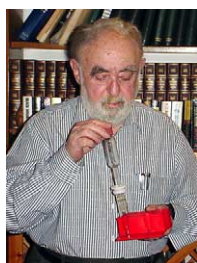


Celebration of inorganic lives: interview with Michael Cais

E. Amitai Halevi*

Department of Chemistry, Technion – Israel Institute of Technology, Technion City, Haifa 32000, Israel



Professor Michael Cais was born in Roumania (October 10, 1924). He received the B.Sc. (in textile chemistry) from the University of Leeds, Leeds, UK, in 1950. Following graduation, he did 1 year post-graduate research on the synthesis and UV spectroscopy of aromatic compounds with Dr. A. Burawoy at the Institute of Technology, Manchester. In 1951, he returned to Israel and began doctoral studies with Profs. Ernest Bergman and David Ginsburg in the Department of Chemistry, Technion—Israel Institute of Technology, Haifa. After receiving the D.Sc. in organic chemistry in September 1955, he was offered a post-doctoral fellowship to do research in natural products chemistry with Prof. Carl Djerassi at Wayne State University, Detroit, MI. He remained at Wayne for 2 years, until the autumn of 1957 when Carl Djerassi went to Syntex, Mexico City, for sabbatical leave. At that time, Michael Cais was offered a position as research chemist with Ethyl Corporation Research Laboratories in Detroit, MI. At Ethyl, he was given the project of developing the organic chemistry of cyclopentadienylmanganese tricarbonyl. In September 1958, Michael Cais was appointed as lecturer in the Chemistry Department at the Technion and he returned to Israel. He was promoted to Senior Lecturer in 1961, Associate Professor in 1964 and Full Professor in 1968. He was elected Chairman of the Department from 1972 to 1976 and President of the Israel Chemical Society from 1967 to 1970. He received the ACS-PRF Faculty Award in 1965; was a Member, Editorial Board, Inor-

ganica Chimica Acta, 1968–1988; Member, Editorial Board, Israel Journal of Chemistry, 1967–1976; Member, Editorial Board, Metal-based Drugs, since 1993. He retired as Professor Emeritus in October 1993.

He has held Visiting Appointments at the Institute of Pharmacology, Bonn University, Bonn, Germany (June–August, 1962); California Institute of Technology, Pasadena, California, USA (1965–1966); Synvar Research Institute, Palo Alto, California, USA (1970–1971); Institute of Physical Chemistry, Basel University, Basel, Switzerland (Kahlbaum Lecturer, June–July, 1973); Institute of Inorganic Chemistry, Technical University, Munich, Germany (June–August, 1978); Laboratoire de Chimie des Organométalliques, Université de Rennes, Rennes, France (March–May, 1979); Memorial Sloan-Kettering Cancer Center, New York, NY, USA (June–August, 1979); Houston Medical Center, Houston, TX, USA (June–August, 1992); University of New South Wales, Sidney, Australia (September 1992–January 1993); Institute of Physical Chemistry, Okazaki, Japan (February–April, 1993).

He was one of the pioneers to begin work in the field of organometallic chemistry in Israel in 1958, and was successful in his efforts to establish international links for Israel in this area. The latter achievement is exemplified by the choice of Israel in 1968 as the venue for the XIth International Conference on Coordination Chemistry (XIth ICC) and his election as Chairman of that Conference.

In his initial research programs at the Technion, he continued working on the chemistry of natural products, synthesis of pharmaceutically active compounds and on development of the chemistry of ferrocene and cyclopentadienylmanganese tricarbonyl. He suggested the trivial name cymantrene for the latter compound, by analogy with the established trivial name ferrocene for bis-(cyclopentadienyl)iron. The name cymantrene has been accepted in the chemical literature. Some of his work with cymantrene resulted in the first published approach to the synthesis of pentalene and benzopentalene through stabilized organometallic precursors. The work with ferrocene led to the elucidation of the properties and structure of α -ferrocenylcarbonium ions

* Tel.: +972-4-8293641; fax: +972-4-8295703.

E-mail address: chr04ha@technion.ac.il (E.A. Halevi).

and the synthesis of metal complexes of the sesquifulvalene and calicene systems. Research in the area of organometal carbonyl complexes led to the discovery of selective hydrogenation of conjugated dienes with arenechromium tricarbonyls as homogeneous catalysts and to mechanistic studies of this catalytic process.

Expansion of his research interests to the area of bio-coordination chemistry, led Cais to the development of the new concept of metalloimmunoassays, whereby metal complexes are used as markers for antigens and/or antibodies, in place of radioisotope markers, for use in diagnostic immunoassays. Work in this area also resulted in the development of a free-radical immunoassay for the detection of cannabinoid metabolites in biological fluids.

The work with biological substrates also led to the discovery and development of novel concepts and devices in separation technology, with potential applications to medical diagnostics, such as non-centrifugation solid–liquid separations and liquid–liquid (solvent extraction) separations. In 1982 Michael Cais received the I-R 100 Award for these developments. Further work in this area also resulted in the development of the concepts of dynamic column liquid chromatography (DCLC), dynamic column solid phase extraction (DC-SPE), and dynamic column affinity chromatography (DC-AC). For the development of DCLC, Michael Cais was awarded, the I-R 100 Award in 1983, for the second year running.

The scientific results and his inventions have been reported in about 150 papers, reviews and worldwide-allowed patents.

Tel.: +972-4-8245259; fax: +972-4-8253542

e-mail: mcais@techunix.technion.ac.il

Relevant Publications

M. Cais (Ed.), *Progress in Coordination Chemistry*, Elsevier, Amsterdam, 1969.

M. Cais, P. Hickmott, A. Modiano, NMR spectroscopy of organic-metal carbonyl complexes, *Annual Reports on NMR Spectroscopy*, vol. 6C, Academic Press, London, 1977, 658 pp.

M. Cais, M.S. Lupin, Mass spectra of metallocenes and related compounds, in: *Advances in Organometallic Chemistry*, vol. 8, Academic Press, New York, 1970, pp. 211–333.

M. Cais, Aromaticity problems in metallocenes, in: *Aromaticity, Pseudo-aromaticity, Anti-aromaticity*, Academic Press, New York, 1971, pp. 96–113.

M. Cais, et al., Metalloimmunoassay, *Nature* 270 (1977) 534.

M. Cais, S. Dani, F.H. Herstein, M. Kapon, Crystal and molecular structure of alpha-alpha-diferrocenylmethylum tetrafluoroborate: a stable carbonium ion salt, *J. Am. Chem. Soc.* 100 (1978) 5554.

M. Cais, Metalloimmunoassay, in: T.T. Ngo (Ed.), *Non-isotopic Immunoassay*, Plenum Press, New York, 1988, pp. 415–438.

M. Cais, Non-centrifugation immunoassays: novel separation systems, *Meth. Enzymol.* 92 (1983) 336–344.

M. Cais, et al., Dynamic column liquid chromatography (DCLC): a novel concept, *J. Chromatogr. Sci.* 22 (1984) 548–553.

P. Ashkenazi, Ch. Yarnitzky, M. Cais, Determination of synthetic food colours by means of a novel sample preparation system, *Anal. Chim. Acta* 248 (1991) 289–299.

E.A.H.—Michael, let us establish some guidelines for this interview. I would like us to focus primarily on the human story, on “Michael the Man”, on how you ended up where you are. Obviously, we shall also cover the highlights of your work. So, let’s go first into your early history. You were born in Roumania and, 26 years later, you graduated from a British university. What happened in-between and how did you come to choose chemistry?

I was born of Jewish parents in Vaslui, a small town in the province of Moldova in the northeastern part of Roumania. My father was the owner of a shop on the main street of the town, where he held the agency for distributing the daily newspapers published in Bucharest, the capital of the country. He also held the agency for selling and servicing the Philips-made radios in Vaslui and surrounding villages. In addition, the shop sold school books, school supplies and general literature books and magazines. Our apartment was situated in back of the shop, and both my parents worked in the shop from early morning to very late in the evening. Even though they had no education themselves beyond primary school, they had a very high regard for learning and aimed to do everything they possibly could to enable my younger sister and me to obtain a university education.

This was not a simple thing for Jews to do in Roumania. Antisemitism was widespread in the whole country. Jews were not allowed to own land or to serve in any public or government offices. Only a few were admitted to universities because of *numerus clausus* regulations. My parents hoped that I would be able to finish the required 8 years of secondary school, pass the obligatory matriculation exam, by which time they would have saved enough money to send me to study abroad, preferably in Paris.

E.A.H.—What happened in your case?

I completed four years of primary school and passed the admittance exam to secondary school in 1935. By the time I completed 5 years of secondary school in the summer of 1940, the situation of Jews in Roumania had become extremely precarious. The Second World War was in full swing, the King of Roumania had been forced to abdicate by a fascist government. The Iron Guard, a Nazi Party, was openly persecuting, kidnapping and beating Jews and was pressing the government to enter the war on the side of Germany. A law was passed that excluded Jews from attending any state school, primary, secondary or university. They were only allowed to attend private Jewish schools in those cities where such schools existed. There was no Jewish secondary school in my town, but my parents were unwilling to give

up their plans for me. They found out that there was a Jewish secondary school in the capital. My mother's brother—a well-established lawyer who had studied in Paris and was probably my parents' role model for me—and two of her sisters lived in Bucharest. My father traveled to Bucharest, a 7-hour train journey, and—after a family council—it was decided that I should come to live in Bucharest with one of my aunts and be enrolled as a pupil in the sixth form of the Jewish secondary school "Cultura". So, I left home—barely 16 years old—and started school in September 1940. My parents were thankful, not only because I was given the chance to continue my schooling; they were glad I had left Vaslui, because some of my non-Jewish former classmates, who had joined the Youth Cadres of the Iron Guard, came around to the shop asking for my whereabouts. They wanted to catch me and beat me up, as they were doing to other Jewish children in the town. A number of my Jewish classmates had been arrested and sent to labor camps in Transnistria, then part of the Ukraine. When my father refused to tell them where I was, they kidnapped him and beat him severely. He was eventually released after payment of a ransom and was ill for a few weeks until he recovered from the beating. I was not aware of any of this.

E.A.H.—Under these circumstances, how long did you continue your stay in Bucharest?

At about that time, the Roumanian Government, led by the dictator Antonescu, decided to declare war on Great Britain and France, on the side of Germany. Following this declaration of war, the Ambassador of Great Britain in Bucharest had to leave Roumania. Before he left, well aware of the persecution of the Jews in Roumania, the ambassador made a humanitarian gesture: he granted to the Jewish Agency in Bucharest 300 "immigration certificates" (official entry visas to the British-mandated Palestine) for children aged 14–16, allowing them to emigrate from Roumania to Palestine. My parents heard about this opportunity from my lawyer uncle, who was active in the affairs of the Jewish Community in Bucharest. My uncle told them that he might be able to obtain one of these "certificates" for me but this would involve payment of a very substantial sum of money to cover expenses for the trip, maintenance for a period of 2 years at some institution in Palestine and bribes to be paid to the Roumanian authorities to obtain an exit permit. After a great deal of soul searching, and in view of the continuous worsening of the Jewish situation in Roumania, my parents decided to make the enormous sacrifice of being separated from their only son, in the belief and hope that going to Palestine would mean saving my life. It is hard for me to describe my own feelings at the prospect of being separated from my family, my home and my friends. All I want to say is: I knew that, as an obedient son, I was going to do what I would be told to do.

E.A.H.—Did you get such a "certificate"?

Yes, I was lucky to get a certificate. At the end of March 1941, a group of 300 children, I among them, embarked

on the ship "Carol I" in the Roumanian port of Constantza for travel to Istanbul, Turkey, the first stage on our way to Palestine. After an overnight passage, we arrived in Istanbul, where we disembarked and were transferred to the Asian part of Turkey. There we boarded a train on which we journeyed for 4 days and nights through Syria and Lebanon, as far as Beirut. From there we traveled for 3 hours by bus until we reached the village of Atlith on the outskirts of the city of Haifa, in—for us—Eretz Israel (the Land of Israel). To our surprise and dismay, our buses stopped at the entrance gates of a concentration camp, surrounded by barbed wire, where immigrants of all ages without "certificates" to enter British-mandated Palestine were imprisoned, some of them for years.

E.A.H.—You left Roumania to escape being sent to a concentration camp and your first stop in Palestine was at a concentration camp! How did you feel?

It was traumatic for all of us. We protested that we had "certificates" given to us by the British Ambassador and therefore were "legal" immigrants. We were told that this was only a formality, a bureaucratic process. We would have to remain in the camp only a short time, until we passed the security check, after which we would be assigned to our final destinations. I do not want to go into any details about the very difficult conditions in the camp. Fortunately, after about 3 weeks in the camp, the authorities began to release the children of our group and send them to different locations in Palestine. I, together with about 10 other children, was allocated by the "Youth Aliyah" Organization (a Jewish Agency Department dealing with the immigration of children into Palestine) to go to an Agricultural School in the Ben Shemen Youth Village. There we were to be given boarding and lodging, attend school 4 hours a day and work in the fields 4 hours a day. The aim of the school was to prepare agricultural workers, who—after 2 years in Ben Shemen—would join a kibbutz or a farming village. In parenthesis, I should point out for our readers that this aim was in line with one of the main aspirations of Zionism. After so many centuries in which Jews lived under antisemitic discriminatory laws which did not allow them to own and work the land, Zionist tenets encouraged Jews to take up working the land upon return to their old, historic country.

