine or the other corresponding alkaloids. We spent several years on that problem. We didn't solve it completely. I continued to work on that problem after I left Prague, and even in Zürich.*

I left Prague because I found that I wanted badly to have an academic position and because the University of Zagreb, in Yugoslavia, offered me one. I was appointed a university docent. That position combined the duties of a full professor with the salary of a poorly paid assistant. I didn't know that at the time. I accepted the position and moved to Zagreb.

In addition to being a teacher, I spent five years continuing the work that I had started in Prague. With the assistance of a few young people, and with the financial help of a small pharmaceutical factory, I was able to organize a modest laboratory. We did quite well until Yugoslavia was occupied by the German army in 1941. I found that I would get into trouble unless I emigrated.

I could emigrate relatively simply because I had an invitation from Professor Richard Kuhn, who was president of the German Chemical Society, to visit Germany to give talks about my work. With this invitation in hand I visited the general of the German occupation army that controlled Zagreb. He gave orders to the Independent State of Croatia to issue passports for me and my wife. My predecessor here, Professor Ruzicka, who was also my former countryman, then invited me to visit him in Switzerland. With his invitation I got a Swiss visa and so I came legally to Switzerland without any heroic attempts to climb mountains or to be refused at frontiers.

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*Vladimir Prelog, Paul Stern, Rativoj Seiwerth, and Suzana Heimbach-Juhasz, "Über die Synthese eines 'vinylfreien Chinaalkaloides' und seine Wirkung auf die Vogelmalaria," Naturwissenschaften, 28 (1940): 750; Prelog, Seiwerth, Heimbach-Juhasz, and Stern, "Synthetische Versuche in der Reihe der China-Alkaloide. II Mitteilung. Über die Synthese der 6'-methoxy-rubanole-(9)," Berichte der Deutschen Chemischen Gesellschaft, 74A (1941): 647-52; Prelog and Alfred Komzak, "Synthetische Versuche in der Reihe der China-Alkaloide. III Mitteilung. Über eine neue Synthese von -Kollidin," ibid., 74B (1941): 1705-6; Prelog and M. Prostenik, "Synthetische Versuche in der Reihe der China-Alkaloide. 4 Mitteilung. Über Homomerochinen und über die partielle Synthese des Chinotoxins," Helvetica Chimica Acta, 26 (1943): 1965-71;and Prelog und E. Zalan, "Synthetische Versuche in der Reihe der China-Alkaloide. 5 Mitteilung. Über die Konfiguration der asymmetrischen Kohlenstoffatome 3, 4, und 8 der China-Alkaloide," ibid., 27 (1944): 535-45.

I came here, I would say, at the right time. Professor Ruzicka had a number of older coworkers or assistants who had immigrated previously to Switzerland, but who no longer felt safe in Switzerland. They therefore emigrated, mostly to the United States, just a few weeks, or even one week, before I arrived.

KOEPPEL: I see. There were a lot of vacancies here.

PRELOG: There were a lot of vacancies for an experienced chemist. I started here as a student and then became a privatdocent. I went through all of the stages of the academic hierarchy. I was a titular professor, which means that I had a title but no salary. I then became an associate professor, a full professor, and, finally, succeded Ruzicka as chairman of the Organic Chemistry Laboratory. I retired in l976 and I am now a student again.

KOEPPEL: Well, you moved up very swiftly. You had stayed in Switzerland once before?

PRELOG: Yes, for four months as a kind of postdoctoral student. I had never before been in a big laboratory. In l937, after I had accumulated some money from my work with the small industry in Zagreb, I spent four months here in the laboratory of Professor Ruzicka. Ruzicka knew therefore that I might be a good coworker. This more or less facilitated my emigration to Switzerland.

KOEPPEL: That proved to be very advantageous. When you came to the Swiss Federal Institute of Technology, what did you find? I know it was very peaceful in Switzerland during the war and everybody who came in from war-torn countries noticed it. How was the working climate?

PRELOG: Oh, it was very good, you know. There were mostly Swiss here. We hardly had any foreigners. At that time the Swiss had to perform their military service on the frontiers. Because of that, they were very eager to work hard. They spent a part of their time doing military service and then came back to work on their Ph.D. theses. I think that the atmosphere was very good. We were cut off from the world's chemical literature, however. We seldom received the Journal of the American Chemical Society. Sometimes, even the mail deliveries from Germany didn't function very well. The journals were very often lost. We could concentrate, however, and work on problems that didn't require much new literature. On the whole, it was pleasant. Of course, we were never sure that the Germans would not occupy Switzerland. The situation was very hot. Yet, in comparison with being already occupied, it was not so bad.

KOEPPEL: You were not afraid that they would invade Switzerland?

PRELOG: I was not afraid that they would invade, no.

KOEPPEL: I know that there was a time when they debated whether they should go through Switzerland or through Holland.

PRELOG: Hitler was a madman. You could never be sure that he wouldn't make completely irrational decisions.

KOEPPEL: Yes. That was true. You had your own journal here then, the Helvetica Chimica Acta. Did they start publishing after you arrived or was that already in existence?

PRELOG: Helvetica Chimica Acta started in 1919 after the First World War ended. We therefore had our own journal. We could publish quickly.

KOEPPEL: You published mostly here?

PRELOG: During that time, yes. I had published before in Czech journals and even in German journals, in Berichte der Deutschen Chemischen Gesellschaft, and in Liebig's Annalen. It was much nicer, however, to publish in Helvetica. Practically everything I did at that time and even later was published there. Only occasionally did I publish in foreign journals. We published most of our experimental work in Helvetica Chimica Acta. That was the tradition. Helvetica Chimica Acta became a respectable journal because a number of very good chemists like Karrer, Ruzicka, Reichstein, and many others, published all of their important work there. It became especially well-known for the work on natural products.

KOEPPEL: Were you on the editorial board?

PRELOG: No, I was never on the editorial board, although I was for some time a member of the committee of the Swiss Chemical Society, and I was also president of the society for two years. Yet, I was never on the editorial board. I wouldn't have done well in that capacity because I am not a great linguist. I think it was wise not to appoint me to the editorial board. By the way, at that time the Helvetica Chimica Acta was edited by the chief editor himself. The editorial board had a very small function, to support the chief editor only when he was in doubt about his decisions.

