CHEMICAL HERITAGE FOUNDATION

# JEROME A. BERSON

Transcript of an Interview
Conducted by

Leon Gortler

at

New Haven, Connecticut

on

21 March 2001

(With Subsequent Corrections and Additions)

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# JEROME A. BERSON

| | |
|---|---|
| 1924 | Born in Sanford, Florida, on 10 May |

## Education

| | |
|---|---|
| 1944 | B.S., chemistry, City College of New York |
| 1947 | A.M., chemistry, Columbia University |
| 1949 | Ph.D., chemistry, Columbia University |

## Professional Experience

| | |
|---|---|
| 1944 | Hoffmann-La Roche |
| 1944-1946 | U.S. Army |
| | University of Southern California |
| 1950-1953 | Assistant Professor |
| 1953-1958 | Associate Professor |
| 1958-1963 | Professor |
| 1963-1969 | University of Wisconsin, Professor |
| | Yale University |
| 1969-1979 | Professor |
| 1979-1992 | Irénée du Pont Professor |
| 1992-1994 | Sterling Professor |
| 1994-present | Sterling Professor Emeritus of Chemistry and Senior Research Scientist |

## Honors

| | |
|---|---|
| 1949 | National Research Council Postdoctoral Fellowship, Harvard University (R.B. Woodward) |
| 1963 | California Section Award, American Chemical Society |
| 1970 | National Academy of Sciences |
| 1971 | American Academy of Arts and Sciences |
| 1978 | James Flack Norris Award in Physical Organic Chemistry, American Chemical Society |
| 1980 | U.S. Senior Scientist Award, Alexander von Humboldt Foundation |

| | |
|---|---|
| 1985 | William H. Nichols Medal, New York Section, American Chemical Society |
| 1987 | Roger Adams Award, American Chemical Society |
| 1992 | Arthur C. Cope Award, American Chemical Society |
| 1998 | Oesper Award, Cincinnati Section, American Chemical Society |
| 2000 | Literature Award of the German Chemical Industry Fund |

# ABSTRACT

**Jerome A. Berson** was born in Florida, the older of two children. His father taught Hebrew, and his mother was a milliner and housewife. As a result of the Depression his father struggled to earn a living, and when Berson was about ten the family moved to the Bronx, New York, and then to Long Island, New York. He graduated from high school at fifteen and then rode a Good Humor tricycle to earn some money before beginning City College of New York, chosen primarily for economic reasons. He finished at City a semester early and began working on penicillin at Hoffmann-LaRoche. From there he was drafted into the U.S. Army, in which he worked as a medic in India until the end of World War II. When he was demobilized he married Bella Zevitovsky, whom he had met when they were undergraduates.

Knowing he could not progress with only a bachelor's degree, Berson, with the help of the GI Bill, enrolled at Columbia University, where his Ph.D. mentor was William von Eggers Doering. Berson wanted to specialize in the chemistry of natural products, but during these early years Doering began to concentrate on physical organic chemistry. He urged Berson to consider academia as a career and was instrumental in arranging for a postdoctoral fellowship for him with R.B. Woodward at Harvard, where one could soak up the atmosphere of natural products chemistry. Berson credits Woodward and Doering with being two of his prime influences. Learning that jobs were found through the old-boy network, Berson wrote letters to many other universities, receiving only rejections until the University of Southern California (USC) offered him a position. Limited resources and manpower at USC caused him to shift his focus to physical organic chemistry. He attended lively, intense seminars at the University of California, Los Angeles, finding Saul Winstein an enormous influence and eventually “almost a friend.”

After thirteen years at USC Berson, by now a fully-fledged physical organic chemist, was recruited to the University of Wisconsin, where he stayed for “six of the happiest years of [his] life.” At Wisconsin he had funding, facilities, students, and colleagues he could only dream of at USC. His students and he worked hard on exciting, evolving problems; Berson calls it a “seminal time” for him. Thermal and carbocationic rearrangements, and the role of orbital symmetry in chemical reactions, were the focus of his laboratory during this period. While at Wisconsin, Berson had taken note of Erich Hückel's work, which with Hund's Rule provided continuing themes in his thinking and research.

Yale University then recruited Berson. The personal reasons he chose to move to Yale included having family nearby and being close to New York City's cultural attractions. Professionally, he noted that Wisconsin's chemistry department, because of its sheer size, was unwieldy to administrate easily as a unit and hence had been divided into sub-units (organic, inorganic, physical, theoretical, et cetera). This fragmentation did not favor cross-disciplinary interactions. He believed that he had much yet to learn, and he found many teachers and colleagues at Yale and elsewhere. The Yale period included many new studies, especially on non-Kekulé molecules.

Throughout the interview Berson discusses his own research; the many important chemists he has worked in collaboration with and learned from, some at Yale and others elsewhere; some of his scientific controversies and their resolutions; the enormous changes permitted by technological advances; funding; the vagaries of research and importance of time and setting for progress. Berson explains his current work in the history and philosophy of

chemistry; he concludes his interview with thoughts on the present and future of organic chemistry and physical organic chemistry.

## INTERVIEWER

Leon Gortler is Professor of Chemistry Emeritus at Brooklyn College of the City University of New York. He holds AB and MS degrees from the University of Chicago and a Ph.D. from Harvard University where he worked with Paul D. Bartlett. He has long been interested in the history of chemistry, in particular the development of physical organic chemistry, and has conducted over fifty oral and videotaped interviews with major American chemists.

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INTERVIEWEE: Jerome A. Berson

INTERVIEWER: Leon Gortler

LOCATION: Yale University
New Haven, Connecticut

DATE: 21 March 2001

GORTLER: This is Leon Gortler interviewing Professor Jerome Berson in his office at Yale University on March 21, 2001. Professor Stephen Weininger of the Worcester Polytechnic Institute is also here participating in the interview. We'll just start at your childhood. I know you were born in Sanford, Florida, on May 10, 1924. How long did you live in Florida?