E.A.H.—What happened next? How did you adjust to the new environment? You must have been glad to go to school again!

I would like to mention first that upon arrival in Palestine I did not have any knowledge of either Hebrew or English. My native tongue was Roumanian; I also had a good knowledge of French, which I had studied for 5 years in my secondary education and also some knowledge of German from 2 years' study in secondary school. By the way, knowing French turned out to be lucky for me, because my roommate in Ben Shemen—who was from Turkey—also spoke French; thus we were able to communicate freely. However, this did not help me at school, where all the studies were conducted in

Hebrew. The 4 hours of my daily school time were devoted solely to the study of speaking, reading and writing Hebrew. I understood and accepted that I had to do this but, of course, it was quite different from taking math, science, etc., the subjects I was used to have in school!

E.A.H.—What about the 4 hours of work in your daily schedule?

With your permission I would like to answer this at some length, because it covers one of the most critical aspects in my subsequent development. The work requirement proved to be the most difficult part for me. Not because I objected to work as such; it was because of the kind of work I had to do. As I told you, Ben Shemen was structured to train agricultural workers. My first assignment was to the vegetable garden. After working at this assignment for several weeks, I came to the conclusion that working the land was the most boring thing in the world for me, that I had no interest in becoming a farmer and that I was not ready to give up my dreams of continuing my studies. I did not hide my feelings from my instructors and teachers, and I requested formally to be transferred to one of the technical secondary schools, which I knew were under the auspices of the “Youth Aliyah” Organization. My request fell on deaf ears, so one day I decided to rebel. I refused to go out to work at my assigned place in the vegetable garden. As punishment, I was transferred to the housekeeping section and was put to do all kinds of menial housework. I had to clean rooms, sweep and wash floors, wash dishes, darn socks, iron the garments of other pupils, and so on. I did this kind of work 4 hours a day, every day except Saturday, for several months. When the administration saw that they could not “break” me, I was called to an interview with the principal of the school. I reiterated my request to be transferred to a technical school because I did not want to become a farmer and wanted to continue my studies up to matriculation. They said that before considering this request, I must take a psycho-technical test to determine whether I had the required abilities. I was sent to Tel Aviv to take the 4-hour test and, happily, I passed with high marks. Upon my return to Ben Shemen with the test results, I was told that there was no free place at any of the technical schools, but since I had passed the test and did not wish to become an agricultural worker, I was being transferred to work and be trained in the locksmith workshop of the school!

E.A.H.—So, you became a qualified locksmith!

Are you kidding? Frankly speaking, doing the housekeeping work had begun to wear me down and even though I had no idea what exactly being a locksmith entailed, I thought I had no choice but to give it a try. In the first assignment, I was given a piece of an iron bar and told that I had to learn how to shape it into a hammerhead. I worked in the locksmith workshop for about 3 months. It was better than doing the housekeeping or the vegetable garden work. At the same time I realized that learning to become a locksmith was not taking me any nearer to achieving my dream of finishing

high school and qualifying for acceptance at a university. I spent many hours thinking about this and slowly arrived at the conclusion that there was no other choice than to get away from Ben Shemen in order to look for other ways to pursue my plans.

E.A.H.—You were 17 years old, you had no money and no relatives to take you in or support you, and yet you considered leaving Ben Shemen, where at least you were assured of boarding and lodging for up to 2 years. Weren't you afraid to contemplate such a step?

You are quite right to ask this question and I assure you that this was a very hard decision to take. I discussed my plan with several of the friends who had been sent together with me from Atlith to Ben Shemen, and tried to persuade them to leave Ben Shemen with me. Some of them had relatives in Tel Aviv and several had other sources of financial support. I knew that, for their own reasons, they too were not happy in Ben Shemen. Thus, I was not surprised that they were willing to consider the idea of running away from Ben Shemen and discuss it.

After lengthy discussions, we formulated our plan and arrived at a decision to act. One rainy morning in October 1941, five of us took our few belongings and—without telling anyone—boarded a bus to Tel Aviv. Upon arrival at the bus station in Tel Aviv we separated. Two of my friends went to their relatives. The remaining three of us walked to an address in Tel Aviv where we knew that, on the third floor, lived the Deputy Director of the “Youth Aliyah” Organization that was supposed to be taking care of us. We rang the bell. When the Deputy Director, a lady in her fifties, opened the door, saw us and heard who we were, she refused to talk to us. We decided that we would not move until she met with us and helped solve our problem. We placed our belongings on the staircase, in front of the door of the apartment, and settled in for a sit-down strike. In retrospect, I believe this was probably the first time such a strike took place in Tel Aviv! We remained there for 3 days and 3 nights, sleeping on the floor, in front of the Deputy Director's door, quietly and without any violent demonstration whatsoever. During all this time the Deputy Director came and went about her business, pretending that we did not exist. Finally, on the morning of the fourth day, she called us into her apartment and told us that since Ben Shemen was not willing to take us back, the “Youth Aliyah” Organization had decided “to wash its hands” of us, “the rebels”. In other words, it refused to take any further responsibility for us. When we claimed that our parents had paid for 2 years of school, with board and lodging, she said that the only thing the organization was prepared to do would be to give each of us the sum of three pounds per month for 3 months, in order to enable us to make our own arrangements. With this payment the “Youth Aliyah” would terminate all their obligations towards us. We were flabbergasted! We were being thrown out on the street! What were we to do? We decided that we had no choice but to accept this offer, even though we had no idea whether it

was possible to subsist on three pounds a month and did not know what would happen to us at the end of three months. We were asked to sign a document declaring that we renounce all further claims on the “Youth Aliyah” Organization. We were then each given three pounds in cash, the first monthly payment of the three offered to us, and ordered to collect our belongings and leave the building.

E.A.H.—This must have been catastrophic for you. You found yourself thrown out on the street, without a sponsor and with your dreams of continuing your studies shattered. What did you do next?

You are quite right. At first this was catastrophic for me because, naively, I had not prepared myself for such an outcome. As you said, I found myself on the streets and it was clear to me and my friends that the first thing we must do was to find a place to stay. We started walking the streets, looking for notices of furnished rooms to rent. Eventually, after several hours of searching, we did find an apartment owned by a widow who was taking in boarders. A room with three beds was available and the rent was one-and-a-half pounds per month per person, including one meal a day, lunch or dinner. We did not hesitate long. It was winter, the rainy season, and evening was approaching. We agreed to take the room and settle in, even though this meant paying half of our total monthly allowance. The important thing was that we had found a place to stay and would not have to sleep on the street! I did not sleep much that night, thinking over my situation and trying to plan what to do next. It became clear to me that the first thing to do was to find some kind of work to earn a living because it would not be possible to subsist for even 3 months on the allowance we had received. The following morning I went to the Youth Employment Office of the Histadruth Trade Union and asked for work, any kind of paying work. It turned out that the only employment available for young people was as temporary menial workers paid by the hour. I had to report at the Employment Office every evening to find out if I would have work on the following day and where. I did all kinds of work for the next few weeks and was glad that I was at least getting some additional income, however small, for my subsistence. One evening, the clerk at the Employment Office, who knew some of my history and was sympathetic to my tribulations, told me that he had found a full-time job for me. “Delfiner”, a well-known textile manufacturing company in Tel Aviv—owned by the Yohananoff family—was looking for an apprentice to be trained to work in the dye-mixing room of the cotton and silk-dyeing section of the plant. The starting salary would be 4 pounds a month, for 8 h a day, 6 days a week, with additional pay for overtime. He asked: “Would you be interested?”. I jumped to embrace him and remember telling him, with tears in my eyes, that this was the answer to all my hopes and prayers. The next day I presented myself at the plant and, after going through some bureaucratic formalities, I began work at the new place.

E.A.H.—Would it be a safe guess that this new employment was also your first close encounter with chemistry and had a bearing on your choice of chemistry as a career?

This would be a very good guess. In your first question in this interview you asked how I came to choose chemistry. We have now reached the point where I can try to answer that part of your question. Let me explain first what was involved in my work in the dye-mixing room. I was apprenticed to Tobias, the Dye Master, whose duty was to formulate and prepare the required mixture of dyes and other appropriate chemicals for each batch of cloth sent for dyeing in the plant. The dye-mixing room stored hundreds of tins and bottles containing every kind of synthetic dye as well as other chemical compounds used in the dyeing process. Tobias was a deaf-mute but he had been trained to speak somehow and could lip-read. He would write the formulation on a special form, with the name and quantity of each dye and chemical to be used in the dyeing process of a particular batch of cloth. He would give me the form and I was supposed to weigh out, or measure, the exact quantities of the dyes and other chemicals, solids or liquids, for that particular formulation. This work, though it may seem pedestrian, entailed a very high degree of responsibility. Any mistake in selecting the right dye prescribed in the formulation, or in weighing out the exact quantity required in the mixture, could cause irreversible damage, by spoiling the whole batch of cloth being dyed.

E.A.H.—Did this responsibility worry you?

Thinking back, I believe that I was awed by the responsibility and worried that if I made a mistake and did not do my work well I would be fired. I realized that I had to be as careful as possible, check and recheck every measurement and selection of the proper chemical. I worked hard and endeavored to learn and memorize the name and location of each dye and chemical and to learn as much as I could about its properties.

E.A.H.—Did you realize that in fact you were doing some form of chemistry?

Not at the beginning. This realization came to me by an evolutionary process. The Dye Master was a very demanding kind of guy but at the same time he was willing to spend time teaching me and supervising my work. I later found out that he was a chemistry graduate from a German university. In addition, Dr. Chazan, the Chief Chemist of the plant, to whom the Dye Master reported, took an interest in me when he saw that I was hardworking and willing to learn how to do my job well. Sometimes he would stop and talk to me and explain some of the processes of cloth dyeing. He once told me that through his chemical work he had invented a new type of synthetic soap. He said that his invention was a secret and—in order to keep it secret—he had to prepare the soap by himself for use in the dyeing processes in the plant. I realized later that he was talking about having invented a synthetic detergent and, in fact, I know that he eventually set up his own company to manufacture and sell this synthetic

soap, which is still being marketed in Israel. Anyway, I came to admire and worship him because of his kind interest in me and it may very well be he who is largely responsible for my becoming interested in chemistry.

E.A.H.—You had now settled down to a job which you liked and your financial situation was more secure. When did you start thinking again about continuing your studies?

I never stopped thinking and dreaming about it. My problem was that I could not hope to attend a regular secondary school because I had to work for a living. I had to find an alternative. I learned that every year the British Council in Palestine held examinations in Jerusalem for the London University Matriculation Certificate. Anyone was permitted to sit for this examination as an external student without any prerequisites. The important thing for me was that this matriculation certificate granted the right to be admitted to a British university. It became obvious to me that sitting for this examination was the only way open for me to try and reach my goals. My major problem was that these examinations were held in English. Whereas I had made reasonably good progress during the past year in learning Hebrew for every day use, my English was very poor—in fact practically non-existent. Therefore, before anything else, I had to learn English. I was given the name of a highly recommended, but expensive, private teacher, a lady who was a graduate of London University in English phonetics. I made an appointment and explained that my aim was to be able to sit for the London Matriculation Certificate exam as early as possible. The teacher agreed to accept me as her pupil for a fee of half a pound per 50-min lesson. I arranged to come to her twice a week. You must understand that this meant a very heavy burden on my budget. My wages at this time had risen to about 6–7 pounds a month including overtime. After paying one-and-a-half pounds for rent (which included one meal a day) and 4 pounds for the English lessons, I had very little left for other needs. This did not really bother me. I was determined to make do with whatever was necessary to achieve my goal.

E.A.H.—What about the other subjects of the examination. How did you prepare for them?

The London University Matriculation required examination in five subjects: two obligatory, English and Mathematics, and three electives, including a foreign language. My electives were Chemistry (naturally), Physics and French. From perusal of the exam syllabus, I learned that most of the subject matter for math, chemistry and physics was known to me from my years of study in the secondary school in Roumania. It mainly remained for me to review all this material in English. I also found out that I should have no problem with the French syllabus, for the same reason. I acquired the required text books and studied every day after work, for 6–8 hours, either on my own or together with two of my friends, who were also preparing themselves for the same exam.

E.A.H.—When did you sit for the exam?

I continued with my studies for the whole of 1942 and part of 1943. I registered to sit for the exams scheduled for June 1943. I took leave from work, went to Jerusalem, rented a room for a week at a youth hostel, took the exams—one every day for 5 days—and returned to my job in Tel Aviv. About 1 month later the British Council in Jerusalem notified me by mail that I had passed all the exams and that the London University Matriculation Certificate was being mailed to me directly from London.