KOEPPEL: I see. Who was the chief editor?

PRELOG: At first, the chief editor for many years was Professor Fritz Fichter in Basel. He was succeeded by Professor Emil Cherbuliez, a professor of organic chemistry in Geneva. Both of the editors were very competent and so the journal became famous. We could publish very quickly because our papers were refereed only in case of doubt. Because everybody knew everybody, everyone could publish rapidly and in spite of that, the journal had a certain standard.

KOEPPEL: The Swiss Chemical Society played a large role. Were most Swiss chemists members of it or was the Society's membership restricted in any way?

PRELOG: Everybody who was working in research, either in academe or in industry, was a member of the Swiss Chemical Society. It was not a professional society; it was purely a scientific society. It has remained a scientific society until this day and it still is not a professional society. It doesn't care about salaries, status of chemists, and their employment.

KOEPPEL: It's not like the American Chemical Society.

PRELOG: Neither like the German Chemical Society, nor the English Chemical Society, which now is called the Royal Chemical Society.

KOEPPEL: I see. You started to work in Zürich with natural products under the influence, I guess, of Professor Leopold Ruzicka. Did you work with him?

PRELOG: When I came here we, of course, discussed what I should do. There was an area here that had been left abandoned by those chemists who had emigrated from Switzerland. I must tell you that some of those chemists became very famous later in the United States.

KOEPPEL: Can you name them?

PRELOG: Yes, of course. One of them was a Polish-born chemist, Dr. Leo Sternbach, who, as you know, discovered Librium and Valium, which in many ways changed medicinal chemistry. When he left he was already employed by Hoffman-LaRoche and joined the branch in Nutley, New Jersey, where he made his discovery. The second was Dr. Rosenkranz who later became president of Syntex in Mexico and who made Syntex a company known worldwide. They were responsible for the development of the pill to a great extent.

KOEPPEL: I never realized that the pill came from Mexico.

PRELOG: In Mexico they had plants containing steroids that were starting materials for the pill. So, it was just the right place to develop the pill. Sternbach and Rosenkranz were not the only people involved in the development of medicinal chemistry, but they were, in the end, among the most important.

KOEPPEL: What was the commercial name of the product?

PRELOG: I don't know. They changed the names all the time because the pill didn't develop all at once.

At that time Ruzicka bought organ extracts from the United States in large quantities. He hoped that it would be

possible with modern methods to isolate some new hormones or some new compounds with high biological activity. He said, "You can do work on natural compounds or any other work you want. You will get for that a couple of coworkers but perhaps you yourself should work on organ extracts and your coworkers should work, for example, on alkaloid chemistry."

From the start I was very interested in the exciting structures of alkaloids. At that time they were very unusual. Today this is no longer so. All of these structures seem very common to us now, but at that time they looked very bizarre. So I worked on organ extracts and at the same time my coworkers worked on alkaloids. I had two coworkers who were more or less assigned to me by Ruzicka.

KOEPPEL: You then published some papers on...

PRELOG: With Ruzicka, on organ extracts.* I was really disappointed about this work. Although we worked hard, we didn't find anything really spectacular.

KOEPPEL: And you got only small amounts, I suppose.

PRELOG: The only new thing we discovered were steroids with a musk odor from the testes of boars. I had forgotten that I isolated them with my own hands, when these compounds became famous. They are sex attractants for swine and are used in animal husbandry. It was also interesting to learn that truffles, which grow under the soil, are detected by swine because they contain one of these steroids with a musk-like odor. The swine are really searching for their sex attractant. It is claimed that it also attracts females and is sold as a perfume.

KOEPPEL: There was a big to-do about musk oil a few years ago.

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*Vladimir Prelog, Leopold Ruzicka, and Paul Stern, "Untersuchungen über Organextrakte. 4 Mitteilung. Zur Kenntnis der unverseifbaren Lipoide aus Schweinemilz," Helvetica Chimica Acta, 26 (1943): 2222-42; V. Prelog and L. Ruzicka, "Untersuchungen über Organextrakte. 5 Mitteilung. Über zwei moschusartig riechende Steroide aus Schweinetestes-Extrakten," ibid., 27 (1944): 61-66; V. Prelog, L. Ruzicka, and P. Wieland, "Steroide und Sexualhormone. 90 Mitteilung. Über die Herstellung der beiden moschusartig riechenden ^{16} - Androstenole-(3) und verwandter Verbindungen," ibid., 27 (1944): 66-71; V. Prelog, L. Ruzicka, and F. Steinmann, "Untersuchungen über Organextrakte. 6 Mitteilung. Über die Isolierung von Chymil-alkohol (d - - Hexadecyl- glycerylather) aus Testes-Extrakten und seine Identitat mit 'Testriol'," ibid., 27 (1944): 674-77; and V. Prelog, L. Ruzicka, F. Meister, and P. Wieland, "Steroide und Sexualhormone. Untersuchungen über den Zusammenhang zwischen Konstitution und Geruch bei Steroiden," ibid., 28 (1945): 618-27.

PRELOG: Anyway, that was a very small discovery. I mention it only because at that time we didn't have the slightest idea about its special qualities.

KOEPPEL: I have to tell you that I worked in the labs near one of your students who worked with musk day in and day out, and I couldn't stand the smell.

PRELOG: Musk must be extremely diluted, otherwise, it is rather irritating.

KOEPPEL: Yes, I know that. So, you stayed with natural products?

PRELOG: Yes, then we started to work on alkaloids. We continued some work on the configuration of cinchona alkaloids and started to work on strychnine. We showed that Robinson's formula is wrong, but we didn't propose a correct formula.* Professor Woodward then also came into the picture. Finally, the formula of strychnine was proven completely.** At that time that was a relatively great achievement. It was not so easy to determine the structure of such polycyclic alkaloids by chemical methods.

KOEPPEL: I understand.

PRELOG: We really worked on strychnine because we didn't have any other alkaloids at our disposition. We found a five-kilo bottle of strychnine in our storeroom. Somebody bought it, I don't know for what purpose.

KOEPPEL: As a rat poison?