BERSON: Until I was about ten, and then we moved to New York City. It was Depression time. My father [Joseph] followed the will of the wisp of making a living and things had sort of collapsed in Florida at that time. That was about 1934, approximately. So we moved, ultimately winding up in the Bronx. I would say the period between 1934 and 1937, or thereabouts, we lived in the Bronx. I went to junior high school in the Bronx and I went to Stuyvesant High School for about two years. Then another one of these family economic crises took us out of the Bronx and took us to a location on Long Island in the town of Long Beach and so we had to move out of New York City. Long Beach was a very different kind of world from the Bronx and Long Beach High School was a very different high school from Stuyvesant High School. Stuyvesant was an exhilarating kind of place at that time and from what I understand it still is. It was very exciting to be there. I was challenged but I loved every day of it. I didn't realize how good it was until we got to Long Beach. This was a school where my graduating class in 1939 was a class of sixty people. There was a chemistry course but there were no labs. They didn't have a chemistry lab. I tried to set up my own lab in the basement of the apartment house we lived in. The landlady was very negative on this, and in any case, it didn't matter because I couldn't afford to buy the chemicals and glassware to stock it with. So it was a frustrating experience and I really didn't do anymore lab work until I got to City College [of New York].

From Long Beach we re-established residence in New York, basically so I could go to City College. I graduated from Long Beach High School at fifteen and I stayed out of school for a year trying to accumulate enough of a nest egg to go to college with. That was a considerable sacrifice for my family because they had been looking forward to my joining the workforce and bringing in some contribution to the household income.

GORTLER: What in the world did you do at fifteen?

BERSON: Well, I worked. I worked that year. I took some courses at the high school in the fall semester. In the spring semester and through the summer I worked as a Good Humor man, riding a Good Humor tricycle-a very heavy, Good Humor tricycle. At this time I was fifteen years old, or something like that, and I worked from 9:30 am until 1:00 am everyday. [laughter]

WEININGER: Let me just interject one thing. You mentioned the absence of labs, which suggests that you already had some interest in chemistry.

BERSON: Oh yes, I did.

WEININGER: How early did that develop?

BERSON: I must have been about eleven. Certainly I remember being very interested in chemistry when we lived in the Bronx. This was even before I started going to Stuyvesant. This was while I was still in junior-high school. Where this interest came from, I'm not really sure. You know, we were taking courses in the junior high school. They were biology courses, but they had chemicals in them. You needed chemicals to make stains and things like that, and I became fascinated by the properties of chemicals. They had odors. They had colors. They were smokes or gasses. Things like that that were phenomena, you know. You could see them. You could smell them. You could sense them directly. And I was just fascinated. What causes these things? What is that all about? I think that may have been where the interest came from. I don't remember a particular teacher or anything like that who stimulated my interest.

GORTLER: Your family probably couldn't have afforded a Gilbert chemistry set.

BERSON: Oh no, they couldn't. I think I received a present from an uncle which was a small Gilbert set, and that sort of kept my interest going. But that was after I had developed this interest. I mean, he wouldn't have made that present had he not been aware of the fact that I was already interested in chemistry.

GORTLER: Do you remember anything from Florida at all? I mean, your schooling there?

BERSON: Yes, I remember. There was no stimulus like that. I have to tell you that my elementary schooling was kind of a mess because we moved around very frequently. I didn't stay at a single school for very long and my parents were very eager to get me out of school. I think the motivation was economic, but it was also that there was no way—I don't know how to say this without sounding like a pompous ass, but, I was making very rapid progress in these schools and by the time I left high school, I was not yet fifteen years old.

GORTLER: You'd been skipping grades.

BERSON: I was skipping grades like crazy. I don't approve of that as a way of raising children and of educating children because there comes a time when a child is emotionally and intellectually ready for a particular subject but it may not be at the time that he's chronologically reached the point where he's able to take that subject. So I strongly disapprove of that and nowadays, of course, they don't do it. So I had always a feeling of specialness, of isolation. So that's one of the main things I remember, that I was always the youngest in the class and looked upon with a certain amount of, well—I had friends, but there was a certain group that looked upon me very suspiciously and I was not a popular kid, let's put it that way. [laughter]

GORTLER: Your father, what did he do?

BERSON: Well, that's a good question. He did lots of different things. I would say that if there were any one thing that you could call his main métier, he was a teacher of Hebrew and he had jobs at several different synagogues and also as a freelance teacher of Hebrew. But that certainly did not sustain him, I mean, the kinds of stipends that a teacher like that could expect were very small and he didn't always have a job because these jobs would end, you know, and so he'd go into some kind of marginal business in an attempt to generate some income for the family. It was just a damned hard time. I mean, I grew up in the midst of the Depression and, of course, it marked me for life. I'm stamped with that.

GORTLER: You still look for bargains. [laughter]

BERSON: Yes, I still do. I mean, it took me a very long time to learn how to have a good time. My family, we never went on a vacation all the time I was growing up. There was no such thing. You know, to get a quarter to go to the movies was a big deal. I don't mean to make too much of this. Let's face it. I have a fairly comfortable situation now. I'm a retired professor and all of that stuff. I don't call myself rich, but I don't really have to worry about those things and my children, bless them, don't worry about those things. [laughter] But it's an indelible mark on me and that has a lot to do with it. And I wasn't the only one. When I went to City College, of course, I'd say most of the kids were like that. So that was a kind of motivating factor. We were always eager to get on with it. You know, we didn't have time to fool around. And there wasn't a lot of frivolity. No fraternity life. Nobody lived on campus. It was all business. And it just took me years to get past that stage of my life.

GORTLER: Your mother [Rebecca]—what role did she play?

BERSON: Well, she was a wonderful woman. She was very loving. Unfortunately, she died early. She died of cancer when she was only forty-eight.

GORTLER: And how old were you at the time?

BERSON: I was nineteen at the time.

GORLTER: She was primarily a housewife?

BERSON: Yes, she was a housewife. Before she got married, and I think for a while after she got married, she was a milliner. She was not highly educated but she loved music and she read, particularly, novels. I remember stories that she told about how she loved opera and we always listened to the opera broadcasts on Saturday afternoon. She told stories about how she used to wait on that freezing sidewalk on 39th Street outside of the old Metropolitan Opera House for standing room tickets when [Enrico] Caruso was singing. [laughter]

GORTLER: Were your parents immigrants?

BERSON: Yes, they were both immigrants. My father came from Vilna [Lithuania], the area around Vilna. I don't know the name of the town. He was always very reticent about talking about his childhood. And my mother grew up in Warsaw. She came from a large family in Warsaw. But they met in this country. They did not come from Europe together.

GORTLER: Do you have any brothers or sisters?