It is hard to express my jubilation. The first thing I did was to send my parents in Roumania a 25-word Red Cross message (the only way one could communicate with hostile countries during the war) informing them of my success. I knew that it would take about 3 months for them to receive my message and another 3 months to receive their reply. Eventually their response arrived, expressing their joy and happiness at my achievement.

E.A.H.—What did you do next, now that you had realized the first part of your dream?

My feeling was very much that of “mission accomplished” and I had to decide what to do next. I felt that there was not much more room for advancement at the textile plant and began to look out for other possibilities. I heard that the Jewish Agency, in its attempts to promote and support the war effort, was looking for volunteer recruits to join a Jewish unit in the British Army for 18-month service in the neighboring countries of Lebanon and Syria. I decided to volunteer and, in August 1943, I found myself in a military camp in the Bekaa Valley, Lebanon, a soldier in 479 General Transport Company, Royal Army Service Corps of the British Army. I will not dwell on details about my time in the army except to say that I was a clerk in charge of the Company office and the Company stores. Our Company did not do any fighting and was mainly engaged in the transportation of troops, supplies and equipment through Lebanon and Syria. Every 2 or 3 months I would be given a week’s leave, which I spent visiting friends in Tel Aviv. At the end of 1944 my company was disbanded, its soldiers were returned to Palestine and discharged from the army.

E.A.H.—I understand that at this time you wanted to begin your studies at a university.

Having managed to save most of my army pay, I thought I had enough money to start with, and planned to enroll at a university to begin my further studies and thus fulfill the second part of my original dream. Obviously, by this stage, I had already decided I wanted to become a chemist! At that time there were only two institutions of higher learning in Palestine: The Hebrew University in Jerusalem and The Technion—Institute of Technology in Haifa. Admittance to either of these institutions required having attained “Bagruth”, the matriculation certificate awarded after a national examination at the end of secondary school studies in Palestine. Thinking that I possessed a matriculation certificate, I applied to be admitted to studies for the 4-year first

degree in chemistry at both institutions, but to my dismay I was informed that neither of these institutions recognized the London University Matriculation Certificate as equivalent to “Bagruth” and, therefore, I was denied admittance by both institutions. The Technion was willing to accept me with the status of a “non-registered student”, which meant that, by paying the full university tuition fees, I would be allowed to attend lectures, participate in lab work and sit for examinations, but I would not be given any official credit towards a degree. I thought that this was better than nothing; at least I would be attending regular courses at a university and thus advance my education. Also, I hoped that if I did well in exams, the university authorities might perhaps eventually reconsider their decision and agree to change my status to that of a regular student.

E.A.H.—When did you start at the Technion under these conditions and how did it work out?

The first thing I had to consider was my financial situation. My meager savings, after paying tuition fees, would not last for more than a few months so I had to find some kind of long-time work that would enable me to earn enough for the university fees and for my upkeep. Let me say that by this time I was reasonably fluent in English and this helped me to find a job as night clerk at the Savoy Hotel, a major hotel *cum* restaurant in Haifa that catered mostly to British government personnel. The working hours were from eight in the evening to six the following morning. This suited me perfectly because it allowed me to attend classes during the day. Furthermore, the conditions of employment included a salary and meals from the hotel kitchen. The duties were relatively light and usually, after eleven o'clock in the evening, I had lots of free time when I could read and study at my desk.

I was very happy. This was the first time since leaving Roumania that I was again really going to school, attending classes, doing laboratory work in chemistry and physics, mixing with fellow students and making new friends. I worked very hard at my studies and enjoyed them. I was not even bothered by the fact that I was not a “registered student”. My employers at the hotel were satisfied with my work and I did not have to worry about keeping the job. In the meanwhile I also began thinking about the possibility of going to Britain after the war to continue my studies. The war was coming to an end and I thought that my service in the British Army would increase my chances of being admitted to a university in the UK as an army veteran. In addition, to prepare myself even better, I enrolled in a correspondence course of London University for the Intermediate London University Examination, which was equivalent to the first year of study at that university. I felt that things were coming along well for me. I was in an up-mood and I could even allow myself to think of my personal life and do something about it.

E.A.H.—What do you mean by “do something” about your personal life?

In our conversation until now, I have attempted to give a factual account of the major events in the course of my life. I tried to avoid being emotional and dwelling too much on my personal sentiments and feelings. Even though I had friends and acquaintances, most of the time I felt alone and lonely. I missed my family very much and longed for a normal family life. Even though I was still under 21, without any tangible means and/or prospects, I began having daring thoughts that perhaps I should consider founding a family of my own. During my army service, and after my release, I had been corresponding with Judy, a girl I had met and dated in Tel Aviv during my leaves from the army. Judy was studying for a Teacher's Diploma at the Lewinsky Teachers College in Tel Aviv. Her parents and brother lived in Hadera, a small town about 30 miles north of Tel Aviv. The more I got to know her, the more I liked and respected her as a person as well as admired her mental qualities. I felt that I could talk to her on any subject or problem and she would respond in an intelligent and sympathetic way. Without realizing it, I was falling in love with her. No wonder, then, that in my daring thoughts of getting married I began thinking about Judy as my future companion in life. Eventually I got up enough courage to ask her if she would marry me and accompany me to England, where we would both continue our studies. I told her that I had nothing to offer but the belief that this was the right thing to do and the will and promise to work hard for our future together. She confessed that she, too, had fallen in love with me and, though she was not yet nineteen, she would be happy to marry me. However, we had to obtain her parents' consent. I had visited with her parents several times in the past but had never given any hint that I planned to marry their daughter. Judy and I went to see them together and told them that we wanted to get married and go to England to continue our studies. They were greatly surprised and told us that they would agree to our marriage but wanted us to remain in Palestine. I explained to them that I had no chance of being admitted to a university in Palestine and that my only chance of continuing my studies was by going to England. Eventually they came around, and we were married in December of 1945. In parenthesis, I want to add that after the end of the war in the summer of 1945, I was very happy to learn that my parents and sister had survived the war, and were safe and sound in Bucharest. We were able to communicate by regular mail and I had informed them of my impending marriage and received their blessing.

E.A.H.—When did you go to England, where did you settle and how did you manage there?

After our marriage we rented a furnished room in Haifa. I continued my work as night clerk and my studies as “non-registered” student at the Technion. Because of my having previously worked and gained experience in the cloth dyeing plant, I decided to continue my studies in the field of textile chemistry. In 1947, I applied to the University of Leeds to be admitted for studies towards a B.Sc.

degree in the textile department. My having served in the British Army and my possession of the London University Matriculation Certificate were sufficient grounds for admittance. Judy, who held a Teacher's Diploma was also admitted to study at the University of Leeds in the Department of Biblical Studies. We arrived in Leeds in September 1947. We had enough money to pay tuition fees for the first year and to subsist for a few months. Luckily, Judy found a position as teacher in a Hebrew school that paid enough for us to live on very frugally. I worked summers in all kinds of job, including one as a weaver in a textile plant in the nearby City of Bradford. One summer, Judy and I worked as instructors in a summer camp in Bognor Regis for Jewish children from London. Thus we were able to earn at least enough to pay our tuition fees at the university.

E.A.H.—Tell us something about your chemistry studies in the textile department.

We had to take all of the usual basic courses in chemistry, such as general, physical, inorganic and organic chemistry. In addition, there were courses on the chemistry and structure of wool, silk, cotton and synthetic fibers. The Head of Department was Prof. J.B. Speakman, a chemist. He was world-famous for his contributions to the elucidation of the structure and chemistry of wool and silk fibers, and was a fantastic teacher. However, the textile department curriculum for a B.Sc. degree included a large number of compulsory courses in textile manufacturing, such as cloth design, structure of the loom, structure of spinning machines, etc. From the beginning, I did very well in the chemistry courses. My previous studies at the Technion gave me a head start and I managed to be among the top three students in the exams in the chemistry subjects. I did not do as well in the textile manufacturing courses. At the end of 3 years' studies, one had to sit for comprehensive examinations in all the subject matter covered over the 3 years. The happy end was that, in the summer of 1950, I passed all the examinations and graduated with the B.Sc. degree of the University of Leeds. To complete my happiness, another very good thing happened at about the same time. My parents and sister, who had survived the war and had been living in Bucharest under the Communist regime, received permission to leave Roumania and immigrated into Israel in the summer of 1950.

E.A.H.—What did you plan to do after your graduation?

As you remember, I told you of my earlier desire to become a chemist. Throughout the 3 years of my studies in Leeds, I carried with me the nagging feeling of wasting time because the major part of my studies consisted of non-chemistry subjects. I was not interested in following a career in textile manufacturing and I wanted to find a way to deepen my knowledge of chemistry.

Let me deviate for a moment at this point. One of our problems of living in Leeds was the weather! We had difficulties not only because of the heavy winters, but because of the bad weather through all the seasons; gray sky, fog and rain a great deal of the time. I even developed a knee prob-

lem, probably some form of rheumatism. Now, it so happened that I had a friend, one of the Ben Shemen "rebels", who was studying chemistry at the University of Manchester. Whilst in Leeds, about once a year, in the summer, we went to spend a weekend with my friend in Manchester. Every time we went there, the weather was absolutely beautiful. So, no wonder I thought it would be nice to transfer to Manchester and continue with my chemistry studies there. Little did we know that our previous visits to Manchester coincided with the 1 or 2 days of that year in which Manchester had nice weather!

E.A.H.—Did you then enroll in the University of Manchester for a post-graduate degree?

No! You see, my B.Sc. was in textiles and Manchester University did not have a textile department, where I felt I had a better chance of being accepted for post-graduate studies. Fortunately, such a department existed at the Manchester Institute of Technology, which at that time was a separate institute, independent of the university. (A few years later this Institute became the College of Technology of the University of Manchester.) I went for an interview with several members of the teaching staff at the Institute of Technology and was very glad that Dr. A. Burawoy, a Senior Lecturer in the Chemistry Department, agreed to accept me as a student for post-graduate studies beginning in the fall of 1950.

E.A.H.—What type of research did you do with Dr. Burawoy? At that time I was a graduate student at University College, London, and recollect that he was involved in a bitter dispute among chemists in Britain.

Dr. Burawoy, a refugee scientist from Germany, was an organic chemist and UV spectroscopist. He became involved in the controversy of resonance versus tautomerism in benzene and its derivatives. By studying and analyzing the UV spectra of suitable benzene derivatives he was trying to prove the existence of equilibria between tautomeric species as opposed to resonance between canonical forms. My research topic was the synthesis of *ortho*-nitrosophenols and their oxime derivatives, followed by the measurement of the UV spectra of these compounds in various solvents. I worked very long hours at the bench, learning and practicing organic synthesis. In addition, I attended advanced courses in organic and physical chemistry, thus filling in the gaps from my undergraduate chemistry studies. Also, I learned to operate the Hilger Uvispek Photoelectric Spectrophotometer and to read the photographic plates in order to analyze the wavelength bands obtained with this instrument. Let me say that this was considered an advanced spectrophotometer at the time. How far from the automatic spectrophotometers of today!

I must tell you that after reading and deciphering hundreds of photographic plates over a period of about a year, my vision deteriorated to the extent that I had to have prescription glasses for shortsightedness. Since then I have had to wear glasses for driving and other activities that require distant vision. On the other hand, maybe because of my having

become shortsighted at a relatively early age, I have never needed reading glasses, even nowadays as I approach 80!

E.A.H.—How long did you stay with Dr. Burawoy and was anything from your research with him published?

Let me first answer the second part of your question. My name was included among the co-authors in two papers published by Burawoy in the November 1955 issue of the *British Journal of the Chemical Society*. To return to the first part of your question, we remained in Manchester for only 1 year because something completely unplanned for happened. In the summer of 1951 we received a message from the Israeli Embassy in London, where we were registered as Israeli citizens after the declaration of the establishment of the State of Israel in 1948, informing us that the Principal of the Reali School in Haifa, one of the most prestigious high schools in Israel, was touring Britain to recruit teachers for his school. The Principal, Mr. Joseph Bentwich, who would be visiting Manchester, had requested to meet with Judy and me. We agreed to the meeting and were curious to hear what he had to say. The Principal invited me to come and teach chemistry in the upper forms of his school and offered Judy a position as English teacher in the lower grades of the school. In addition to the regular teacher's salary, he offered to provide us with rent-free housing for as long as we would be teaching in his school. He would also cover part of the travel costs to Israel. Considering the state of our finances at the time, this was a very tempting offer. Nevertheless, I told the Principal that it was difficult for me to consider his offer because it meant that I would have to give up my plans to continue my studies towards the doctorate. He said that, in his opinion, it should be possible for me to continue the doctoral studies in the Chemistry Department of the Technion in Haifa and suggested that I try to get approval from the relevant authorities to make my research in Manchester part of my eventual doctoral thesis at the Technion. He promised to give me his full support to carry out such a program if I was prepared to teach chemistry in his school at the same time.