PRELOG: Perhaps, I don't know. I then read about one hundred and forty papers by Hermann Leuchs, about fifty papers by Sir Robert Robinson, and thirty papers by Heinrich Wieland. We didn't have much literature to read during the war, so it was possible to
spend quite a lot of time in the library reading old papers. We were very lucky. In our first experiments we found something wrong with Robinson's formula. (It had been thought to be correct for several years.) That discovery made us well-known because Robinson was considered at that time to be the best chemist in the world. So, being able to find something wrong with his formula was very important.

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*Vladimir Prelog and S. Szpilfogel, "Die Konstitution des Strychnins," Experientia, 1 (1945): 197-98.

**Robert Robinson, "The Constitution of Strychnine," Experientia, 2 (1946): 28-29. Also, R.B. Woodward, W.J. Brehm, and A.L. Nelson, "The Structure of Strychnine," Journal of the American Chemical Society, 69 (1947): 2250.

KOEPPEL: What was wrong with his formula?

PRELOG: Oh, the size of the rings was not so easily determined. He put a five-membered ring in place of a six-membered ring. Our first discovery was that this ring can't be a five-membered ring.

KOEPPEL: Well, you already had a lot of experience with polycyclic compounds. Did you synthesize adamantane?

PRELOG: Yes. That was more or less a secondary research activity, but we had in fact been the first to synthesize adamantane. By doing so we also proved its structure. The structure of adamantane had been known, but it had been more or less a matter of intuition, supported by a Debye-Scherrer X-ray diagram that didn't really prove the structure. It showed only that the proposed formula was compatible with the X-ray diagram.

KOEPPEL: Was your formulation two-dimensional, or did you propose a three-dimensional structure?

PRELOG: Not I, but Lukes was really the one who first proposed the right formula, more or less intuitively, because the crystals of adamantane are tetrahedral. He proposed it because a hydrocarbon, $C_{10}H_{16}$, with a melting point of about 280°C, was quite unusual. This is possible only because the molecule is almost perfectly spherical, and therefore, fits the lattice of the crystal very well. The other point was the tetrahedral crystal structure. From those two bits of knowledge and by using intuition, he proposed the structure. The powder diagrams didn't specify the position of the individual atoms in this case. Therefore, our synthesis represented a synthetic structure proof. We wrote only two papers about adamantane, but they made quite an impression.*

KOEPPEL: You did that before you came to Zürich.

PRELOG: Yes, that happened in Zagreb.

KOEPPEL: Could you tell me a little bit about Woodward. You published several papers with him.**

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*Vladimir Prelog and Rativoj Seiwerth, "Über die Synthese des Adamantans," Berichte der Deutschen Chemischen Gesellschaft, 74B (1941): 1644-48; and Prelog and Seiwerth, "Über eine neue, ergiebigere Darstellung des Adamantans," ibid., 74B (1941): 1769-72.

**D.H.R. Barton, O. Jeger, V. Prelog, and R.B. Woodward, "The Constitution of Cevine and Some Related Alkaloids," Experientia 10 (1954): 81-90; F. Gautschi, Jeger, Prelog, and Woodward, "Über die Konstitution der Decevinsaure," Helvetica Chimica Acta, 37 (1954): 2280-2294; Jeger, Mirza, Prelog,

PRELOG: Woodward first came here in 1948. His trip was sponsored by the Swiss-American Foundation that was founded by American branches of Swiss firms. In the beginning, after the war, there was little contact between Swiss and American chemists. To promote these contacts, the Foundation sent American chemists to Switzerland every year. One of the first was Professor Woodward. At that time he was not fully accepted by the American chemical establishment.

KOEPPEL: Do you know why?

PRELOG: Yes, but I don't want to talk about that! Woodward was very young.

KOEPPEL: How old was he?

PRELOG: At that time he was about thirty-one years old. He had had some conflicts with American chemists, especially the older ones, because he was very self-confident. He realized that he knew much more chemistry than these people and he irritated them. Some of them, of course, recognized him, but the others just thought that he was not a pleasant fellow. Ruzicka, my predecessor, who was already at that time a Nobel Prize winner, accepted him fully because he recognized that Woodward was a great man. So, I too accepted him immediately and we became very good friends during his first stay here in Switzerland. This friendship lasted until his premature death a few years ago.

KOEPPEL: Was he here one year, or...

PRELOG: No, no, no, he was here only for a few days.

KOEPPEL: Oh, I see.

PRELOG: He was already at Harvard, but he was, I think, only an associate professor. He was soon promoted. We really thought that he would be a very good addition to our staff.

KOEPPEL: Did you offer him a position?

PRELOG: Well, he considered it very seriously, but then he became so famous...

Ch. Vogel, and Woodward, "Die Konstitution der Hexan-tetracarbonsaure aus Cevin und Germin," ibid., 37 (1954): 2295-2301; Jeger, Prelog, E. Sundt, and Woodward, "Die Konstitution des Ringes F und die absolute Konfiguration des Kohlenstoffatoms 25 des Cevins," ibid., 37 (1954): 2302-2306. Gautschi, Jeger, Prelog, and Woodward, "Absolute Konfiguration des Kohlenstoff- atoms 10 in Cevin und verwandten Alkaloiden," ibid., 38 (1955): 296-303; and F. Mathys, Prelog, and Woodward, "4,5,- Dihydro-2,3, 6,7-dibenzoxepindion-(4,5)," ibid., 39 (1956): 1095-1099.

KOEPPEL: What about the Woodward Institute?

PRELOG: Well, when he became so famous we were not able to offer him a position. He didn't have any teaching duties at Harvard, at least no teaching duties he didn't want. If he didn't want to teach, he didn't have to. Here it would be impossible to have a professor who didn't teach. Yet, we always wanted to bind him more closely to Switzerland. Finally, I persuaded the CIBA Company to organize an institute in Basel in which he could do whatever he wanted. If he produced something of practical value it could be used by CIBA and if he didn't it would still be good chemistry. The Woodward Institute, organized in Basel by the CIBA Company, consisted of a laboratory with about six coworkers. There was a kind of lieutenant who directed the research during Woodward's absence.

KOEPPEL: Who was that?

PRELOG: Oh, there were several of them. There was Dr. Karl Heussler. He was replaced by Dr. Ivan Ernst who was later replaced by Dr. Jacques Gosteli. The three CIBA chemists were assigned to the position temporarily; they were, so to say on "loan" from CIBA.