BERSON: I have a younger sister, who lives in Allentown, Pennsylvania now. I keep close to her and she has two sons.

GORTLER: Did she get a college education?

BERSON: No, she never went to college. I think at the time that she would have been thinking about going to college, my mother died. My father was out of work at that time and I think that it was just too much hassle. She wasn't motivated as strongly. He was not pushing her or encouraging her, so it just never happened. She's an intelligent woman, but it just never happened.

GORTLER: So your decision to go to college was essentially <u>your</u> decision to go to college.

BERSON: Yes, it was somewhat of a family struggle to have that happen. I mean, once I got into it, I don't think my parents ever raised the issue with me again, but I could feel the pressure. You can't fool around there. You've got to keep driving. And in fact I graduated a semester early and I went to work immediately at Hoffmann-La Roche and for that short period of time that I worked there, before I was drafted and went into the army, I was able to bring some money into the household.

GORTLER: So you knew you were going to be drafted at some point?

BERSON: Oh yes, no question. That was another motivation to get my undergraduate degree before that happened. But, you know, we're talking about 1943 or that ballpark. That was the depths of the War [World War II]. The Russians were taking a shellacking. Well, they had "won" the Battle of Stalingrad at the cost of I don't know how many millions of people killed. The second front had not yet been opened. It was not so obvious that we were out of the woods on the war. Everybody who was able-bodied was being drafted.

GORTLER: Before we get to your wartime experience, let's go back and deal with City College. You decided on City College because it was a free college?

BERSON: Definitely, yes.

GORTLER: And so you were not considering other colleges?

BERSON: Well, look, I was considering all kinds of places. I was considering MIT [Massachusetts Institute of Technology], and I wrote to MIT and they sent back their bulletin and the various pieces of literature, and I looked at the cost of tuition and, "pffftht." [laughter]

GORTLER: You weren't going to make it selling ice cream. [laughter]

BERSON: That's right. I mean, it was totally out of the question. Now, I did apply to places that I thought perhaps could give me scholarship support. But we have to keep in mind—I mean, in my own defense here—I was unsuccessful in doing that. I was not able to find a place that wanted to give me a scholarship, but they were much rarer in those days. I think that it was harder to get them. The idea of—what's the word I'm trying to think of—merit-based admissions rather than ability to pay, I think that was decades in the future. So the people who tended to go to private colleges were those who could afford to go. There was no state university system in New York at that time. So City College was it. I guess Brooklyn College had opened by then, so it could have been Brooklyn, but I didn't know anybody who knew anything about Brooklyn College. You know, your decisions at that age are based upon piles and piles of ignorance. You don't really know what you're doing. My parents certainly didn't know this. They weren't able to guide me. The school counselors were not very helpful, so I was pretty much on my own and that's the way it ended up.

GORTLER: City College had a good reputation.

BERSON: Well, it was. It was a good school. I'd say the students were terrific. The faculty was, for the most part, less than terrific.

GORTLER: Were there people who influenced you a great deal there? Tell me a little bit about the courses you took and the people that may have had some influence.

BERSON: Well, yes. I'd say that freshman chemistry I took with Abraham Mazur. He was a very good influence. He was a very good teacher and he had a kind of passion for the subject that just pervaded the atmosphere when you were around him. He was a strong influence on me, I'd say. Some of the other teachers, I won't mention names, were borderline cases, but another one who made a very good impression on me was David Perlman, who taught the course in qualitative organic analysis. That was my first introduction to chemical theory. Now at that time, Perlman was teaching a rather elementary form of resonance theory. This is 1943 or 1944, in that ballpark, so the theory was not very popular yet and Perlman was considered to be quite avant-garde. I don't know if there was anybody else around in those days who was teaching that. Even at Columbia [University].

GORTLER: Perlman and David Davidson, who was at Brooklyn College, put together a qualitative organic chemistry scheme and they had a book out that they used for many years at Brooklyn.

BERSON: Right. They were very close friends.

WEININGER: So there was nothing in your organic textbook about resonance. There were no resonance structures.

BERSON: Oh, absolutely not.

WEININGER: Do you remember your textbooks?

BERSON: Yes, in fact, I think I have a copy of it still. Francis Earl Ray. Do you remember that textbook? It had a red cover. Ray's book makes reference to resonance, but he didn't really have a firm grasp of what it meant. He represented the resonance forms as individual components of an equilibrium mixture. Another book that I took along with me to the army was a book by [George] Richter. He was at Rice University.

WEININGER: Oh, yes.

BERSON: So I really spent a lot of time with that one after hours when I was in the army.

GORTLER: [James B.] Conant's book was around at that time, I guess.

BERSON: Conant's book was probably around. The other one that I should have been reading, but it was too heavy to be carrying around in my barracks bag was Gilman's "Treatise" (1), the two volume "Treatise." [laughter] In fact, I was so eager to have that book that I bought a copy and I sent the two volumes home to my wife, Bella, who was not my wife at that time but wife-to-be. I asked her to keep them for me, so it was kind of a sentimental gesture because I felt that somehow I was close to those books even though I didn't have a chance to read them. [laughter]

GORTLER: That's very interesting. Did you do any research when you were at City College?

BERSON: No. There was really not an opportunity to do that. Most of the people who taught on the faculty at that time, well the ones who were active, had some research going on but it wasn't on campus. They tended to be doing research at P&S [Columbia Physicians and Surgeons], and there was a whole group of biochemists that worked at P&S. Some of them worked, I guess, with [Rudolph] Schoenheimer. [David] Rittenberg ultimately became a member of that group and others worked with other biochemists at P&S. So for a while there, because these people were very passionate about their research and about their science, although I didn't play any direct role in it, it sort of spilled over and for some time I felt that I wanted to be a biochemist.

But that changed when I went to Hoffmann-La Roche. I was there for only five months but I worked on the penicillin problem-the structure of penicillin, which was at a balance point then, a fulcrum, because some of that work was classified. I suspect that there was a lot more known about the structure of penicillin than was available around the labs at Hoffmann-La Roche. Now maybe some of the senior people knew, but certainly the lab assistants like I was did not know that. So we were told that we were working on the structure of penicillin, but it was pretty clear that we had crude preparations; powders, we never had crystalline penicillin in our hands. And we didn't really know what we were doing. So basically the work was isolation work. It was a problem on how do you get this stuff pure enough following biological assays so that you can ultimately get it crystalline and begin to work on the structure. Well, as I say, there were many other laboratories around the country and overseas, in Britain, particularly, who were working on that. And Hoffmann-La Roche never really made a dent in that field.