This was an offer I could not refuse. I understood the risks involved. I also realized that I would be taking upon myself very heavy responsibilities. I had no teaching experience and could not know whether I would be a good teacher. It also meant that I would have to put in very long working days to find time both for full-time teaching and for doing research in the laboratory. However, the latter issue was the least of my concerns; I was used to working long hours. After much deliberation we decided to accept the offer and returned to Israel in August of 1951.

E.A.H.—One of the risks involved in this plan was that you could not know for certain whether the Technion would admit you for doctoral studies. How did this work out?

I should mention that before I decided to accept the Principal's offer, I had discussed the whole thing with Dr. Burawoy. He was very understanding, and told me that he would have no objection to the eventual inclusion of the

research I had carried out under his supervision, in the doctoral thesis that I would eventually submit at the Technion. He even offered to read and edit the draft I would write on the Manchester work as part of the thesis, if necessary. This was very encouraging because I thought it would increase my chances with the Technion, and it helped me decide to take the risk that you rightly mentioned.

It turned out that, luckily for me, at that time—the end of 1951 and beginning of 1952—Prof. E.D. Bergman, of the Hebrew University of Jerusalem, a world-class scientist and the doyen of organic chemists in Israel, was also a permanent Visiting Professor at the Technion. He had been asked to help develop organic chemistry research at the Technion and was interested in attracting research students in this field. He was willing to accept me as his student and agreed to consider my work in Manchester as part of my eventual doctorate thesis.

One of Prof. Bergman's interests was in the area of polycyclic aromatic compounds and their carcinogenic properties. He proposed that I work on the synthesis and spectroscopic properties of triphenylene and its derivatives. Relatively few modes of entry into the triphenylene series had been worked out at that time and he thought this would be a suitable topic for a doctoral thesis. Obviously, I accepted his suggestion without hesitation! Now that I was a chemistry doctoral student at the Technion, you can imagine my happiness that the major risk involved in my decision to return to Israel had been eliminated. Nor could I help remembering that, 6 years earlier, the Technion had refused to admit me as a "registered" student for a B.Sc. degree in Chemistry!

E.A.H.—How did you combine your teaching duties and your research? What was your daily schedule?

The housing that was provided to us under the conditions of my employment was located on the campus of the Reali High School, which was situated on top of Mount Carmel, Haifa. This was convenient for my teaching duties, which were Sunday to Friday, between 8 A.M. and 2 P.M.; I did not have to waste time on travel to the school. However, this was less convenient for reaching the lab at the Technion, located at the time in mid-town Haifa. We did not have a car, a luxury at the time, and I had to travel by bus, a 50-minute ride each way. I would arrive at the lab about 3 P.M. and worked there until about 9 P.M. Upon my return home I had to prepare my lectures for the next day's teaching schedule. Fortunately, there were many school holidays as well as the 3-month summer vacations when I could put in about 12 hours a day in the lab. This enabled me to come along reasonably well in my research. Prof. Bergman, on his weekly visits at the Technion, reviewed my research results and advised me on how to continue. This state of affairs continued for about 2 years until the summer of 1954, when a new development occurred.

E.A.H.—You are of course referring to the arrival of Prof. David Ginsburg at the Technion. I say this because at about that time David Ginsburg invited me to join the Department of Chemistry at the Technion.

Yes! As you know, Dr. David Ginsburg, an American scientist who had joined the Organic Chemistry Department at the Weizmann Institute of Science in Rehovoth, was a rising star among the young organic chemists in Israel. He had achieved world-wide recognition in the chemical community for his work on the total synthesis of morphine. Ernst Bergman, who had been asked by the Technion to help strengthen its Chemistry Department, was empowered by the Technion authorities to offer David Ginsburg the appointment of Professor of Chemistry and Head of the Department of Chemistry at the Technion. Ginsburg accepted this offer and he took up his appointment in June 1954.

E.A.H.—How did this development affect you?

With Ginsburg's appointment, Bergman ceased being a Visiting Professor at the Technion. Ginsburg, with Bergman's approval, suggested that I stop the work on triphenylene. They thought I had enough research material to include a chapter on this topic in my thesis. At the same time, Ginsburg thought that, in order to have enough material overall for my thesis, I should begin work on a new topic, under his supervision. Ginsburg was interested at that time in the total synthesis of the alkaloid colchicine, a tricyclic compound with two seven-membered rings, by methods developed by him in his synthesis of morphine. He proposed that I work on the synthesis of suitable intermediates in the tropone series, aimed at developing feasible paths towards an attempted total synthesis of colchicine. I enthusiastically agreed to start on this project because it meant I would be gaining experience in new methods of synthesis and would be introduced to the field of natural products chemistry, which was probably the most fashionable topic in organic chemistry at that time. Let me also mention here that when Ginsburg agreed to accept the appointment at the Technion, he also demanded—and received—substantial funds both for hiring new staff and for the purchase of teaching and research equipment. The facilities and working conditions in the laboratory were significantly modernized and enlarged. This had a highly beneficial effect on my research work. I was able to make very satisfactory progress, gaining experience in modern research methods while getting results in my new research project. Not least helpful was the fact that I could talk with my research supervisor on a daily basis, rather than—as before—once a week during Bergman's visits to the Technion.

E.A.H.—How much longer did you have to continue in order to complete your work for the doctorate and when did you get your degree?

By the summer of 1955, one year after Ginsburg's arrival at the Technion, he told me that I had accumulated sufficient research results and could start working on the manuscript for my thesis. It took me about 3 months and several drafts, which I had to type myself since I could not afford a professional typist. In September 1955, I submitted the thesis to the Doctoral Committee appointed for my examination. In order to connect between the three different topics of the

research I had carried out, I entitled my thesis "Synthetic and Spectroscopic Studies in the Aromatic Series".

At that time, as you know, the regulations at the Technion were that a doctoral student had to "defend his thesis" in an examination before a Doctoral Committee. The examination took place in the main lecture hall in an open public session that anyone could attend. The candidate was given 50 minutes to present his work, after which each of the three committee members asked the candidate questions pertaining to the research as well as general chemistry questions. At the end of the examination, the committee members would retire for about 15 minutes, after which they would return to the lecture hall and announce their decision as to whether the candidate had passed or failed the doctoral exam.

The members of my committee were Profs. Ginsburg (Chairman), Bergman and Kalugai. I was able to answer all the questions asked by the examiners, except one. Let me tell you about this question. In my thesis, in reviewing the literature in the introduction to the chapter on the triphenylene work, I mentioned that some X-ray measurements on the crystal structure of triphenylene "agreed fairly well with Coulson's theoretical calculations made by the molecular orbital theory". Prof. Kalugai asked me to explain "what was the molecular orbital theory". I was stunned by the question! I knew practically nothing about molecular orbital theory. To my very great embarrassment, I had no choice but to say so in answer to the examiner's question. You can imagine my trepidation while waiting for the return of the committee members from their deliberations. The committee returned after about 10 minutes, which to me seemed like 10 hours. The Chairman called me to the podium, congratulated me and announced publicly that I had passed the examination for the Doctor of Science degree. This was the first Doctorate in Organic Chemistry awarded by the Department of Chemistry at the Technion. I remember that I had tears of happiness in my eyes. However, I can tell you that when I speak of that moment even to day, nearly 50 years later, I can recollect the embarrassing and, for me, traumatic experience of that examination. It does not even help that, after the examination, Ginsburg told me he knew that Kalugai did not have the faintest idea of what molecular orbital theory was about and was merely asking for information!

E.A.H.—After finishing the doctorate you went to USA for post-doctoral research with Carl Djerassi. Why this particular choice?

When Ginsburg told me that I could start writing the thesis, he also asked me if I had any plans for what I was going to do after finishing the doctorate. I told him that I would very much like to continue in academia and was interested in continuing research on the chemistry of natural products. He said that there might be an opening in his department, but one of the necessary conditions for such a position was post-doctoral experience at a university abroad. He suggested that I apply for a post-doctoral fellowship, gave me the names of several scientists known for their work on nat-

ural products chemistry and suggested that I write to them. I applied for a post-doctoral fellowship to all of them, giving Ginsburg's name as reference and received several offers in return, among them one from Carl Djerassi, at that time a professor at Wayne State University in Detroit, MI. After consultation with Ginsburg, and upon his recommendation, I decided to accept Djerassi's offer, even though, financially, the stipend that he offered was the lowest one!

E.A.H.—How long did you stay with Djerassi and what did you work on with him?

Accompanied by my wife and 3 year old daughter, I arrived in Detroit towards the end of September 1955 and continued in Djerassi's group until September 1957. My major research project was the determination of the structure and absolute configuration of cafestol, a pentacyclic diterpene constituent of coffee. The work consisted partly in extracting cafestol from coffee oil, supplied by General Foods Company, from whom Djerassi had a research grant. I extracted gallons of coffee oil by soxhlet extraction. During these extraction operations the whole lab, and in particular my clothing and hands, were imbued with the aroma of coffee!

Djerassi's group at Wayne consisted of about 20 people, including doctoral students and post-doctoral fellows from all over the world. Djerassi would come in the lab twice a day, stopping to talk and discuss the work with every one in the lab. There was very good interaction among all the people in the group. Everybody was familiar with everyone else's work. We had weekly group seminars where we discussed the research going on in the lab as well as current topics in the chemical literature. Pioneering work was going on in the lab in the areas of mass spectrometry and optical rotatory dispersion as tools for the structural elucidation of natural products.

In September 1957, Djerassi decided to take a year's leave of absence to go to the pharmaceutical company Syntex Mexico, for whom he was a consultant on the development of the "pill". He took several of the people in his group to work with him at Syntex and he asked me to join him as well. I told him that I had planned to remain with him in Detroit for another year because my wife, who was working on her Master's Degree at the University of Detroit, needed another year to complete her studies. I explained to him that even though this was a very tempting offer, I would not leave my family alone in Detroit to go to Mexico and that, regretfully, I could not accept his offer.

E.A.H.—You went to work for Ethyl Corporation instead. Why did you choose Ethyl?

I already knew in the summer, the time when scouts from industry visit universities to interview graduating students for potential employment, that Djerassi would be away from Detroit. I took advantage of the occasion and presented myself to be interviewed by representatives of several companies in the Detroit area, one of which was Ethyl Corporation. In all of these interviews I explained, up front, that I was from Israel and was looking for a

temporary 1 year research position in organic chemistry. Ethyl Corporation was the only company that made me an offer of employment under these conditions. As you know, Ethyl at the time was—and probably still is—the biggest producer of tetraethyl lead (TEL), the anti-knock additive to car fuel. TEL was considered one of the main sources of pollution of the atmosphere, and Ethyl was very interested in finding new anti-knock agents to replace TEL or reduce its use. It was known that ferrocene, a new organometallic compound, which had been first reported by Pauson and Kealy, as well as another group, in 1951, had combustion-improving properties. Similarly, cyclopentadienylmanganese tricarbonyl, discovered by Wilkinson and Piper in 1955, was found to be a combustion-improver. By 1957, Ethyl Corporation had developed pilot-plant capabilities for the manufacture of cyclopentadienylmanganese tricarbonyl (a crystalline yellow-colored solid) and its derivative, methylcyclopentadienylmanganese tricarbonyl (a yellow-colored liquid). Ethyl wanted to investigate the organic chemistry of these two compounds, which were thought to be chemically similar to ferrocene. They wanted to test as many manganese-containing derivatives as possible for anti-knock properties as a potential substitute for TEL. I was asked whether I would be prepared to work on such a project. Even though the area of organometallic and coordination chemistry was a complete departure from the fields of chemistry in which I had worked before, the project seemed fascinating to me. The discovery of ferrocene had opened up an entirely new field in the area of organometallic and coordination chemistry. Moreover, I was offered a salary that was nearly three times as much as I was making from my post-doctoral fellowship! I was very happy to accept the Ethyl offer.

E.A.H.—In retrospect, it seems that Ethyl Corporation was instrumental in causing your entrance into coordination chemistry. Did your work at Ethyl progress well enough to have had this effect on you?

In retrospect, I think that agreeing to work for Ethyl was probably one of the most auspicious decisions I took on shaping the direction of my scientific career. Soon after I began work on the cyclopentadienylmanganese tricarbonyl project, I realized, from perusing the chemical literature, that I had before me a golden opportunity that rarely befalls a young chemist in the early stages of his research career. There were very few reported data on the chemistry of this new compound. This was probably due to the fact that preparing cyclopentadienylmanganese tricarbonyl in quantities sufficient for the investigation of its chemical properties was not an easy task. Here I was, having unlimited quantities of a rare starting material and the whole gamut of known chemical reactions of aromatic compounds before me. In addition, by this time, ferrocene chemistry had become abundant in the literature. All I had to do was to develop the right conditions to carry out with cyclopentadienylmanganese tricarbonyl reactions similar to those reported for *ferrocene*. I

had me a ball! I was running four or five reactions simultaneously. After work-up in the isolation and purification of the reaction products, I had several new compounds every week in sufficient quantities to send for chemical analysis as well as for anti-knock testing. I can say without equivocation that this was my most productive period ever in doing chemical work at the bench!