KOEPPEL: What was the relationship between the Woodward Institute and the ETH?

PRELOG: None whatsoever.

KOEPPEL: How about the vitamin B_{12} synthesis with Eschenmoser?

PRELOG: Nothing was done on vitamin B_{12} at the Woodward Institute in Basel. Work on B_{12} was initiated at Harvard. Soon afterward, Professor Eschenmoser of the ETH decided to work on B_{12} . He knew that Woodward was working on that topic but he was not afraid to proceed on his own. Initially, Woodward and Eschenmoser worked independently. Slowly, however, they realized that the task was so difficult and so time-consuming that they decided it would be best if each of the groups worked on a certain part of the project. Finally, they decided to unite their efforts. They exchanged experience, results, and even compounds. They cooperated very closely. Each contributed his own share and finally it was crowned with success. German chemists considered that achievement the Mount Everest of synthesis.

KOEPPEL: Yes, a wonderful piece of work.

PRELOG: It didn't have anything to do with the Woodward Institute in Basel. The Woodward Institute never touched anything in connection with vitamin B_{12} . It was done either in Zürich by Eschenmoser or in Harvard by Woodward. It was a problem that didn't have any practical aim because vitamin B_{12} can be obtained so cheaply from microbial cultures. Considering all of the

difficulties to produce it synthetically it will never be--well you should never say never--but at least I can't think now that synthesis will be a viable source of vitamin B_{12} .

KOEPPEL: Well, I really would like to ask you now about stereochemistry. You received the Nobel Prize in 1975 for your contribution to the stereochemistry of organic molecules and for reactions involving stereospecific pathways. I would like to know how you became so involved in stereochemistry.

PRELOG: Through work on alkaloids. Many alkaloids, as most other natural compounds, have a number of asymmetric carbon atoms. This is the reason why a number of stereoisomers are possible. It was necessary, first, to specify the stereoisomers of interest. If, for example, you have sixty-four stereoisomers and only one is a natural compound that is biologically active, you have to be able first to assign to this molecule a model or a stereoformula. Secondly, you have to have a certain language, symbols, descriptors, to speak about it. Finally, you need to be able to prepare this specific stereoisomer. These problems were not solved at that time, or were only poorly solved.

While doing our work we needed symbols to talk about our results. Slowly, therefore, our interest in stereochemistry became stronger and stronger. It started with our attempt to determine the configuration of cinchona alkaloids. The constitution of quinine was known, but it has four asymmetric carbon atoms, and therefore there are sixteen stereoisomers. Quinine, which has antimalarial activity, is one of the sixteen. You have to have descriptors that enable you to distinguish quinine from its stereoisomers. That was one problem.

Furthermore, you need to have a method that enables you to determine the three-dimensional structure. At that time, X-ray analysis was not well developed. It was used successfully in only very few cases. It was also very tedious. So, we used chemical methods in order to be able to determine the spatial distribution of the atoms. These methods evolved slowly, part by part. So, if you read the Nobel Prize lecture* you see that our achievements were not unique. We were not the only people, of course, to do this kind of research. There were many others. Perhaps, however, we had a bigger impact. It was a matter of luck.

KOEPPEL: You have a very interesting story about how you got together with Cahn and Ingold in Manchester. Would you care to tell it?

PRELOG: Well, as you know, it involved precisely this matter about which I've spoken, descriptors. For specification of spatial distribution of atoms, Emil Fischer, one of the

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* Vladimir Prelog, "Chirality in Chemistry," Les Prix Nobel en 1975, (Stockholm: P.A. Norstedt & Soner, 1976) pp. 137-150

greatest chemists of all times, had developed descriptors to specify carbohydrates. But these were insufficient when applied to alkaloids. Using them led very soon into great difficulties. Cahn, who was editor of the English Chemical Society's Journal at that time, decided to clarify the matter. He had noticed that the stereochemical symbols were inconsistent and controversial. He therefore had asked Ingold for advice. In 1951 Ingold suggested a tentative solution.* It did not prove to be a totally satisfactory one. A meeting of the Chemical Society was convened in Manchester [31 March-2 April, 1954].

KOEPPEL: Did Cahn and Ingold suggest at that time to use the sequence rules?

PRELOG: Yes, they suggested the so-called sequence rules.

KOEPPEL: Which are still applied.

PRELOG: Yes, but not in the same way as they suggested. During the anniversary meeting in Manchester, the Society held a symposium
on dynamic stereochemistry.** After the symposium, the ICI organized a ball at the Octagon House in Blackley near Manchester. Everybody danced except for Ingold, Cahn, and myself. Not being proficient dancers, we drank beer and discussed chemistry.

Cahn and Ingold asked me what I thought about their proposal and I said, "It's terrible. It will make a bigger mess than we have now." Instead of telling me to go to hell, they were kind enough to ask me to write a joint paper about the issue. I immediately accepted. We met several times in London and in Switzerland before we established our principles. After we were more or less satisfied with our principles, we worked on the details. In 1956, we published our first paper, in Experientia.*** There, we laid down the basic principles of what is now called the CIP system. The system was then accepted by Professor Friedrich Richter for use in Beilstein's Handbuch der Organischen Chemie. Our system was used to specify about one hundred and fifty thousand compounds in Beilstein. In general, our system worked well, even though small inconsistencies were discovered. For about ten years we continued

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*Robert S. Cahn and Christopher K. Ingold, "Specification of Configuration about Quadricovalent Asymmetric Atoms," Journal of the Chemical Society, 1951: 612-622.

**"Symposium on Dynamic Stereochemistry." A meeting held on 31 March 1954, with the Royal Institute of Chemistry, the Society of Chemical Industry, and the Institute of Petroleum.

***Robert S. Cahn, Christopher K. Ingold, and Vladimir Prelog, "The Specification of Asymmetric Configuration of Organic Chemistry," Experientia, 12 (1956): 81-94.

to improve it. In 1966 we published a second paper.* In that paper we considered all of the difficulties found by the editors of Beilstein. We called it the "Beilstein test."

KOEPPEL: I see. You used the actual examples to weed out the imperfections.

PRELOG: Yes, by that we improved the system. The basic principle remained, but the applications had to be made more exact. In 1982, I published a third paper with Professor Günter Helmchen.** When we wanted to apply the system to computers, we found that computers didn't always understand us. So, we had to improve it.