GORTLER: Were they one of the pharmaceutical firms that was producing it by fermentation?

BERSON: They were producing it, I don't know in how large a quantity, because they were doing it by surface culture whereas the mass production was being done by deep fermentation and that was being done, I think, at Abbot [Laboratories] and Pfizer. They were the main contributors.

GORTLER: And I think a few people had visions of synthesizing it. Some people at Merck [& Company] might have been trying to synthesize it.

BERSON: Yes, I suspect so. That was perhaps ten years later in the middle 1950s.

GORTLER: [John] Sheehan did that work.

BERSON: Sheehan did that, finally, yes. You know, I think now the thing is that it costs more to throw penicillin away than it does to make it, so the job is now to just make modifications. Total synthesis is not worthwhile.

GORTLER: Right. It never has been.

BERSON: This is a big digression we've gone into here. What I started out to say at the beginning was that experience at Hoffmann-La Roche gave me an interest, a powerful interest, in the chemistry of natural products, and that I carried with me through the army years and right into graduate school.

GORTLER: Your transition from natural products to other areas is one important aspect of this interview. How about other influential courses at City College? Maybe philosophy came into this?

BERSON: I took a philosophy course, which was called "logic and scientific method." It was a complete turnoff because it was very formal and no one ever brought it into the domain of how do we apply this to the work of the working scientist. I mean it's all very well to say that if I want to prove things syllogistically I have to follow certain rules to avoid a mistake in logic, but what's the relationship between that and how we do our work? That problem is something that I'm still worrying about fifty or sixty years later. In fact, I'm trying to write a book on that now.

GORTLER: Well, that's why I asked that question. I thought maybe your early interest had been piqued by some course you had taken.

BERSON: It may have been at that point, but it was more of a matter of frustration and a feeling of deep ignorance than having an eye-opening experience. I had a very good writing course, speaking of writing. My freshman year everyone was required to take a compulsory course in themes and you had to write a theme a week. Then we had a sit-down critique, half an hour or forty-five minutes, one-on-one, with the professor in the course, not a teaching assistant. And I happened to have an outstanding professor. This is bad because I can't remember his name now. I think it was Edward Mack. He was just a wonderful teacher. Someone in high school had told me that I could write, and the first thing that this guy did was to disabuse me of that notion [laughter] because I didn't have a clue as to what I was doing. But then he set me on the right track. He was really a very strong influence.

Another group of courses that I took, which I found fascinating, were courses in German. We were required to take either German or French and I chose German because I had had French in high school. Well, high school French, you know, isn't very much. The German courses I took, and I had started out planning to take only two years, but after I had finished two years, the instructor in the course said to me, "Well, I'm sure you're going to continue taking German." I said, "Well, I know it's not a requirement for me." He says, "Take German. It might save your life someday." Well, that never happened, fortunately, but the air at that time was pregnant with those thoughts because this was 1942 or 1943 and it was perfectly clear that I was going to go into the army. If I was sent to the right place, it might come in handy. Well that was not really a very strong motivation, but in retrospect, I have to say that I was so interested in the subject and the language and the literature that I did continue and I took two more years of German. I took four years of German in college. I would say my German now-it's an exaggeration to say that I can speak German. When I travel in Germany, which I have done frequently, and in fact lived in Germany for a while, five weeks or something like that at a stretch and at one time three months, I could negotiate. I could go to the grocery store or the cleaning store. I lived in town and I was able to get along. So that basis was there and, of course, it gets rusty if you don't use it, but it comes back and you grind the rust off if you're thrown into the milieu and you have to use it. So that is still with me.

[END OF TAPE, SIDE 1]

BERSON: Well, I was just telling the story about Toby Sommer who's a former student of Sam Danishevsky. He's now working at Brandeis [University]. He wrote me after he read the book and he said that he had been very interested in what I wrote about [Johannes] Thiele. One of the things I had in my book was a quotation from [Richard] Willstätter's autobiography. Toby read that, and for reasons that are too complicated to go into here, he was extremely interested in exactly what kind of a guy was Thiele? So not only did he read what I had translated from my German copy of Willstätter's autobiography, but he went to the library and got a copy of the English translation of Willstätter's book which I don't have and our library doesn't have. And he compared the professional translator's translation to mine and he found a discrepancy. [laughter] So I had to write him back saying look, I don't want to get into an argument with Dr. Lily Hornig. She's a professional translator and I wouldn't presume to challenge her, but I pointed out that she had translated, and I think mis-translated, a word from Willstätter's book, which led to this switch in interpretation that caught Toby's eye and he was extremely interested in. Well, I'm not sure I convinced Toby who doesn't know German, but in any case, I could stop that steamroller at least temporarily. [laughter]

GORTLER: Well, let's get back onto the chronology of your career. From Hoffmann-La Roche you were taken into the army, and then the question is: What did you do in the army? Were you able to use any of your chemistry there?

BERSON: Well, not really. I ended up in the medical corps. I was trained to be a combat medic, really, and I remember we asked, "Well, are we going to get any weapons if we go into combat?" [laughter] They said, "No, you aren't going to get any weapons." So we asked, "Well, how are we supposed to protect ourselves?" They said, "Well, we gave you that little plastic card with a red cross on it. You're supposed to show this." [laughter]

GORTLER: I think the mortality rate of medics was probably higher than—

BERSON: It was very high. Well, fortunately I never got exposed to that, for complicated reasons. Because, about the time that we were supposed to go overseas—we were ticketed, I think, it was pretty obvious, to go to a location in the Pacific. We were shipped to Fort Lewis, Washington. From there we were supposed to be shipped overseas to some destination, which we were never told. What became clear to us after a while, when we were not shipped over, is that we were going through a second basic training course, only this time it was an infantry basic training course. So we were issued weapons. We did fire for record on the firing range. We did go through the infiltration course. We did twenty-five mile hikes with full-field pack, steel helmet, rifle and bayonet, [laughter] and we did do bayonet drill. So I knew how to kill somebody with a bayonet. So I asked myself, well, I'm supposed to be a medic. I'm not supposed to do this! We were never told why we were doing this, but in retrospect it seems pretty clear to me that they were beginning to be very worried. This was about the fall of 1944 and the Germans were mounting this drive that was going to lead to the Battle of the Bulge. The Allied troops were being pressured. They were under considerable pressure because the Germans were just throwing everything into this attack. So I think that we were being trained to be replacement troops, infantry troops. But by the time we got through that basic training course, I think the tide had turned and the Allies were again in control of the situation. The Battle of the Bulge was over then. That was around December or January, 1944 or 1945, in that break period. And that's about when we ended our basic training.