E.A.H.—What was the publication policy at Ethyl?

Like any other industrial company, Ethyl would allow publication only after it had taken the necessary steps to protect its intellectual property by submitting the appropriate patent applications. Here was an additional bonus for me in my experience at Ethyl. The company had an in-house patent department with several patent attorneys who would meet regularly with the research scientists to discuss their work and to determine whether there was any new patentable material. Due to my productivity in the lab, I had very frequent meetings with one of the patent attorneys to discuss my results and to go over draft patent applications with him. Because most of my compounds were new, and thus patentable, and because of Ethyl's interest in manganese compounds as potential anti-knock additives, Ethyl applied for patents on all of the compounds I prepared during my stay with Ethyl. This intensive interaction with the patent attorney enabled me to learn a great deal about the use of suitable patent language and the rules involved in preparing patent applications. Eventually 15 patents, with my name as co-inventor, together with Dr. John Kozikowsky, who was working in parallel with me on the chemistry of methylcyclopentadienylmanganese tricarbonyl, were allowed to Ethyl. This was not bad for 1 year's work! Especially so, since I was also remunerated with the proverbial One US Dollar for each patent allowed!

E.A.H.—Scientifically, this was an eventful year for you. Did anything else happen during this year that had a bearing on your future?

Several additional events that occurred during this year required me to make decisions about my future. David Ginsburg, with whom I had kept in touch, wrote to offer me an appointment as Lecturer in the Department of Chemistry at the Technion. I also had an offer to come and work with Frantz Sondheimer, who at that time was Head of the Organic Chemistry Department at the prestigious Weizmann Institute of Science. Additionally, Dr. Gus Liggett, the Research Director at Ethyl Corporation, had asked me to continue working at Ethyl with a promotion in grade and a raise in salary. The latter offer, though very enticing (a salary of four to five times higher than any offer from Israel), I rejected outright. Our daughter Daphna was approaching school age and, considering my past history, my wife and I were determined to live and bring up our children in Israel, where Jews would never be persecuted and discriminated against merely for being Jewish. I had to decide between Haifa and Rehovoth. On one of Carl Djerassi's frequent visits to Detroit from Mexico, to meet with his students who were continu-

ing their work at Wayne, I met with him to ask his advice. He knew both Sondheimer and Ginsburg well. Carl told me that if I go to Sondheimer, I would have to work only on topics of his choosing. On the other hand, Ginsburg would give me independence and encourage me to work in areas of my own interest. Obviously, I chose to accept Ginsburg's offer and we returned to Israel in September 1958. I never had reason to regret this decision!

E.A.H.—What happened to your expectation of research independence when you joined the Technion? Could you choose your own area of research?

First, let me mention that, while still in the States, I had received Ginsburg's permission to apply to the ACS-Petroleum Research Fund for a research grant. My application was approved, so I was able to bring my own research funds with me. This in itself established my research independence. My problem was to decide on the direction of my research program. As I mentioned before, natural products chemistry was the fashionable area of research. In addition, organic chemistry was dominant in Israeli chemical research. No one in Israel was doing organometallic chemistry research at that time. Indeed, for quite a few years I remained a "lone wolf" in Israel carrying out research in this area.

I must mention here that before I left Detroit, Ethyl Corporation had agreed that if I wanted to continue investigating the chemistry of cyclopentadienylmanganese tricarbonyl and its derivatives in Israel, they would supply any quantities of starting materials I required. Ginsburg encouraged me to continue working in this field. He too was aware that organometallic chemistry was a rapidly expanding field of research and was glad to have someone in his department working in this area. Nevertheless, I was not yet ready to stop working on some topic connected with natural products chemistry. So, I entered into a collaborative research project with Ginsburg on the isolation and characterization of the constituents of *Catha Edulis*, a plant that was presumed to have narcotic properties. My first doctoral student at the Technion, Asher Mandelbaum, the top student in his class, agreed to take this topic for his thesis. As you know, Asher subsequently joined the staff of our department and became our expert on mass spectrometry. He retired as Professor Emeritus last year.

E.A.H.—How many people did you have working with you to start with?

I had a good start. In addition to Asher, I had two research assistants supported from the PRF research grant funds. I also had my own work bench in the lab and managed to do quite a bit of chemistry myself.

E.A.H.—You said you were "a lone wolf" in organometallic chemistry in Israel. What contacts did you make with scientists abroad in this field?

My first direct contacts were made in September 1959 when I attended the XVIIth IUPAC International Congress in Munich, Germany. I presented a paper on the UV Spectra

of Organometallic Compounds on work carried out jointly with Richard Lundquist while still at Ethyl Corporation. In fact Ethyl paid for my travel expenses to Munich. At this congress I had the opportunity to meet and talk with many of the leading people working in the field of organometallic chemistry. In particular, I became friendly with E.O. Fischer and Peter Pauson, a friendship that continued for many years. Subsequent to this Congress, I began to attend the International Conferences on Organometallic and Coordination Chemistry regularly and got to know, and make friends with, many colleagues in these fields, world-wide. I was invited to participate in the meetings of the International Organizing Committee of these Conferences, as the representative of Israel. All of these contacts helped me eventually to bring the XIth ICCG to Israel in 1968.

E.A.H.—We'll come back to the XIth ICCG later. Let us talk some more about your research. I notice that one of your early Visiting Appointments was at the Institute of Pharmacology in Bonn, Germany. Why there?

In 1961 I initiated a joint research project with Prof. William Taub, of the Weizmann Institute of Science, on the synthesis of a new class of delta-lactones. Taub, a leading scientist in Israel on Pharmaceutical Chemistry, also held an appointment as Visiting Professor at the Technion, where he taught a graduate course every year on the chemistry of pharmaceutical compounds. We also collaborated on this project with Prof. Domenjoz, Head of the Institute of Pharmacology at the University of Bonn, who was testing the pharmacological properties of our compounds. At about the same time, I had been asked to serve as secretary and coordinator of the Pharmaceutical Committee of the Israel National Research Council. One of my tasks in this extracurricular activity was to investigate and prepare a report on the feasibility of setting up pharmacological testing facilities in Israel to serve the country's pharmaceutical industry. Visiting with Domenjoz was very helpful in the preparation of my report. What's more, during my 3-month stay in Bonn, I even had the opportunity to do some work in the lab and managed to get enough results to publish a paper with Domenjoz.

Let me tell you an amusing story in connection with my service on the National Research Council. In the summer of 1962, I was invited to present a paper at an International Symposium on "The Theory and Structure of Complex Compounds" in Wroclaw, Poland. At that time Poland was part of the Soviet bloc and, as an Israeli citizen, I was worried about traveling to Poland. I happened to talk about this at one of the National Research Council meetings. The Chairman of the Council told me that I should not worry, he had a solution for me. As a member of the Council, which was a Government institution, I was entitled to travel on a diplomatic passport and he would recommend that I receive one. So, for 1 year, I enjoyed the perks and benefits of traveling on a diplomatic passport!

E.A.H.—Let's return to organometallic chemistry. What were the next milestones in your progress?

Perhaps I should first mention some personal, non-chemical milestones. In 1961, I was given tenure and promoted to the rank of Senior Lecturer, followed 3 years later by promotion to Associate Professor and then, in 1968, to Full Professor. Also, a mundane but important event: in the summer of 1964, the Chemistry Department moved from the old, mid-town Technion campus, to its own, very spacious building on the new campus, that was being built at that time, on the eastern slopes of Mount Carmel. As you know, this was the largest, best equipped and most imposing building on the new campus. This achievement was due mostly to Ginsburg's standing on the Technion Faculty and to his talent for soliciting funds from donors, members of Technion Friends Societies throughout the world. I was given an office and two laboratories with room for about 10–12 research students. It did not take too long to fill up this space with graduate students who chose to work with me for their master's and/or doctoral degree, as well as with post-doctoral fellows, whom I could support with funds received from two major 5 year grants that I had obtained from the US Air Force and the US Department of Agriculture for research in organometallic chemistry. Another important event for me was my forthcoming sabbatical at the California Institute of Technology.

E.A.H.—How did you come to choose CalTech for your sabbatical?

As you know, the employment conditions at the Technion entitle the academic staff to take a paid sabbatical year after each 6 year period of teaching and research. I was due for a sabbatical for the 1965–1966 academic year. In 1964, for the inauguration of our new building, Ginsburg organized an international symposium, attended by many distinguished chemists from all over the world. One of these distinguished visitors was Jack Roberts, at that time Head of Chemistry at CalTech. I discussed with him the possibility of my coming to CalTech on sabbatical leave. He told me he would be glad to arrange such an appointment for me but said that he did not have the funds to support my stay there. I explained to him that I did not require any funds, because I had fortunately just received a PRF Faculty Award from the American Chemical Society, and could use it for any research purpose I desired. I assured Jack that this award, together with my sabbatical leave stipend, were enough to support my stay at CalTech. Upon his return to Pasadena, Jack Roberts sent me confirmation of a Visiting Appointment at CalTech for the 1965–1966 academic year. Accompanied by my wife and two daughters, I arrived in Los Angeles in September 1965. We rented an apartment in Hollywood, one block from a school for the children and half way between UCLA, where Judy had enrolled to attend classes in linguistics, and Pasadena, where CalTech was located.

E.A.H.—Tell us about your sabbatical at CalTech and why was it important to you?

First, I wish to mention that I was given a very warm welcome at CalTech by the Chemistry Department staff in

general and by Jack Roberts in particular. I was given a nice office furnished with a large desk, which—I was told—had been Pauling's desk!

The major reason for choosing CalTech was because I had decided to use my sabbatical to “go back to school”. I thought that CalTech, one of the most famous schools in the world, would be ideal for my purpose. I felt that after 6 years of hectic activity to establish my position at the Technion, I needed a pause in which I would devote time to filling in some gaps in my own chemical education. The “trauma” of having failed to answer the molecular orbital question in my doctoral exam 10 years earlier was still on my mind and I had to do something about it.

After settling in at CalTech, I requested permission from various faculty members to attend their regular courses for both undergraduate and graduate students. For example, I took such courses as theory and practice of NMR, quantum chemistry, group theory, chemical reaction mechanism and some others. I learned how to use the computer (at that time data were entered by means of punched cards) for carrying out simulations of NMR spectra and doing Huckel molecular orbital calculations. In addition, I attended departmental as well as group seminars, and lectures by visiting scientists. Altogether, I had a very busy schedule and enjoyed myself immensely. I even collaborated with John Richards and one of his Ph.D. students, in a study of NMR spectra of alpha-ferrocenylcarbonium ions. I was also busy maintaining a regular correspondence with my group at the Technion. I had arranged for one of my post-doctorate fellows, Dr. Dennis Dell, to be in charge of my group and to send me monthly progress reports from each one of the 10 co-workers in my group.

One of the highlights of my sabbatical was an invitation to lecture on my work on alpha-ferrocenylcarbonium ions at one of the famous Winstein Seminars at UCLA. These seminars began at 7 P.M. with a 1-hour lecture by the invited speaker, which was followed by questions from the audience and discussion that continued until around midnight. I assure you that this was an unforgettable experience! To be “grilled” on your work for 4 hours by some of the best minds in the chemical world and to end up feeling good about yourself is something that is not easily forgotten!

The last thing I did at the end of my sabbatical was to make a stop in Sweden on my way back to Israel. I had enrolled to attend a 3-week Lowdin workshop on theoretical chemistry in Abisko. I must make it clear that I had neither the intention nor the inclination to become a theoretical chemist. I did not have the necessary qualifications for this. My purpose was simply to add to the education acquired in my studies at CalTech. I am sure I did gain from attending this workshop and I can say that, all in all, Abisko was a very interesting intellectual experience. Perhaps I should add that I also enjoyed having had the opportunity to experience the phenomena of “midnight sun” and the “twenty-four hour day of continued daylight”!

E.A.H.—I know that after your return home from sabbatical you became involved in a number of extra-curricular, chemistry-linked, activities. Will you tell us about them?

The heaviest responsibility awaiting me upon my return to Haifa was to start work on the preparation and organization of the forthcoming International Conference on Coordination Chemistry (XIth ICCC) due to take place in Israel on September 8–18, 1968. I felt that this forthcoming conference was going to be of paramount importance to the development of coordination chemistry research in Israel. I worked very hard on this project for nearly 2 years and, with your permission, I would like to go into it at some length.