KOEPPEL: That's another test, isn't it? The "computer test."

PRELOG: That's another test, yes. Beilstein's editors, of course, had to test it again and they found small difficulties. Therefore, we will have to publish a fourth paper.

KOEPPEL: You will?

PRELOG: Yes. Chemical Abstracts also used the CIP system. I visited them recently. They now have registered in the Chemical Abstracts "on-line service" 6,600,000 compounds, of which 1,300,000 were specified by the CIP system.

KOEPPEL: Optically active compounds?

PRELOG: Optically active, and some optically inactive, stereoisomers.

KOEPPEL: Well, CIP stands, of course, for Cahn, Ingold, Prelog. We still call it the R&S system in more elementary education.

PRELOG: The CIP system doesn't only use the R and S descriptors, but also M and P and others.

KOEPPEL: Yes, I'm aware of that now. And u and l?

PRELOG: And all kinds of other descriptors. Of course, for students R and S are most important. For all practical purposes, it has to be a very general system that will not fail to meet our growing needs. We want to make it so perfect that it

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*Robert S. Cahn, Christopher K. Ingold, and Vladimir Prelog, "Specification of Molecular Chirality," Angewandte Chemie, International Edition, 5 (4), (1966): 385-415.

**V. Prelog and G. Helmchen, "Basic Principles of the CIP-System and Proposals for a Revision," Angewandte Chemie, International Edition, 21 (1982): 567-583.

can be used on every so-called stereogenic unit--the part of the molecule which generates stereoisomers. That, of course, is not an easy thing to do. Think about all of the possibilities you can have.

KOEPPEL: Yes, like helices?

PRELOG: All kinds of conformations, including helices.

KOEPPEL: You also pioneered the inclusion of conformations into the stereochemical system.

PRELOG: Yes, we did. We can specify conformations. Initially, many concepts that were coined and used in stereochemistry were not accurately defined. What is a configuration? What is a conformation? Which of the isomers are conformational? Which are configurational? Usages developed pragmatically, which means that there was a specific case, and a concept was developed for this very special case. Then it was used for other cases, rightly or wrongly. So, a certain order had to be developed. We tried to contribute something to that.

I think that Confucius said "If I become emperor of China, I would first define words correctly. If words aren't correctly defined then laws can't be written. If laws are not clear, then justice can't be done. If justice is not done, then people become restless. Finally, if people are restless, the empire is in danger." So, the first thing for the statesman to do is to give words their correct meaning.

KOEPPEL: Yes. Yes, indeed.

PRELOG: It is like this also in other sciences. I think that it is very important that we understand each other, including when we speak with nonspecialists. Most people who are very active don't care about language. They think that everybody will understand them anyway and that it is more important to make discoveries than to improve language. I do not agree with that attitude. We are the linguists of science.

KOEPPEL: Yes, well, you seem to be also mathematically oriented in your approach.

PRELOG: Not very much. I learned mathematics as an amateur.

KOEPPEL: You did?

PRELOG: I never had a good formal education in advanced mathematics.

KOEPPEL: I get the feeling from reading your papers that you approach the field in the way van't Hoff approached it. It was novel then, but he approached stereochemistry from a mathematical viewpoint.

PRELOG: I don't think that these older chemists knew much mathematics.

KOEPPEL: Not in the modern sense.

PRELOG: They used mathematics instinctively. I don't think, for example, that van't Hoff was a mathematician. But he did possess intuition. It was then possible to use elementary mathematics and elementary geometry in order to deal with chemical problems. I had to learn my mathematics as an autodidact. I discussed it sometimes with colleagues who are experts. Mostly, however, they were not interested in the problems of organic chemistry.

KOEPPEL: Certainly not in the geometrical aspects.

PRELOG: Geometrical problems in chemistry are too simple for them so that they are not interested in them. They are also not interested in chemical problems because these require a knowledge of chemistry that they don't possess.

KOEPPEL: Well, you have some very famous predecessors who were also dealing with stereochemistry at the Swiss Federal Institute of Technology. Was there any influence upon you from Wislicenus, or Victor Meyer?

PRELOG: You mention a very interesting matter. As you probably know, I have many famous predecessors. The first professor here was Georg Staedeler. True, he was not as famous as his successor, Johannes Wislicenus, one of the founders of stereochemistry. He was succeeded by Victor Meyer who coined the words stereochemistry, stereoisomer, enantiomer, and diastereomer. His successor was Arthur Hantzsch, who was not only one of the founders of the stereochemistry of nitrogen but also a founder of physical organic chemistry. His pupil, Alfred Werner, was a professor at the University of Zürich and founded the stereochemistry of octahedral complexes. Hantzsch's successor was Eugen Bamberger. Unfortunately, he had an accident through which he lost his memory. Accordingly, he had to retire at a very early age. His successor was Richard Willstatter, who won a Nobel Prize. Hermann Staudinger succeeded him. He too won a Nobel Prize. His successor was Richard Kuhn and Kuhn's was Ruzicka. I am the Institute's fifth Nobel Prize winner.

KOEPPEL: Kuhn won the Nobel Prize also?

PRELOG: Yes, including Ruzicka five successive directors of this laboratory had won Nobel Prizes. It is not so often that a single laboratory or a specific institution has directors who win five successive Nobel Prizes. I hope that this tradition will continue.

KOEPPEL: When did you learn about winning the Nobel Prize? How did the message get to you?

PRELOG: I got a phone call at about half past one in the afternoon from our radio station.

KOEPPEL: Oh, they heard it first?

PRELOG: I didn't have the slightest idea about it. The second call came from the president of our city, Dr. Sigmund Widmer. I don't know how he knew. Of course, many others followed. The telegram from Stockholm came much later. Well, you see, I was relatively old.

KOEPPEL: You had just retired?

PRELOG: It occurred one year before retirement.

KOEPPEL: One year before retirement. You were still active; you were teaching.

PRELOG: Yes, I was teaching courses.

KOEPPEL: How did your students react?

PRELOG: In Switzerland we don't make a great fuss about a Nobel Prize. I came to the Institute after lunch. I didn't hurry; I took a street car. They didn't expect me to arrive that way; they thought that I would at least take a taxicab. The lobby was full of students and colleagues who already had prepared some champagne and things like that.