So I think that they changed their plans again and we were sent overseas to Calcutta, India, where we were assigned to take over what was called the 29th Medical Laboratory, which was connected to the Army Base Hospital in Calcutta. So that's where I stayed for the next thirteen months, working as a lab tech. So you could say that some of my experience in science, generally, came in handy. You know, when I had to look at somebody's urine sample to see if there were red blood corpuscles in it, I could recognize what a red blood corpuscle looked like. And we were trained in the medics to take blood samples. So if the MPs brought in a drunk late at night, there always had to be somebody in the lab prepared to wake up out of a sound sleep and take a blood sample out of a guy. One night they brought in a guy who must have been six foot six and he must have weighed three hundred pounds. They had two rather smallish MPs trying to control this guy and he was very angry. [laughter] He saw me standing there with this syringe. I thought he was going to take my head off. Anyway, they finally had to club him into submission in order for me to get a sample out of him.

So that was my contribution. It was not a very big one to the war effort. I should say that at one time I did try to get into the Air Force, but that was in 1943 when I was still in college. The war was a central thing in those days and I was very crazy and sort of determined to get into it in some direct way. But my eyesight wouldn't allow me to go into the Air Force. I also tried to get into the meteorology program. You could be trained to become a meteorologist. I was rejected for that also, so I just waited for them to draft me to tell me what to do.

WEININGER: Did City College have a program where guys were coming in to be trained?

BERSON: V-12 or something like that. Yes, they did have a V-12 program. They had an ROTC [Reserve Officer Training Corps] program. But I was never sent back to college then. I mean, I didn't know how to do that and I think you had to go into the Army before you were sent back for V-12. I was in the midst of my studies and that was kind of a diversionary thing and so I didn't get into that. In any case, that's not what I wanted. I didn't want to go to college in the Army. If I was going to go to college, I'd try to stay in and finish as a civilian. If I was going to go into the Army, I wanted to be in it.

GORTLER: You came out of the army and I think you got married right away?

BERSON: Three weeks. [laughter]

GORTLER: I assume you had met your wife in college?

BERSON: Yes, we had met before. We had met in 1942, actually, and we had been keeping company until I went in, almost two years. By then there was kind of an understanding. We didn't have a formal engagement, but there was an understanding. So she was working full-time then and didn't have time to prepare the wedding. Since I had just been released and school hadn't started yet at Columbia, which is where I was going to go, the problem was dumped in my lap and I had to make all the arrangements for the wedding within three weeks. How I ever did that, I don't know, but we did it.

GORTLER: It was a small wedding.

BERSON: It was about a hundred and twenty odd people. I mean, families were involved. You couldn't elope or, you know, have a small wedding. It had to be a big deal. So it was.

GORTLER: If we can talk briefly about the role of your wife [Bella Zevitovsky Berson] in your career.

BERSON: Well, absolutely central. I mean, she's just the most important person in my life and she is so strong and so smart and so calm and focused. I don't really know what I would be without her. She has a way of just being in charge of situations. I've learned a lot from her, and I admire her tremendously, and besides the other aspects of being man and wife, she is really just a unique person—admirable in every respect. So she was a student at NYU [New York University] when I met her and she graduated from NYU in 1945. She was Phi Beta Kappa there. At one time I had dreams that we would go to graduate school together. She was interested in biochemistry and I was interested in chemistry, so we thought that would be a match. But as time went on, she decided that's not what she wanted to do. She really wanted to have a family, so ultimately she didn't go to graduate school. She worked for a while. She worked in [Robert C.] Elderfield's lab at Columbia on the anti-malarial project. And when I was a post-doc at Harvard, she worked in the analytical lab at MIT. So she was a professional chemist at the bachelor's level.

But then when we moved to Los Angeles, we had our first child and she stayed home for the next seventeen years while we raised those three children. At the end of that time, it was just about the time we moved to Wisconsin, she went to graduate school in library science and she got a master's degree at Wisconsin in library science. When we came to Yale, she went to work at the Yale Library and very quickly she became Associate Director of the Library and ultimately Director of the Medical Library at Yale. So she had a very high degree of responsibility and I think she was just a terrific asset to that whole operation. She's retired and she continues to do some volunteer work at the library and she also does other volunteer work.

Our children are now grown. The oldest is Ruth. This is going to sound like bragging, but okay, so be it. They're wonderful kids. Ruth will be fifty in December. God, is that possible? She is an art historian. She worked for a number of years at the Art Museums of San Francisco, and then she was Deputy Director at the Zimmerli Museum in New Jersey at Rutgers [University]. Now, she's gone back to San Francisco and she is the Exhibitions Director at the San Francisco Museum of Modern Art. Her major scholarly field has been the Impressionists, and she wrote a two-volume catalogue and scholarly reference on the first eight Impressionist exhibitions. It weighs about 20 pounds. That work apparently has been very highly regarded, and just this past month she was invested as a *Chevalier de l'ordre des Arts et des Lettres* of the French Academy. So she's really a world-renowned art historian.

So that's Ruthie, and then our middle child is David who is a professor at Brown University in Neuroscience. He's done work in a lot of different fields, but he's just now reached a point where he's made what is apparently a very important breakthrough in the mechanism of the circadian rhythm—what controls the circadian rhythm, particularly in mammals and presumably also in humans. He has identified, apparently, a group of cells and he's identified a pigment. He hasn't isolated it. He doesn't know the structure. But he has characterized it spectroscopically. It's not one of the visual pigments. It's in a separate set of cells that produces a separate pigment that is especially, apparently, evolutionarily developed for the purpose of responding to the circadian rhythm, the diurnal changes in the light levels. He's terribly afraid he's going to be scooped because a lot of people in the field are working on it. He's preparing a paper for *Science* now, which I hope that he finishes up pretty damn soon and gets into publication. But it's really beautiful work and very, very exciting. So that's David.