The first priority was finding the necessary financial support for the conference. I contacted all of the five universities in Israel, a number of Israel Government Ministries, The Israel Academy of Sciences, The National Council for Research and Development and the Israel Atomic Energy Commission. I claimed that the ICCC would be the most important international scientific conference to take place in Israel to date. My arguments must have been convincing because I received firm financial commitments and pledges from all the above organizations. These commitments, together with the expected income from participation fees, assured the conference budget. The Israel Chemical Society and IUPAC, the International Union of Pure and Applied Chemistry, were co-sponsors of the conference. The organizing committee of XIth ICCC included David Ginsburg as Honorary President, me as Chairman of the Conference, Frank Herbstein as Secretary, and one representative from each of the five Israeli universities. The conference was to take place at two venues: 8–12 September in Haifa and 15–18 September in Jerusalem. Izhak Marcus, of the Hebrew University of Jerusalem, as co-Chairman was responsible for the Jerusalem part of the conference, which was held jointly with the Fifth International Conference on Solvent Extraction Chemistry (Vth ICSEC).

The previous ICCCs had established a successful organizational framework for these meetings and many traditions had evolved. Nevertheless, I thought that perhaps time was ripe to experiment with some changes in the structure of the conference program. We decided to emphasize a few selected topics by organizing plenary symposia with contributions from a panel of five speakers and to allow ample discussion time for audience participation. Each symposium would consist of one main lecture (40 minutes) followed by four shorter lectures (20 minutes each). After a coffee break (20 minutes) the plenary would reconvene for the discussion. The five previous speakers would then become a discussion panel, which would answer questions and comments from the floor. Previously appointed discussion leaders would lead the discussion. We selected three topics for three plenary symposia in Haifa and two topics for two plenary symposia in Jerusalem. We also had three 1-hour plenary lectures, two in Haifa and one in Jerusalem. The plenary lectures and symposia were held in the morning sessions. In addition, about 150 invited papers (20 minutes each) were

presented in afternoon parallel sessions, four in Haifa and two in Jerusalem.

E.A.H.—How did you select the topics for the conference and for the symposia?

The choice of topics for the symposia and plenary lectures was partly governed by the results of an opinion poll conducted among coordination chemists throughout the world. The first circular of the XIth ICCC was distributed during April and May, 1967, to more than 2500 chemists. We requested recipients, irrespective of whether or not they planned to attend the conference, to make four selections in order of preference from a list of eight topics that were being considered by us for our conference topics. By December 1967 we had received about 600 replies from 35 countries, in which 95% of the respondents indicated the intention to participate in the XIth ICCC. This was a gratifying result in itself, considering the turmoil which had just occurred in our geographical part of the world.

E.A.H.—Are you referring to the June 1967 “Six Day War”?

Yes! You remember the tension and fear that were prevalent in our country at that time. Every one thought that war against Israel was imminent. Let me give you an illustration of the atmosphere by recalling a personal example. At that time my research grant from the US Department of Agriculture was in progress, and one of their senior scientists, Dr. E.N. Frankel, had joined my group as Visiting Scientist in September 1966 for a 1 year stay, accompanied by his wife and five children. At the end of May 1967, the situation had grown so tense that Dr. Frankel decided to return to the USA immediately. He and his family sailed by ship from Haifa to New York. By the time he landed in New York, 2 weeks later, the “Six Day War” was over! Upon landing, Dr. Frankel sent me a cable that he wanted to return to Haifa to complete his 1 year stay. He came back, this time without his family and continued his work in my lab for the remaining three months of his originally intended stay.

I believe that the above example gives an illustration of what might have occurred in the minds of the potential participants between the receipt of our conference first circular in May 1967 and their subsequent confirmation of intention to participate in the conference.

E.A.H.—What sort of response did you get from the scientists you wanted to invite for the plenary and symposia main lectures?

The response was tremendous. Not only from the scientists invited for the main lectures, but also from most of the leading coordination chemists from all over the world, who were willing to participate in the conference whether invited to present a paper or not. I would like to mention some names. I apologize in advance to all those whose names deserve mention but are omitted because of my poor memory.

Among the main plenary lecturers we had Manfred Eigen, Gottingen (Germany) (subsequently a Nobel Laureate), Arthur Adamson, Los Angeles, USA, Albert Eschen-

moser, Zurich, Switzerland, Jack Halpern, Chicago, USA, Owen Mills, Manchester, UK, Henry Freiser, Tucson, USA, Leonard Katzin, Argonne, USA.

Additional names of participants in symposia and session lecturers: E.O. Fischer, Munich (subsequently a Nobel Laureate), J.C. Bailar Jr., Urbana, Stan Kirschner, Detroit, Larry Dahl, Madison, Ron Nyholm, London, Joe Chatt, Birmingham, Gordon Stone, Bristol, Paul Heimbach, Mulheim, Leslie Orgel, San Diego, Jannik Bjerum, Copenhagen, Ugo Croatto, Padova, Fausto Calderazzo, Pisa, Umberto Beluco, Padova, Luigi Sacconi, Florence, Jan. Reedijk, Leyden, Kazuo Yamasaki, Nagoya, and many others. We received a total of 252 abstracts for the Haifa sessions and 61 abstracts for the Jerusalem part. The Proceedings of the Conference, which included all of the abstracts submitted, were published by Elsevier Publishing Company in a hard cover, 850-page, book titled “Progress in Coordination Chemistry”. This book was distributed to all the conference participants and could also be purchased from Elsevier.

E.A.H.—Having participated in the Conference I can testify that XIth ICCC was an exceptionally successful meeting. In retrospect, to what do you attribute this success?

Thank you for your compliment and for your question. I would like to address my comments, in particular, to those readers who might become involved in the organization of future conferences; they may find this information to be of some use to them.

First and foremost, I attribute the success of the conference to the participation of a very high number of leading coordination chemists and to what I believe was the high scientific level of the papers presented by the participants. I would like to take this opportunity to express again my deepest appreciation and grateful thanks to all the participating scientists for their contribution to make this conference a success.

An additional factor which, I believe, contributed to the success of the conference was the very rich social program that we had organized for all the participants, not only for “accompanying persons”, as is customary at such meetings. This was made possible by the generous financial sponsorship I had managed to obtain prior to the conference. To start with, the registration fee for active participants was only US \$20.00 per registrant and US \$8.00 per accompanying person. (Compare this to current registration fees of US \$500 and more.) All the registrants were entitled to receive free tickets for nearly all the events, including transportation on the shuttle service between hotels and the conference location, the social functions and all but two of the nine excursions: (1) an archeological visit and beach party followed by a gala performance in the excavated Roman Amphitheater at Caesarea on the shore of the Mediterranean Sea (US \$8.00/person), and (2) the conference banquet (US \$7.00/person). The following events were offered: on Sunday evening, 8 September, the opening ceremony and reception by the President of the Technion—Israel Institute of

Technology; on Monday, an evening reception by the Mayor of Haifa, followed by a Folklore Show; on Tuesday morning a fashion show for the ladies program; on Tuesday evening, all the foreign participants (over four hundred of them), in groups of 10–12, were invited to spend the evening and have dinner in an Israeli home (this was the first time such an event occurred at an international conference); on Wednesday afternoon and evening, the Caesarea outing; on Thursday morning the ladies program provided a visit to a Women's Army Base. The Conference Banquet took place on Thursday evening. On Sunday, 12 September, the Jerusalem part of the conference was opened with a lecture on "Masada" by Prof. Yigael Yadin, the famous archeologist who had been responsible for the excavations at Masada. Following the lecture, there was a reception by the President of the Hebrew University of Jerusalem. On Tuesday the participants were invited to a reception by the Mayor of Jerusalem at the Israel National Museum, which included a tour of the museum.

The 3-day interval between the Haifa and the Jerusalem sessions (Friday, 13 September to Sunday, 12 September) was left free, in order to enable participants in the conference to join excursions and sightseeing tours offered by the official travel agency appointed by the conference.

E.A.H.—What happened after the conference?

On the day after the conference ended, I took my family to Eilat and spent a whole week on the beach. Believe me, I needed a rest! Upon our return to Haifa, I still had some work to do winding up the affairs of the conference, such as preparing an audited financial report for the sponsors. I was pleased to be able to report that we had stayed within the budget and even had a small surplus.

Most important for me was being able to resume full contact with my research group. There was only one more extra curricular activity to which I had to devote some of my time: In September 1967, I had been elected President of the Israel Chemical Society for a 3 year term. This was not a full-time position and I had no problem coping, especially compared with the work involved in organizing the conference.

E.A.H.—In 1970–1971, you went for your sabbatical to the Synvar Research Institute, in Palo Alto, CA. Why did you make this particular choice?

My research in organometallic and coordination chemistry was progressing quite satisfactorily. However, for some time I had begun to recognize that an important area in chemical research was evolving in the direction of bio-organic and bio-inorganic chemistry. More and more I was driven to the idea that, considering my background in natural products chemistry and experience in organic synthesis, I should find an entry into research in this developing field.

I learned of Synvar from two of our colleagues in the Chemistry Department who had gone there on sabbatical as Visiting Research Fellows. The Synvar Research Institute had been set up as a joint venture between Syntex, the pharmaceutical company, and Varian, the instrument makers, both located in Palo Alto. The declared aims of Synvar

were, among others, to use the principles and knowledge of chemistry, physics and biology in the development of novel analytical methods with potential industrial applications. I also learned that one of the areas of research at Synvar was the development of non-radioactive methods for immunoassays and thought that this might be an interesting vehicle for my entry into the field of bio-organic and/or bio-inorganic chemistry.

The Research Director of the Institute was Dr. Ted Ullman, whom I did not know personally at the time. However, one of the most influential members of the Board of Directors at Synvar was Carl Djerassi, who—in the meantime—had moved to Stanford University as Professor of Chemistry and was still strongly connected to Syntex. I wrote to Carl to enquire about the possibility of spending my forthcoming sabbatical at Synvar. He replied that he would be glad to support and recommend my appointment as a Visiting Research Fellow at Synvar. Not surprisingly, with Carl's recommendation, my application to Synvar for such an appointment was approved, and in August 1970 I arrived in Palo Alto accompanied by my family.

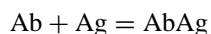
E.A.H.—What work did you do at Synvar?

One of the major areas of research at Synvar was the use of stable nitroxide radicals as spin-labels for the qualitative and/or quantitative detection by electron spin resonance (ESR) of various substrates in biological fluids. The idea was to replace the radioactive isotopes used in radioimmunoassay (RIA) by stable nitroxide radicals and thus remove the hazards of working with radioactive materials. Instead of using gamma- and/or beta-counters to measure the radioactivity in the analytical process, one would use an ESR instrument to detect and measure the spin-label signal. This was very much in the interest of Varian, one of the major makers of ESR instruments.

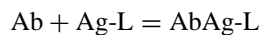
E.A.H.—Let me interrupt you at this point. Some readers of this interview, including myself, may not be too familiar with the area of immunoassay. Would you give us a few definitions and a brief description of the principles involved in the development of an immunoassay? I assume that this would also answer my previous question about the kind of work you did at Synvar.

Antigens (Ag) are substances which, upon introduction into the body of an animal species, trigger the formation of antibodies (Ab). Antibodies are glycoproteins formed in pertinent cells of the organism on intrusion of antigenic substances. Antisera are sera that contain antibodies. Haptens are small molecules (mol. wt. <5000) that exhibit antigenic properties only when covalently bonded to a macromolecular carrier.

The specific recognition and binding of an antigen by an antibody with sufficient binding affinity forms the basis of the immunological reaction equilibrium:



If the antigen Ag is replaced by a labeled antigen Ag-L, it is possible that a similar equilibrium will be established:



provided that the label L does not cause immunological changes in the antigen, i.e. that the antibody Ab exhibits equal—or very nearly equal—recognition of both the unlabeled antigen (Ag) and the labeled-antigen (Ag-L). In this case, the binding constant (or affinity constant), K is the same, or very nearly the same, for the complexes AbAg and AbAg-L. If mixtures of variable amounts of antigen (Ag) and a constant amount of the labeled antigen (Ag-L) are allowed to compete for a limited and constant concentration of antibody-binding sites, the reaction mixture—upon equilibration—will consist of a “free” antigen phase (unbound Ag and Ag-L) and a “bound” phase of antibody–antigen complexes (AbAg and AbAg-L). After separation of the two phases, the amount of label present in either the “free” or the “bound” phase is determined by the appropriate analytical method. Preparation of a calibration curve, plotted for standardized amounts of labeled antigen and unlabeled antigen, provides the means of determining the quantity of analyzed substance in unknown samples.

The work in this area at Synvar comprised the following steps in the development of a spin-label immunoassay: (1) synthesis of suitable stable nitroxide radicals to be used as spin-labels; (2) attachment of the spin-labels, by the methods of organic synthesis, to hapten molecules which would subsequently be analyzed for their presence in biological fluids; (3) attachment of the hapten molecule by a covalent bond to a high-molecular-weight compound found in the serum of animal biological fluids, for example bovine serum albumin (BSA), to obtain the antigen; (4) immunization of animals such as rabbits or sheep by injection of a solution of the antigen, to produce and then isolate antibodies produced in the serum of the animals. These antibodies were then expected to specifically recognize the presence of the analyte molecules in human biological fluids, such as urine or blood serum; (5) utilization of the reagents produced in (1)–(4) to develop the immunoassay protocol, as described above.