KOEPPEL: Oh, I think that was quite nice.

PRELOG: We had a small celebration but it was nothing much. In Zürich, it is not so rare an occurrence.

KOEPPEL: The Swiss are a little spoiled in this respect.

PRELOG: Well, I think, it is very nice that they are not hero worshippers. We are a democratic country.

KOEPPEL: That's true.

PRELOG: In addition to the Nobel Prize winners at ETH whom I mentioned, Professors Karrer and Werner at the University of Zürich also won Nobel Prizes. All of them were treated as ordinary citizens. When you win the Nobel Prize you get into the newspapers and other media, but only for a very few days.

KOEPPEL: You get interviewed.

PRELOG: You get interviewed, but not so much. People don't make much fuss. It's very pleasant, I must say.

KOEPPEL: Well, in science maybe it's so...

PRELOG: It's much more popular to win the prize in literature.

KOEPPEL: Tell me about your teaching here at the Swiss Federal Institute of Technology. Did you teach organic chemistry like your predecessor?

PRELOG: Oh, yes. Even during Ruzicka's time, I taught elementary organic chemistry.

KOEPPEL: One, two, and three, or what?

PRELOG: One and two at that time. There were two organic chemistry courses.

KOEPPEL: And how many students on average did you have?

PRELOG: Oh, we had about one hundred students in the chemistry department. They were rather fewer in the natural sciences department. About one hundred twenty students or so usually attended the lectures. Doctoral candidates also came to hear the lectures a second time, especially during Ruzicka's time. For about sixteen years I taught the first and the second course in organic chemistry. Later, colleagues shared this difficult job with me. I had to give courses every morning from eight to nine, from Monday through Saturday. We also had some seminars in the afternoons. For several years, I had to examine practically everybody.

KOEPPEL: That's a heavy load. You had teaching assistants for your laboratory?

PRELOG: Laboratory work was almost completely in the hands of teaching assistants. So, I didn't worry very much about that. The program was well organized.

KOEPPEL: Tell me a little more about your present system. Is it still the same as it used to be?

PRELOG: No, we used to have a much simpler system. Professor Ruzicka and myself gave the same courses for pharmaceutical students, chemistry students, and natural science students as well. All of them were in one lecture. That's now all specialized. They now offer special courses for chemistry majors, biochemistry students, and pharmaceutical students.

KOEPPEL: I see.

PRELOG: There are about four organic chemistry courses taught during four semesters. It has changed substantially. I don't even know exactly what they do now.

KOEPPEL: Did you use a textbook or did you give a lecture that you prepared?

PRELOG: I tried to prepare my own lecture.

KOEPPEL: When did you become chairman of the laboratory?

PRELOG: On October l, 1957. Ruzicka was seventy when he retired. I mentioned in my historical lecture, by becoming chairman I reached my level of incompetence!

KOEPPEL: I doubt that, but go on.

PRELOG: I tried to step down.

KOEPPEL: Did you not like it?

PRELOG: Professor Ruzicka had been assisted by Dr. Bruno Engel who took care of administrative duties. Among other things, he ordered apparatus and chemicals. He organized everything. I was content to be chairman so long as I didn't have to deal with these matters. For some unknown reason, however, Engel committed suicide a few years after I became chairman and I was left with many of his duties. We couldn't replace him because he was very competent and any successor would have been judged by his standards.

I found that I had to do something about these, for me, unpleasant administrative duties. They were very time-consuming, especially for a conscientious person. This laboratory employed about two hundred people. That number includes staff, doctoral candidates, postdoctoral students, technicians, and so on. When you have to be boss of two hundred people, you run into statistics. Among two hundred people, statistically you will have your thieves and you will have fires. You will have to meet police and you have to meet firemen. There are also many other things like health rules. During my time, being chairman became more and more tedious. People didn't care to hear about this increasing complexity, yet they didn't stop saying that the chairman is responsible for everything.

KOEPPEL: Yes.

PRELOG: So, I disliked being chairman very much. Fortunately, we organized a kind of rotating chairmanship. I had managed to get the number of full professors increased from three to eight. When we increased our staff to eight full professors, we decided that each should be chairman for one year.

KOEPPEL: Oh, I see.

PRELOG: However, we made all of the big decisions together. We would talk to each other if we didn't agree. This was sometimes not so easy. Futhermore, I was to be excluded from this chairmanship because of my previous great meritorious service! So, I was not chairman for a number of years before I retired.

KOEPPEL: You were chairman one more time or not?

PRELOG: No, no, not after 1965.

KOEPPEL: And when did you retire?

PRELOG: I retired in 1976. For eleven years I was more or less the primus inter pares. They called me their "Dorf-altester", which means the oldest man in the village.

KOEPPEL: That's what I read in a news clipping after you won the Roger Adams Award in the United States from the American Chemical Society.

PRELOG: The rotating chairmanship has worked well so far. We had very able people who got offers from all kinds of foreign universities. Eschenmoser and Arigoni got offers from Harvard. Jack Dunitz got offers from Yale and Cornell, Heilbronner, from Basel.

KOEPPEL: They didn't accept those offers?

PRELOG: Well, they were all associate professors at that time. So, first, I managed to get them promoted to the rank of full professor. If they would have always had to work under one chairman, they would perhaps have accepted a position where they would have been more independent. Having a collegial chairmanship meant that all of the full professors were equal. Everybody is a formal chairman for a year. None of them need feel as if he were in a dependent position.

KOEPPEL: That's very important?

PRELOG: That's very important because some of them like to be independent. I think that some of them would be tempted by an offer to become chairman and to organize things as they like. Some would perhaps feel better if they were independent and would leave Zürich. By organizing the collegial chairmanship, however, I managed to keep them all together. We lost only Professor Heilbronner who moved to Basel to become professor of physical chemistry. All of the others stayed.

KOEPPEL: Very good strategy. It seemed just the opposite under Professor Ruzicka.

PRELOG: The custom here, at our school, was that there was one chair and one full professor. I was, as far as I know, the first so-called personal full professor. Ruzicka was the chairman and I was "his" full professor. Then, I became his successor. At first, there were two associate professors. We then added a few more associate professors. They then got tempting offers. Finally, we ended up with eight full professors.