And then the youngest son is Jonathan who is a show business type, and the most recent activity of his is as the field director for a pyrotechnics display company. They're called Performance Pyrotechnics Associates and they're based near St. Louis. They do shows in connection with public events, dramatic presentations, the Super Bowl fireworks they did, July 4th fireworks on the Schuylkill River in Philadelphia, that sort of thing, the massive displays.

When Hong Kong was turned over to the Chinese mainland people in the early 1990s, he did the display on a barge out in the middle of Hong Kong Harbor. We have some photographs of that. He's very good at what he does, and we are very proud of him. So there are the kids. They're all married now and we have four grandchildren.

GORTLER: That takes care of the next question, which was about your children. I'd say you covered it all. When did you decide to go to graduate school and how did you decide to go to Columbia?

BERSON: Well, there again, ignorance was in control of the situation. I didn't really know what I was doing. Through the rumor mill, I don't know quite how, while I was an undergraduate, and also when I was in the army, some of the people in our outfit were chemists. One guy had a master's degree in chemistry, in fact. So these people were a little more—maybe a lot more—au courant than I was about where were the places to go for graduate work. How did I decide I wanted to go to graduate school? Well, I just became aware of how ignorant I was when I worked at Hoffmann-La Roche, and I wanted to put myself in a position where I was an independent operator, not a lab technician. Do you know what I mean? Where I had a Ph.D., because I could see that the people who had real fun in the lab at Hoffmann-La Roche were the Ph.D.s, not the lab techs. [laughter] Basically it wasn't that we were doing menial work. I mean, we didn't have to mop the floor or anything. But because we clearly did not know much about what we were doing, we weren't given a lot of intellectual responsibility and the people who were calling the shots were the ones who did know what they were doing. So I said, well, it's pretty obvious that I have to learn what I'm doing. And the only way I can see to do that is to go to graduate school and get a Ph.D.

So somehow, I don't know exactly how, I got the idea that the places that I was particularly interested in were Wisconsin, and where I got that idea from I don't really know except that of course it was a good school in those days and it still is, but why that came to mind I can't remember. Harvard also was floating around out there as being a good place to go. And then my father began to lean on me. He was very eager for me to go to school someplace near New York because that's where he was. So I chose to apply to Columbia. Well, Wisconsin accepted me. Harvard did not accept me. Their excuse was that they had a lot of people coming back from the Army who had been there as graduate students. That may have been partially true, but I suspect that I may not have been accepted there anyway. But in any case, Columbia accepted me. So Bella's parents also were getting antsy about our leaving town, so that kind of left Wisconsin out of the picture. The combination of pressures left me pretty much with Columbia as the choice. Fortunately they did take me, and so I went there. So again, you see this was not a highly intellectual decision. In fact, the most attractive thing that I knew, personally, about Columbia chemistry at that time, was that Bill [William von Eggers] Doering was there. Now why was he attractive? Bill Doering, at that time it was something like 1944, he would have been twenty-seven years old.

WEININGER: You'd read about him in *Life* magazine?

BERSON: I'd read about him in *Time* magazine. I said, this guy works on natural products. He synthesizes alkaloids. That's just what I want to do. So I'm going to Columbia and he's certainly one of the people that I'm going to want to be interested in. Well, that turned out to be a mistake, because by the time I got to Columbia, the other two people in natural products were Charlie Dawson, who was working on the active principle of poison ivy, urushiol. Everybody who worked on that project got poison ivy—terrible cases of poison ivy. I had come back from India with a bad fungus infection. In fact, I had been sick a couple of times in India. I had had bacillary dysentery. I'd had amoebic dysentery. And I had this fungus infection that I was still carrying around with me. I said, do I need another skin disease at this point in my life? [laughter] So that was the end of that natural product avenue.

Another one was Elderfield who, in fact, had worked on alkaloids when he had been at Rockefeller but was doing very little of that at this stage. At this point, he was almost entirely involved in the anti-malarial project, so all of his work was synthesis of these analogs of anti-malarial drugs. You know it was typical medicinal chemistry research—making derivatives and having them tested. And I wasn't terribly interested in that. So *faut de mieux*, what could I do? I went to Doering.

WEININGER: [David] Curtin wasn't there yet?

BERSON: Curtin was there, but he was clearly a physical organic chemist. And I didn't want to do physical organic. I didn't even know there was such a thing. So I went to Doering. I had taken his course and it was very physical organic, no natural products in it at all to speak of. I went to him and I said, “You're not doing any more natural products work?” He said no. So we talked for an hour about how important physical organic chemistry was. I couldn't really get him interested in doing any natural products. He didn't have any problems in that area. So I kept badgering him and he finally thought of something. There were some leftover residues from some work that Don [Donald S.] Noyce had done on a natural products problem. Now what this material was, I just can't remember. It was not an alkaloid. I don't know. I don't think they ever published anything on it, so I haven't even been able to look it up. I suppose I could go back and get a copy of his thesis and find it.

GORTLER: Don Noyce was working on the structure of a mold metabolite. The work wasn't published as far as I know.

BERSON: But that was the project that Bill Doering gave me. Don had isolated some things and he had worked on this structure. I don't know that they ever reached a point of sufficient certainty on the results to publish the thing, but in any case, what was leftover were the things in the mother-liquors. Everybody knew it was in there, but nobody had really worked on it. So Bill brought out this flask [laughter] with kind of some mud at the bottom of it, and he said, "Here, maybe you can find out some things that Don didn't have time to work on and you'll have a natural products isolation and identification problem." Well, this was exactly what I thought I wanted because that's where my interests had gone after I'd been at Hoffmann-La Roche. So I started to work on this. Well, I should have known better than that. I mean, Bill clearly was not interested in this project. He didn't have any ideas about how to go about it. You know, you think in about 1947, chromatography had just been invented and it was very crude. There was no thin layer chromatography. There was certainly no gas chromatography. There was no liquid phase chromatography. You know, exchange chromatography—all of those things remained to be invented.

WEININGER: You probably had UV [ultraviolet] and you had crude IR [infrared].

BERSON: Crude IR. We didn't have IR until about the moment I started research, we got the first infrared machine.

WEININGER: A single-beam instrument?