In the protocol using the ESR system, an aqueous solution containing appropriate known amounts of specific antibodies and spin-labeled hapten was titrated with increasing amounts of the unlabeled hapten. After an incubation period, a precipitating agent was added to the reaction solution to induce precipitation of the high-molecular-weight antibody. The precipitate, which contained the “bound” fraction, was separated from the liquid by centrifugation. The supernatant liquid, containing the “free” fraction was monitored with the ESR instrument to determine the amount of competitively displaced spin-labeled hapten. The absence of “free” (non-antibody-bound) labeled analyte ESR signal in the supernatant liquid indicated that no unlabeled analyte had been present in the urine or serum sample to compete with the spin-labeled analyte in binding to the antibody. In other words, the result was a negative test. An ESR signal in the su-

pernatant liquid showed the presence of “free” spin-labeled analyte. This indicated that competing unlabeled analyte had been present in the original urine or serum sample, and was therefore a positive test. A semi-quantitative result could be obtained by running appropriate calibration curves.

Without going into further detail, I worked on all the above steps, except the immunization of animals. The latter step was carried out on a special animal farm owned by Synvar, somewhere in California. My project was to develop a spin-label immunoassay for the detection of barbiturate metabolites in human biological fluids. I must say that I really enjoyed working again full time at the bench. The work progressed quite well. I could follow and apply general procedures which had already been established in previous work at Synvar. By that time, the researchers at Synvar had advanced very far in the development of a spin-label immunoassay for morphine metabolites in both urine and blood serum. In fact they were already testing for morphine in urine samples of heroin addicts, collected from drug rehabilitation centers. By mid-1971 Synvar had a well-tested working spin-label immunoassay for the screening of urine samples from suspected heroin users. The test was able to detect the presence or absence of morphine metabolites.

The success of this test came to the attention of the Pentagon authorities, who at that time had a serious problem with identifying heroin addicts among the returning veterans from Vietnam before their return to the States. The Synvar urine spin-label immunoassay appeared ideal for large screening operations, so Synvar was offered a contract to send a team to Vietnam to set up screening operations among the American troops. The Synvar team took an ESR instrument with them and was able to carry out the screening of many thousands of soldiers over a period of several months. The success of this operation was a turning point in the future development of Synvar. Subsequently, Synvar was incorporated as a company and changed its name to Syva Corporation, because the name Synvar had already been appropriated by a synthetic varnish company. Within a relatively short time, Syva became successful in the manufacture and sale of spin-label immunoassay kits for the detection of a large number of metabolites, including the barbiturates on which I had been working during my stay at Synvar.

E.A.H.—How did the work you carried out during your stay at Synvar meet your expectations of entering a new field of research?

I remained at Synvar until August 1971. While doing work on the bench on the immunoassay project, I also spent many hours reading as much as possible on the subject of immunology, a completely new area for me. During all this time I was trying to think of a way to connect this new knowledge I was acquiring to my expertise in organometallic and coordination chemistry. One day an inspired thought flashed through my mind: If one could use spin-labels to develop non-radioactive immunoassays, why not use non-radioactive metal atoms as labels in non-radioactive immunoassays? The

metal atoms, in the form of their organometallic or coordination derivatives, could be attached to analytes by suitable chemical reactions, just as the stable nitroxide radicals were being attached for use in the spin-label immunoassays. Instead of utilizing ESR for detection of the label, one could employ one of the many analytical methods already available for the detection of metal atoms. I became very excited by this idea. I went to discuss it with Ted Ullman and to ask if Synvar might be interested in collaborating with me in this area of research. Ted thought that it was an interesting idea but did not believe that it was compatible with the expertise at Synvar and its research programs. However, he said, Synvar would be interested in entering into a collaboration with me, after my return to Israel, in the development of additional spin-label immunoassays, such as, for example, the detection of marijuana and hashish metabolites in the urine of users of these drugs. I gladly agreed to this proposition, because it provided me with a mechanism to continue working in this new field and to prepare the ground in my laboratory for work on my new idea. We agreed that Synvar would cover half the cost of a Varian ESR instrument for my laboratory in return for my submitting regular progress reports to Synvar on the spin-label research. We also agreed that I was free to work on the idea of metal-labels without any obligation towards Synvar.

E.A.H.—What happened after your return from your sabbatical?

We returned to Haifa in September 1971 not knowing beforehand that I would be faced by a surprising development. Some of my colleagues suggested to me that I should submit my candidacy in the forthcoming November elections for Chairman of the Department of Chemistry for the term beginning 1 January 1972. I was very reluctant to do so because I knew that the position was very demanding. I did not like the idea of a full-time job doing administrative work. Furthermore, I was afraid that this would interfere with my research plans, in particular with my intention to set up the new immunoassay project. I want to remind you, Amitai, that I turned to you and asked that you should be the candidate to stand for election as Department Chairman. For your own good reasons, you refused to do so and tried to convince me that I should be a candidate. David Ginsburg, who had been Chairman for many years, put a lot of pressure on me to accept the candidacy. I agreed finally and was elected Department Chairman, a position I held for the years 1972–1976. I believe I did a reasonably good job but—in retrospect—I think that this was the most difficult period of my life in academia. Remember that during that time we also went through the traumatic experience of the 1973 Yom Kipur war!

E.A.H.—I know that in spite of taking up this new position you did proceed with your plans to initiate the immunoassay program in your lab. How did you go about it and what happened to your other research projects?

The organometallic chemistry research was coming along very well. We were getting good results in the work on the catalytic properties of arenechromium tricarbonyl complexes in the stereospecific and regioselective hydrogenation of conjugated dienes. Need, I remind you that you were my consultant on reaction kinetics and that the two of us published a joint paper on one of the hydrogenation topics?

The work on alpha-ferrocenylcarbonium ions was very productive. A milestone in this work occurred when one of my doctorate students, Sanda Dani, managed to obtain a stable crystalline salt of such a carbonium ion, and we were able to determine its crystal structure in collaboration with Frank Herbstein, the crystallography expert in our department. About half of the people in my group were working on these and related topics. The other half agreed to help me set up the immunoassay project and begin research in this area.

My aim was to become self-sufficient in all the various facets of the project. I was glad to associate Dr. Harriett Gershon, the immunology expert in the Technion's School of Medicine, as consultant to the project. With her help we set up an animal room on the roof of our building, with 24 rabbit cages, for immunization in the production of antibodies. All the students and technicians working on the project were required to undergo training in the immunization of the rabbits, collection of the blood and isolation of the anti-sera.

In January of 1972, as agreed with Synvar, we received the ESR instrument from Varian. Everyone in my group was trained to use the ESR machine and to carry out calibration curves with the nitroxide spin labels. Alfred Modiano, one of the more experienced technicians in my group, learned to synthesize the various nitroxide radicals needed for our work.

By agreement with the Haifa branch of the Department of Drug Control in the Ministry of Health, I received a permit to obtain various kinds of abusive drugs from pharmaceutical companies and store them in a special safe in the laboratory. They included barbiturates, methadone, amphetamines and kilogram quantities of hashish, the last from the police stocks of confiscated drugs for use in our research; I had to submit monthly reports to the Ministry of Health on the amounts of drugs used in experiments during that month.

We set up facilities for the extraction and isolation of the cannabinoid constituents of hashish. I already had experience with such extractions from my work on *Catha Edulis*. We also collaborated on the hashish work with Prof. Raphael Mechoulam of the Hebrew University of Jerusalem, who was the first to synthesize tetrahydrocannabinol (THC), the active constituent of hashish and marijuana. He sent us samples of various THC derivatives for comparison with the products that were isolated and synthesized in our laboratory.

We were now ready to proceed with the development of a spin-label immunoassay for the detection of hashish and marijuana metabolites in the urines of users of these drugs.

E.A.H.—How successful were you in developing this assay, and how long did it take you to complete this project?

Remember that we started the immunology work from scratch. The chemical work was no problem. The most important aspect was the production of specific antibodies for the recognition and binding of cannabinoid derivatives. We knew from reports in the literature that a number of laboratories in Europe, USA and Canada were trying to develop such antibodies. Some of these reports stated that they may have developed antibodies, but they were of rather low specificity and not suitable for the development of an immunoassay. This was rather discouraging, but on careful perusal of these reports I noticed two interesting points: first, all these reports emanated from biological laboratories; second, the experimental descriptions in these reports convinced me that the researchers involved were not chemists with experience in the isolation of pure compounds from natural products. I came to the conclusion that the low specificity of their antibodies was due to their having used impure mixtures of antigens in the immunization process. Consequently, I instructed my coworkers to pay very careful attention to the various purification and characterization steps in the preparation of the cannabinoid antigens used for immunization of our rabbits. My assumption must have been correct, because we obtained antibodies of very high specificity. In fact, following publication of our data, Dr. S.P.M. Lems, of the Immunochemistry Department, Central Laboratory of The Netherlands, Red Cross Blood Transfusion Service, informed us that he was carrying out comparative studies of cannabinoid anti-sera from various laboratories in Europe and requested samples of our anti-sera for inclusion in his tests. Subsequently, Dr. Lems reported to us that our cannabinoid anti-sera were found to be the most highly specific of all the anti-sera tested.

To cut this long story short, once we had good antibodies, we felt we had in our hands the means of developing a working spin-label immunoassay for the detection of hashish and marijuana metabolites. It took us about 2 years to complete all the various aspects of the production of a satisfactory free radical immunoassay, and to be confident enough to publish our results jointly with Mechoulam and Gershon in FEBS Letters in July 1975. Naturally, during all this time we fulfilled our obligation to Synvar, who were kept fully informed of our progress through quarterly reports. Eventually, Syva marketed their own spin-label immunoassay kit for the detection of hashish and marijuana metabolites in urine.

E.A.H.—When did you start working on your concept of using metal-labels in immunoassays?

We decided from the start that in parallel with the work on the spin-label work we must also begin working on the metal-labeling project. In order to develop a strategy to prove the feasibility of the concept, we had to decide on an approach to two major problems in the task before us: (1) choice of the analytical method to be used in the assay for metal detection and (2) the development of suitable chemical reactions for the attachment of coordination metal com-

plexes to various types of organic compounds known to be analytes in existing immunoassays.

The analytical methods under consideration were emission, absorption and fluorescence spectrometry, electrochemical methods, neutron activation, etc. The method of choice for us was atomic absorption spectrometry (AAS). Our department possessed two flameless-operation AAS instruments: a Perkin-Elmer 403 with HGA-70 graphite furnace and deuterium background corrector as well as an Instrumentation 351 with 455 flameless unit and programmable calculation data system kit. These instruments were available for use by my research group. In addition, we had the benefit of expert advice by Prof. Magda Ariel, from the Analytical Chemistry section in our Department. I insisted that everyone working on the metal-label project become proficient in the use of the AAS instruments.

As model analyte compounds in the chemical work, we chose the steroid hormones estrone, estradiol and estriol, barbiturates, such as phenobarbitone and seconal, and cannabinoid derivatives. We prepared our own antibodies to these compounds. The extensive chemistry of transition metal-organic complexes that had been developed in the previous two decades provided a rich and versatile source for the synthesis of “metal-labeled” haptens and antigens. We were able to produce metal-labeled analytes, which we designated metallohapten and/or metalloantigen, by attaching a variety of metal complexes to the above-mentioned model analyte molecules. To give several examples, we attached Fe atoms by means of ferrocene derivatives; Mn atoms through cymantrene derivatives; Pt and Rh atoms through cyclooctadiene-acetylacetonate complexes; Pt and Pd through functionalized *ortho*-catecholato complexes; Cr and Co atoms through functionalized *tris*-acetylacetonate complexes.

We thus had in our hands the components required to begin testing the feasibility of the metal-label immunoassay concept. After much hard work and many problems, we were able to show that the concept was feasible, and in October 1977 we sent a communication, entitled “Metalloimmunoassay”, to the prestigious journal *Nature*. This article summarized over 5 years of work by many co-workers, graduate students and post-doctorate fellows. All of them, nine in all, were named as co-authors of this communication. To our delight, after only 3 weeks we received notification that the article had been accepted for publication without any comments by referees requesting revisions and/or corrections! The article was published in the 8 December 1977 issue of *Nature*.

The publication of Metalloimmunoassay (MIA) in *Nature* was timely for us. Bio-inorganic chemistry was becoming a very fashionable research area, in particular due to Prof. B. Rosenberg’s discovery of the anti-tumor properties of platinum complexes. I thought that our experience in developing methods for binding metal complexes to haptens and antigens might find applications in this interesting field as well.