KOEPPEL: Are you well funded? How is research funded? Does it come partly from industry or the government?

PRELOG: We always got quite a reasonable amount of money from the school for teaching and research. Additionally, we were supported strongly by industry. Ruzicka was very successful in gaining support from industry because his work was interesting for it. I continued that tradition.

KOEPPEL: That was CIBA-Geigy or...?

PRELOG: That was CIBA at that time. After the merger it became CIBA-Geigy.

KOEPPEL: Were there others?

PRELOG: No, we got little from the others. It was very difficult to work with several firms.

KOEPPEL: I see.

PRELOG: I was already on the board of CIBA and later when they merged with Geigy, on the board of CIBA-Geigy. In the United States they would call it the board of directors, and we call it "Verwaltungsrat."

KOEPPEL: Yes, but did that not constitute a conflict of interest in any way?

PRELOG: No, we tried to behave in such a way that it was not a conflict. Not everybody liked it though.

KOEPPEL: They did not dictate your research?

PRELOG: No. Our principle was always that we shouldn't work on problems that are more or less given to us by industry. They didn't ask us to work on a project of immediate interest to them. We always worked on what we wanted to do. We thought that if something practical came out of our work then, of course, the firm that supported us would have the right to use it. It's a very complicated situation that needs quite a lot of tact and understanding from both sides. At that time it was much easier to have that type of cooperation. Today it would be much more difficult. However, the Swiss National Science Foundation was then organized and quite a lot of money is now given by it to the Laboratory. We got quite a lot of money through the Swiss National Science Foundation which is like the National Science Foundation in the United States. It is a semi-official organization that supports research. You have to propose a project and the support is only temporary. You always have to invent new projects and write proposals, like in the United States.

KOEPPEL: Yes.

PRELOG: In Switzerland, we have a great advantage compared to the United States. We don't pay any overhead to our school. In the United States, if you receive a grant from institutions like the National Science Foundation or the National Institutes of Health, a great part of it goes to the school as so-called overhead. This means that the school takes a part of this money for administration or even for teaching. That's not the case here. So, we get money either from industry or from the Swiss Science Foundation, and we use this money fully without paying any overhead. Additionally, we are still supported by the school.

KOEPPEL: You did develop some products commercially. I'm thinking of rifamycin.

PRELOG: Yes, but, we were interested in structures. Industry is interested mainly in biological activity. They can use, for example, an antibiotic without knowing anything about its structure, but they can improve it by knowing its structure. If they know the structure they can predict certain properties, and so they are interested in structure as well as biological activity. At that time it was difficult to determine structure in their own laboratories. Doing so was too expensive for them. So we did research on structures and on the basis of this research they developed their product further. It was in some ways a very nice form of symbiosis because although there were different interests they proceeded in parallel fashion.

KOEPPEL: Right.

PRELOG: We were interested in what the molecules were like. They needed to know the molecular structure to do chemical work or to find some properties of the compounds they used. Yet, they also did biological work for us, which is also sometimes necessary during isolation and purification. So, it was a very convenient arrangement. We also cooperated very nicely with the microbiological research group at the Institute for Special Botany at the ETH directed by Professor Gäuman, who helped us to isolate the microbes and cultivated them for us. Both groups were supported by industry. It was a triangle of industry, microbiology, and organic chemistry. This type of arrangement doesn't work as well any more as it worked in our times. Everything was smaller then; too many people are now competing in this field.

KOEPPEL: Research is so costly now, isn't it, with instrumentation...

PRELOG: Research needs more and more instrumentation. I mention in some lectures and in some historical surveys that chemistry changed with the introduction of physical methods, as much as the art of war changed through the invention of firearms. In the old days people who were very strong physically, and very shrewd, became heroes. With a gun,

however, even a weak man could kill the greatest hero from behind a corner. So it was with research in the old days. It was very cheap. Today, the costs are increased by a factor of between ten and a hundred. As a result of this, people who give money and who are very often not competent, ask themselves what use this large amount of money serves, and if it is used properly. This makes things much more complicated. It is very difficult for these incompetent people to make up their minds, especially if they are not experts. They always want more and more detailed reports, more and more detailed projects. With respect to research, which they don't really understand, they have to ask experts. Experts, if they are good, could do something better than, for example, writing a report about a bad project. The man who initiated a bad project will more or less fight and experts have to be very careful abut what they say and propose. So, the whole thing became much more difficult.

I lived during the very good times. We owe very much to the Russians for those good times. When Sputnik went up in 1957 the Americans decided to spend money for science, and Switzerland did also. So, it was very easy for me to get the necessary funds. We could do whatever we could justify. We never lacked money. This is not so any more. Money always becomes tighter and research is always more and more expensive.

KOEPPEL: You seem to have lived, in the 1950s, in a period of great transition from the simple classical approach to the modern approach.

PRELOG: My predecessor said to Professor Scherrer who was professor of physics: "What we need from the physicists are ringstands and clamps." Now the situation had changed.

KOEPPEL: Indeed it has. Could you tell me something about your relationships with scientists from the United States? You have given so many guest lectures there.

PRELOG: In my time, you know, I met a great number of American chemists.

KOEPPEL: Who are the people you met?

PRELOG: Oh.

KOEPPEL: Your friends.

PRELOG: Dozens.

KOEPPEL: Could you name a few? To tie it together.

PRELOG: The whole group at Harvard was always very friendly. I don't know in which order to name the others, there are so many.

KOEPPEL: It doesn't matter.

PRELOG: We knew very well the people at Urbana, Illinois, which was a great center of research. The senior member there was Roger Adams.

KOEPPEL: Yes, that's what I wanted to ask you.

PRELOG: Adams was a great friend of Ruzicka and he continued to be a great friend of mine.

KOEPPEL: Did he do work on many membered rings?

PRELOG: Not so much. He did a few of them, but he worked also on natural compounds. He had a great and enduring esteem for Ruzicka. There were also very good friends at MIT, Caltech, Columbia, Yale, Cornell, Amherst, UCLA, Madison, Chicago, Purdue, Berkeley. It is so difficult to mention them all because I don't like to emphasize one rather than the other.

KOEPPEL: Did you know any of the older famous chemists, like Gilbert Newton Lewis?