BERSON: It was a single beam instrument. It was in [Ralph] Halford's lab. Up to that time I don't know how they had been doing IR spectra. They had been doing them a point at a time, I suppose. But they got the first continuous recording, single-beam spectrometer that was put out then. It was not Baird. It may have been Perkin-Elmer. Probably the first Perkin-Elmer—Perkin-Elmer 12B, or something like that. I'm short-circuiting the whole thing. I never was able to get anything out of Don Noyce's residues. I worked five months on that thing and it was total frustration. I went to Bill and I said, "You've got to get me off this project. I want to do some chemistry. I don't want to fool around with these oils and tars." So he put me on another project and that project was the one that constituted my thesis. But what I meant to say with regard to infrared was that the solution of that problem, which was a structural problem, depended upon an infrared spectrum, and as far as I know, I was the first one to use infrared spectroscopy at Columbia to solve an organic structure. So that was my Ph.D. thesis.

GORTLER: I was wondering about that problem because essentially you showed that the structure of diisohomogenol in the literature was correct but some of the oxidation products of the—

BERSON: The structures of the products were wrong. That's right.

[END OF TAPE, SIDE 2]

GORTLER: You were talking about your experiences at Columbia and your research. Once you got on this project, Doering probably didn't have a hell of a lot of interest in the project.

BERSON: No, he didn't, because I don't know whether that came through in the publication that we wrote (2), but he had an idea about this work that was he was building up a large intellectual construct concerning the nature of a series of different rearrangements at different oxidation states. They were related to the ketol rearrangement that you may have seen in the steroid series. If you have an α-ketol, under certain conditions, it transposes the carbonyl and the hydroxyl by a migration of carbon. So when he saw these papers in the literature, these papers by Alexander Müller, he thought that the structures that Müller was writing for these decomposition products were wrong and he had a different set of structures that he thought was a more likely set. Those compounds would undergo rearrangements under some of the reaction conditions that Müller had been talking about, to give products of a different structure from Müller's structures, but the rearrangement would fit into this scheme on the α-hydroxyketone rearrangement. So that was the guiding principal of this.

If it had turned out that Doering's hypothesis for these structures was correct, then I think he would have taken more interest in the project because it would have fit into this scheme. But, well, here's what happened on that. He said, "Why don't you just look into this. I don't think these structures are right. I think that what's going on is this α-ketol rearrangement, but I haven't really done a lot of reading and I haven't done a lot of thinking about what these structures might be. Why don't you just go into the library and read up on all that stuff." So I did that, and there were about ten of those papers. I collected all the notes that I had made—there was no Xerox in those days so you had to take notes—and I took all that stuff home one weekend. I laid it out and it quickly became very clear to me that Müller was certainly wrong, but Doering was also wrong. I mean, I don't say this with any glee because he really hadn't put a lot of effort into this. He just had a hope that maybe this would fall into that category. But my hypothesis for this was something completely different and something not terribly interesting and it was something that I thought could be verified in a few rather simple, straightforward experiments. So I worked all that weekend. I was very excited about this because I thought I saw the whole picture. I took it into Doering on Monday and laid the whole thing out for him and he said, "Well, that looks plausible and I have a few more ideas about experiments that you could try and why don't you go ahead and start off on that line." It quickly became obvious that all of that was correct, that my hypothesis was correct, and within eleven months I did the whole job. That involved not only this infrared thing, but also a lot of other structural work and transformations—not only reformulating Müller's transformations, but finding other new transformations that verified the structure. It was all very uninteresting chemistry and it didn't lead anywhere. Nope. Doering didn't put anybody else on any problem like that after I finished.

GORTLER: You must have had a certain sense of accomplishment when you were done this.

BERSON: Oh yes, I did. It confirmed my interest in natural products chemistry because these reactions that Müller had reported were reactions of oxidation products of diisohomogenol a dimer of isohomogenol, which is the methyl ether of isoeugenol. Can you visualize that?

[Insert figure 1 picture]

Then Müller carried out certain oxidation studies on the diisohomogenol and that led to these products. Well, what he was formulating as the products of oxidation seemed to me to be very improbable. He was attacking them at unactivated positions with the oxidizing agent and all of the rationalizations of these structures seemed to me to be very forced. Whereas, if you just assumed that the primary oxidation product wasn't what he thought, which was a hydroxy-ketone, but instead was a diketone, which was my hypothesis, then everything fell into place. It was a diketone that resulted from the ring opening of the hydro portion of the hydrindane. But that really made me think I was a natural products chemist. I was very naïve.

GORTLER: Even though at this point you were sort of being inundated by all this physical organic chemistry.

BERSON: Yes, right. Around the lab, I mean, there was something like eighteen people at the lab and I was the only natural products chemist, so called.

GORTLER: Were there other people in the lab that you became friendly with?

BERSON: Oh sure. I mean, Andy [Andrew] Streitwieser was there at that time. Ken Wiberg was there at that time. Herb Meislich, who subsequently taught at City College, was there. Who were some of the other people around? I had friends in the Elderfield group—Al Gray and Geraldine Lynch, at that time her name was. Al Wolf was in our group at that time. Dick [Richard] Young was in our group. Morty Levitz. And Doering's first wife, Ruth Haines, was in our group. In fact, I took over her lab space when she graduated. They weren't married. Oh, wait a minute. They did get married, I guess, just before she graduated.

GORTLER: Was there a fellow by the name of Bob Odum?

BERSON: Bob Odum was there, yes, toward the end of my stay. And Chuck [Charles] DePuy was there. A fellow named Dick [Richard] Urban was there. What's become of some of these people, I don't really know. Is Bob Odum still around?

GORTLER: He retired from Brooklyn College a number of years ago. He lives in upstate New York.

BERSON: I see. But he stayed in Brooklyn all that time?

GORTLER: He was at Brooklyn College from the late 1950s to somewhere in the late 1980s.

WEININGER: I think he came just when I finished. I finished Brooklyn in 1957.

GORTLER: Oh yes, that's right. I keep forgetting you're a Brooklyn College graduate.

BERSON: Let's see. There were people in the Curtin group that I knew. I knew Elbert Harris. Was that the fellow who worked with Curtin? And Peter Pollack. They worked with Curtin on the migratory aptitudes and the Curtin-Hammett idea. Ed Tristram who subsequently worked at Merck was in Curtin's group at that time.

WEININGER: Did you have any interaction with Louis [P.] Hammett?

BERSON: Yes, that's an interesting point. I took a course with Hammett. I didn't take it for credit because I didn't need it. I was very concentrated on my work at that time and I was trying to make a clear path for myself, so I got to know him in my coursework. He was also a member of my Ph.D. committee.