In October 1978, I visited Prof. Rosenberg at Michigan State University in East Lansing to discuss with him some of my thoughts on this subject. For example, one of the ideas I suggested was the possibility that binding a *cis*-platinum complex to an estrogen steroid molecule might provide a “magic bullet” that would be selectively recognized by the estrogen receptors on the tumor cells in breast or ovarian cancers. Rosenberg was receptive to these ideas and encouraged me to go ahead with research in this direction. Our own facilities to do work in this field were quite limited and we lacked the necessary expertise. Consequently I entered into collaboration with several groups. In fact, this was the reason for my Visiting Appointment at the Memorial Sloane-Kettering Cancer Center in New York for 3 months in the summer of 1979. I asked Moshe Shimoni, a talented and industrious doctorate student, to come with me and, in collaboration with several of the scientists at Sloane-Kettering, we synthesized mercury derivatives of estradiol and tested their selective recognition by estrogen receptors in mammary-tumor-bearing rats. We did not get conclusive results because of difficulties in the determination of mercury by atomic absorption. However, in 1982 we repeated some of this work in collaboration with a group in Israel led by Dr. J. Shani, using radioactive ^{203}Hg in preparing the mercuriestradiol derivatives. The results showed conclusively that the selective accumulation of mercury in the mammary-tumor tissue of the tested rats was greater by a factor of more than 10 compared to other tissues. In fact, the paper reporting these results was awarded the first prize in the competition for the Genia Czerniak Award in nuclear medicine and radiopharmacology, held in Israel in 1982.

E.A.H.—Let’s go back to the development of MIA. You mentioned that you encountered problems in this development. What were these problems and how did you overcome them?

As I said, we encountered many problems. Some of the major ones were inherent in the protocol of an immunoassay. If you remember, the end point of such a protocol involves determining the relative proportions of the “free” and “bound” labeled reagent, after the physical separation of these two fractions. A variety of methods to separate “bound” from “free” fractions had been described in the literature. However, the large majority of the practical methods available required the addition of a precipitating or adsorbing reagent after the primary incubation step, to be followed by incubation, centrifugation and the decantation steps. For the MIA system, the required addition of a precipitating reagent constitutes a highly critical and error-prone step, since the reagent must be ultra-pure insofar as metal ion content is concerned. The analytical method in MIA, as in other immunoassay systems, must determine the labeling-metal atom content in concentrations of $\mu\text{g/ml}$ or lower. Consequently, the introduction of any additional reagent into the protein-binding reaction system carries with it the danger of contamination with the same metal atom or ion being used for the labeling of the antigen.

In a flash of inspiration, it occurred to me that a potentially useful solution to this problem was to investigate the possibility of using solvent extraction methods to separate the “free” from the “bound” fractions, instead of using precipitating or adsorbing reagents. Metal-free organic solvents of analytical reagent or purum grade were readily available and did not require additional purification. I asked Moshe Shimoni, who had previous experience in immunoassays, to start investigating this idea as part of his doctoral work. After a number of initial experiments, it transpired that the use of an extraction solvent for the required separation eliminated the need for centrifugation. Instead of performing this step, one could mix the aqueous and organic phases with a short (20–30 s) vortex operation. Then, after the spontaneous phase separation, aliquots could be taken with a pipette from the solvent and/or aqueous phase and transferred to another tube or vial to be taken to the analytical instrument. We soon found out that the method, as just described, involved too many error-prone manipulatory steps. It was clear that we had to find a way to permit the whole assay, including the solvent extraction and complete segregation of phases, to be carried out in the same tube. After testing a number of approaches, we finally designed a device which consisted of two parts: (1) a polypropylene test tube, the assay tube, in which mixing of the aqueous immunoassay mixture and the extracting organic solvent would take place; (2) a piston rod that we called a mixer-separator piston, also made of polypropylene, with a channel traversing its vertical axis and shaped at its upper end in the form of a collecting container. Slightly above its lower end, the piston was fitted with a sealing element, such as a rubber or Teflon O-ring. When the mixer-separator is pushed down into the assay tube, the O-ring seals the tube hermetically. The upper liquid phase is aspirated through the channel and is transferred into the collecting container. At a predetermined distance from the upper end of the mixer-separator piston the collecting container is wider than the assay tube. In this way, on pushing the piston down into the assay tube as far as it would go (until stopped by the contact between the collecting container and the rim of the assay tube), it is possible to achieve quantitative collection of a predetermined volume of liquid as well as the required physical separation between the two liquid phases.

E.A.H.—How did this new device perform in practice?

We had to use an established immunoassay system to test the efficacy of the device and to carry out comparative studies in order to better analyze the results obtained in the MIA work. We had become convinced that the solvent extraction method need not be limited to the MIA system, and felt that this approach could also have interesting potential for use with immunoassays in which markers other than metal atoms or ions were used for labeling the haptens. We decided to choose RIA, the most sensitive assay available, for our comparative studies. This necessitated the transformation of

one of my two labs into a radioactive work area and we had to acquire beta- and gamma-counters for the RIA tests.

We bought commercial RIA kits, for testing estriol, digoxin and thyroxine. The reagents were labeled with either tritium for beta-counting or (125)iodine for gamma-counting. We carried out parallel comparative experiments: one experiment, following exactly the instructions in the commercial kit protocol and a second experiment with the same reagents, but following our solvent extraction method with the new device. The results were highly satisfactory and we were able to demonstrate conclusively the feasibility and generality of the solvent extraction separation method in immunoassay protocols.

However, though successful, we were aware that use of this method in immunoassays was limited to relatively low-molecular-weight haptens for which suitable extraction solvents could be found. On the other hand, it occurred to me that the concept of the design and operation of our device could be applied to the development of a novel solvent extraction apparatus to replace the ubiquitous separatory funnel. Interestingly, the separatory funnel in its presently familiar shape was first described by the famous Swedish chemist Berzelius in his textbook published in 1841. It is surprising that in spite of the many well-known drawbacks and problems encountered—especially by students—in the operation of separatory funnels, no significant conceptual changes in the design of the separatory funnel have occurred over such a long period of time. With the help of technicians in the glass blowing workshop of the Chemistry Department, we constructed prototypes of a new glass instrument for laboratory liquid–liquid extraction, based on the principles of operation in the immunoassay solvent extraction device. One could say that we invented the “separatory cylinder” to replace the “separatory funnel”! I coined the name Mixxor (from the words “mixer” and “extractor”) for this new instrument. I am pleased to say that the Mixxor is currently available commercially for small and medium volumes (2, 5, 10, 20 and 50 ml) in solvent extraction operations and is in use in many laboratories worldwide. You may be interested to know that the web search engines Google and Overture come up with more than one hundred web references in response to a search request for the item “mixxor”.

E.A.H.—I believe that you expanded the Mixxor liquid–liquid separation method to a new device for solid–liquid separations and to a novel concept in liquid chromatography. Would you tell us something about these developments?

For those unfamiliar with immunoassays, let me explain that the most widely used procedures are based on adsorption (charcoal, silicates), fractional precipitation (ammonium sulfate, ethanol, dioxin, polyethylene glycol), double antibody and solid phase reagents, all of which end up with a system of suspended particles in a liquid medium. The selection of any particular procedure is determined by consideration of many interrelated factors, such as solubility of the compound, char-

acteristics of the antiserum, fraction to be counted, degree of non-specific binding, and type of radioisotope. However, one feature that is common to all of these techniques is the need for a centrifugation step to effect aggregation of the suspended solid particles, followed by a decantation (or suction) step to separate the solid and liquid phases physically. Our success with the non-centrifugation, non-decantation device in the solvent extraction procedure opened the way to the development of a modified device which, subsequent to mass transfer between a fluid and particles suspended in it, would achieve a solid–liquid separation by allowing for mass transport through a selective barrier. Clearly, for such a separator to be useful in immunoassays, it should—among other things—eliminate both the centrifugation and decantation manipulations. Moreover, the separator device should be suitable for use with any of the aforementioned separating reagents, without prejudicing the freedom of selection of any particular reagent, as may be dictated by a consideration of the various interrelated factors enumerated above.

The piston of the mixer-separator used in the solvent extraction procedure was modified as follows. The lower end of the piston had a cavity, in which a membrane of choice was fitted and held tightly in place by a ring disc. A sealing element (O-ring), at a predetermined distance from the membrane cavity, allowed the piston to fit snugly into the test tube and slide along its inner walls. A circular groove was designed on the piston segment, between the membrane cavity and the O-ring. The opening on top of the collection chamber could be closed with a tight fitting cap. The whole device was made of polypropylene.

On operation, the mixer-separator piston is pushed down into the test tube. This causes the liquid phase to be aspirated through the orifice bore of the ring disc, then through the axial channel, and finally to accumulate in the collection container. The membrane in the cavity at the bottom of the piston acts as a selective barrier, preventing the solid particles from being transported together with the liquid phase into the upper container. The groove between the membrane cavity and the O-ring plays a crucial role in the performance of this device. During the downward movement of the piston, the groove serves to entrap a predetermined amount of air (an “air pocket”) which—on compression—acts as a cushion, relieving part of the pressure resulting from the resistance of the membrane to liquid flow. Upon decompression any liquid that may have crept up into the space between the inner wall of the test tube and the outer walls of the terminal end of the piston is forced back into the tube. The manual operation of the steps involved in the use of this device in an immunoassay protocol is very simple and can be easily carried out by a technician. We have also designed and built a simple automatic instrument that can process up to 40 assay tubes simultaneously in less than 3 minutes.

As with the previously described solvent extraction device, we used the solid–liquid separator to carry out comparative RIA experiments with commercial kits and obtained excellent results. The methodology and design of

the separator practically eliminate potential contact with the radioactive reaction mixture, thus ensuring maximum safety from radiation hazards. Our results show that the use of this separator provides a feasible, practical alternative to centrifugation and decantation in the immunoassay protocol. Furthermore, beside immunoassays, this device has many other potential applications in fields where selective filtration is required. Indeed, a slightly modified version of this device is currently being produced and marketed under the generic name “syringeless filter” by a well-known filtration products company that acquired the patent rights for our invention.

E.A.H.—What about applications to chromatography?

The principle of a hollow piston moving up and down inside an outer tube under hermetically closed conditions, as applied in the liquid–liquid extraction and solid–liquid separation devices, was so simple that it induced thoughts in the direction of other potential applications. For an experimental chemist like me, it was inevitable that such thoughts would lead towards the field of liquid chromatography, which was being used routinely in our laboratory. As you know, in conventional liquid chromatography of all types, the mobile phase percolates through a stationary phase as a result of a pressure drop induced by various means, e.g. gravity, pumping systems, gas pressure cylinders and capillary forces. Except for the last, all these driving forces are external to the stationary column. In the case where capillary forces alone are responsible for movement of the mobile phase, the flow is not uniform along the chromatographic bed and eventually stops.

We applied our methodology to the development of a new concept, which I called dynamic column liquid chromatography (DCLC). In DCLC, flow of the mobile phase is achieved by forcing a densely packed chromatographic column through the eluent in a system that is completely closed, except for the column outlet. Under such conditions, an intrinsic pressure develops in the system that causes the mobile liquid phase to flow through the moving chromatographic bed in a direction opposite to the movement of the packed column. This is in direct contrast to the principle of a conventional syringe pump, in which the liquid is forced out in the same direction as that of the plunger movement.

An important, unique feature incorporated in the DCLC system is that the flow rate of the mobile phase is fully controlled by the movement of the column. No flow occurs when the column is at rest. Another important aspect featured in the DCLC concept is that, as a consequence of the intrinsic pressure that develops in the closed system, external pumping systems can be replaced by a simple mechanical device that holds the dynamic column and governs its movement.

Without going into further detail, I can tell you that we designed special glass chromatography columns which were pushed through syringe reservoirs by means of a simple me-

chanical instrument and were able to prove the feasibility of the DCLC concept. We also applied the dynamic column methodology to the development of a solid phase extraction device (DC-SPE). We published our results in the appropriate chromatography journals.

E.A.H.—What is the I-R100 Award mentioned in your biographical sketch?

The Chicago-based magazine, *Industrial Research and Development*, runs a competition every year in which a panel of distinguished scientists and industrialists select the “100 Most significant New Technical Inventions of the Year”. The I-R100 Award, in the form of an engraved silver plaque, is presented at a ceremonial black-tie banquet held at the Museum of Science and Industry in Chicago, where the selected inventions are exhibited over a period of 1 month in one of the halls of the Museum. In 1982 we received an award “for the development of solid–liquid and liquid–liquid separating devices” and again in 1983, “for the development of dynamic liquid chromatography column”. It was very flattering for us to find ourselves on the list of awards together with recipients from prestigious companies and institutions such as, Argonne National Laboratory, Bell Laboratories, Dow Chemical Co., E.I. Du Pont, General Electric, Los Alamos National Laboratory, Oak Ridge National Laboratory, Standard Oil Company of California, Westinghouse Electric Corp., to mention just a few.

E.A.H.—Is there anything more that you’d like to tell us?

In August 1982, I gave a lecture at the Gordon Research Conferences entitled “Serendipity in a Bio-Organometallic Chemistry Research Project”. The Oxford Concise Dictionary defines serendipity: “the faculty of making happy and unexpected discoveries by accident”. I think serendipity has made my life interesting. There’s never been a dull moment, and, if I may quote my favorite Frank Sinatra song, “I did it my way”!

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