PRELOG: No. I never met him. He was a generation before me.

KOEPPEL: How about Linus Pauling?

PRELOG: I have known Linus Pauling very well since 1948. I had many, many encounters with him.

KOEPPEL: Did you have any special friends visiting you here?

PRELOG: Oh, yes. Again, however, it is so difficult to name all of them.

KOEPPEL: Because you have so many.

PRELOG: Yes. There were too many to be mentioned individually. I have been altogether perhaps--I counted once--at more than one hundred and sixty places. A great number of them were in the United States.

KOEPPEL: Yes, I have your whole lecture list here.

PRELOG: But these are only named lectures. These are only lectures which bear a certain kind of honor. I have also been invited to many meetings and symposia organized by the American Chemical Society.

KOEPPEL: Yes, I see.

PRELOG: And as I think about how bad my English is, I wonder, you know...

KOEPPEL: It's not. It's not bad at all, considering that you just talked English for two hours, how could it be bad! I met

you in Atlantic City at the stereochemical symposium at the 168th annual meeting of the American Chemical Society. I mean I remet you.

PRELOG: I remember that meeting very well. The annual meeting of the American Chemical Society in 1974.

KOEPPEL: Now, to conclude gradually. Well, first of all, I see that you are still active. You have recently published a paper on chromatography, on the separation of enantiomers.*

PRELOG: That is now my hobby, the separation of enantiomers by partition between liquid phases. We are interested in this field because liquid membranes play a great role in biology. Liquid membranes that will separate enantiomers of biogenic amines or other biologically active compounds are interesting from a biological standpoint. We study such systems where the situation is simpler than in biological systems, as models for complicated biological membranes. We are working in coopera-tion with the electrochemists of our laboratory, e.g., Professor Willy Simon, who is studying the electrochemical behavior of such liquid membranes. That's more or less the only field I am now working at experimentally. I still have one postdoctoral student working in this field.

KOEPPEL: Did you write any books?

PRELOG: No.

KOEPPEL: No textbooks?

PRELOG: I wrote chapters for monographs, but not textbooks. I remember that quite some time ago we had a Japanese visitor. It was very difficult to talk to him because he spoke only a few words of German or English--I don't really remember. Anyway, at the end of his visit he said to Professor Ruzicka, "I think that you are a better chemist than Karrer."

Ruzicka was very proud. He said, "Why do you think that I am greater?"

He responded, "You never wrote a textbook." So, we decided that we would never spoil our reputation by writing a textbook. I am also not a very good writer.

KOEPPEL: Well, it's the bi-tri-quadri-lingual background that is distracting.

PRELOG: It takes me quite a lot of time to write a paper. I write everything five times before I publish. The idea of writing a book horrifies me.

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*V. Prelog, Z. Stojanac and K. Kovacevic, "Über die Enantio-merentrennung durch Verteilung zwischen Flüssigen Phasen," Helvetica Chimica Acta, 65 (1982): 377-384.

KOEPPEL: You may be a little bit in limbo, because you say that you forgot your mother language and then maybe you didn't get quite as deeply into your next languages.

PRELOG: Yes, you know, either you have to learn a language very young, or you have to be very talented.

KOEPPEL: I know you don't have a crystal ball, but what is your idea of the future of chemistry or of chemical education?

PRELOG: Chemistry is a very big field and it's so important because everything that happens in the world is related to it. It is so important to know in order to understand what's going on in the world. So, we have really just started and I think...

KOEPPEL: It will survive?

PRELOG: It will never stop. Consider, for example, such a complicated process like memory. Evidently, memory is something chemical. Yet we are far from understanding it. We have to do a lot of fundamental work to understand it. We don't have the necessary tools yet, but they do improve every day. Of course, Einstein said, "We live in a time of more and more perfect methods and more and more confused aims." We always have to think of what we really want to do because the possibilities now are really tremendous.

KOEPPEL: Yes, they are frightening.

PRELOG: If you take a chain of one hundred amino acids in a protein, and twenty different amino acids, you can make 10^{100} possible combinations. There are, as far as we know, 10^{86} atoms in the world and many, many proteins have hundreds or thousands of amino acids. Now, we know that we will never be able to make all of these possible isomeric proteins even though we could synthesize many of them with existing methods. If you say I want to combine a hundred amino acids in a certain sequence to a protein, you can do it. It will take years of effort, however, and require several very able coworkers. Yet, if you fail to put only a very few amino acids into the right sequence, you will not have the expected activity. Which one of these syntheses should be done? Should we spend a million dollars to prepare one of these isomers which might be of no value in the end? This is our problem. We have to be clear about the aim, about what we really want to do because we can now do much more than we were able to do before. We improve our methods every day. They become easier, faster, and more specific.

KOEPPEL: Professor Prelog, before we conclude the interview, I would like to ask whether you have any letters, papers, or

manuscripts on file. Where will your papers be stored? Are you collecting them?

PRELOG: Unfortunately, I have too many of them. It would be very difficult to sort out what is important and what is not important. I think that I shall keep the correspondence with Cahn, Ingold, and other people who contributed to the CIP system.

KOEPPEL: Where are these letters located? Are they kept right at the Institute?

PRELOG: I have them here now, but I shall perhaps deposit them into the archive of the library of the Swiss Federal Institute of Technology. The library does quite a good job collecting the correspondence and other papers of some of the members of the faculty. The library, for example, will keep all of the important correspondence that Ruzicka left. It has a special place where it keeps the correspondence and manuscripts of Thomas Mann, who was a kind of professor here during his later years. It also has the correspondence of Carl Gustav Jung and some other important members of the ETH. I think the library's staff does it professionally and very well. I don't think that I have many letters worth preserving. Some of them, of course, are more important than others, but I think that it would be a formidable task to select them and to store them. I think that I will not leave too much of the correspondence to the archives of the Swiss Federal Institute.

KOEPPEL: You will donate only what is relevant to your scientific work.

PRELOG: Only very relevant. Otherwise, very soon even the Federal Institute of Technology wouldn't have enough space.

KOEPPEL: Professor Prelog, I thank you for the interview you gave me. You have given me so much interesting information about your life, about your work and your relationship with scientists, including those in America. It has been a great experience. Thank you very much.

INDEX