GORTLER: Tell me what you thought of his course.

BERSON: I thought it was terrible.

GORTLER: [laughter] You're not alone.

BERSON: Did you take it?

WEININGER: No. But I've talked to a lot of people who were at Columbia.

BERSON: Well, I mean, he was obviously a very smart man and one of the key figures in the field of physical organic chemistry. Hardly anybody knew as much or had originated as much as he had. But, let's face it, he was not very dedicated to teaching. He'd come in and just sort of natter and stop in mid-sentence and look out the window. There'd be a pregnant pause. Twenty-five seconds would be ticking off, thirty seconds. [laughter] Not a word was being said. Everybody was shifting about uneasily. So he was not a dynamically attractive personality. But speaking of Hammett, I did get to know Ernie Grunwald there who came as a post-doc with Hammett at about that time. I also knew another fellow. It's very bad to get old. I can't remember names anymore. I must have known several of Hammett's students, but I just can't remember the names. I knew some of the physical chemistry students. I knew Dick [Richard] Bernstein slightly. He was ahead of me in graduate school so we didn't overlap that much. He worked with Tuffy Taylor at that time. I knew a fellow named Howard Reiss who was a statistical mechanicist who worked with [Victor] LaMer.

WEININGER: Did you take a course with LaMer.

BERSON: I didn't take a course with LaMer. It's too bad about Hammett because I really grew to appreciate his book only much later. When it became clear to me that I was going to be a physical organic chemist and not a natural products chemist, I said, well, this is where one should learn this stuff.

GORTLER: What about your relationship with Doering?

BERSON: Well, it was very much a mentor-student kind of relationship, although he wasn't that much older than I was. He was seven years older than I. When I met him, I think he was still an assistant professor or maybe had just been promoted to a tenured associate professor. So it was very early in his career. He had a huge group, not only at Columbia, but he also had this other group up at Hickrill.

GORTLER: Was that the Katonah lab?

BERSON: Yes. So it was not easy to get to see him.

GORTLER: Wasn't a private individual funding the Katonah lab.

BERSON: A woman named Ruth Weill, who was Doering's first graduate student, was the wife of a rather wealthy stockbroker, I guess he was. She was very interested in chemistry and she wanted to continue working as a chemist, but she didn't want to hire herself out in industry. She wanted to work at home. And basically I think that they built the laboratory at Katonah for Ruth Weill to work at, under the conditions that she persuade Doering to come and be the director of it. This is my understanding of what that story was, and so they set this up and they had several people working up there. The person who was the sort of "on the scene" executive officer of the lab was Larry Knox and so I got to meet Larry.

WEININGER: That was [Paul D.] Bartlett's student?

BERSON: Yes, he was a student of Bartlett. The Bartlett-Knox work. That's right. And Knox also became famous again with Doering in the synthesis of tropylium ion. Larry was just a hell of a good chemist. He had golden hands and I don't know what ever became of him. I think he died some time ago, at a fairly early age, if I'm not mistaken.

GORTLER: He was black, wasn't he?

BERSON: Yes, he was very rare for a Ph.D. chemist at that time. He was really a very talented guy. And I thought a very nice guy. I liked him. But I don't know what happened to him.

Doering gave me a lot of flexibility as a graduate student. In the beginning he was very—what's the word I want—controlling, not only to me, but also to other students. He would not hesitate to speak his mind and tell you where you were wrong and why you were never going to amount to anything, and sort of that kind of admonitory presence, which left you with no illusions; that he was all business and you were not to take this any way but seriously. I probably resented that at the time because, well, just normal rebellion, you know. But in retrospect it was probably good for me. Also in retrospect, I realize that he was pushing me very hard during that time. You see, I was at Columbia less than two-and-a-half years. As I look back on that, it was a combination of circumstances. First of all, there was this unexpectedly easy project that I had and second, Doering was very eager for me to get out and get on with it. Third, I was working like a beast. [laughter] I mean, that combination added up to a very quick trajectory through Columbia and the result of it was that I don't really think I knew as much as I should have known when I graduated.

GORTLER: One of the questions I have and I'm sure Steve has, is when did you start to move over into physical organic chemistry? Obviously it wasn't at that stage.

BERSON: It wasn't at that stage, no.

GORTLER: We'll get back to that question. How were you supporting yourself?

BERSON: The GI Bill. Almost entirely on the GI Bill and I was a teaching assistant, so that combination. I could not have gone to graduate school without the GI Bill, and that was true of almost everybody in my graduate class. So, you know, that was really Uncle Sam. That was the payback.

GORTLER: Actually, that was probably one of the heydays of the American university.

BERSON: Well, that was a very special group of guys because we were all convinced that now is the time. We had a spent a couple or three years, sometimes more, in the army. Some of these guys had been in combat. We had people coming back from service in the Pacific with malaria, you know, a lifelong affliction with malaria. I mean, it was a very serious bunch of people. Not much fooling around. So there was inherent talent, but there was also seriousness of purpose. And the atmosphere was just great. It just couldn't have been better. It was a very, very stimulating environment.

WEININGER: And they were probably grateful to have come back at all.

BERSON: Well, a lot of us, you know, we were at a place in our lives where we didn't have any—just a few years before we had no dream of ever being in that situation. You know, I thought if I was lucky I would go to college and I'd go to work for a paint company or something like that and be a formulations chemist. I didn't know anything about any of the rest of this stuff.

Well, picking up on your question of how did I get to be interested in physical organic chemistry. Doering wanted me to do post-doctoral work. I didn't have any dream of that when I was a graduate student. I hadn't given it much thought. I thought I'd go and get an industrial job somewhere like people were trying to do. One day Doering walked into the lab and asked, "Have you given any thought to the rest of your life?", or something like that. [laughter] I said, "Well, no, not really." [laughter] He said, "I think you should try to get an academic job." The thought had never even crossed my mind. He said, "But you'll have to have a post-doc first." And I said, "Well, okay. How do I do that?" He said, "Well, there's a very small number of people that you should even consider working for. In fact, I'd say the only one you should consider working for is [Robert B.] Woodward. Why don't you write to Woodward and see what he can do for you." So I wrote to Woodward. In fact, Doering—and this is to show you how hard he was pushing me—had a party at his house in Woodward's honor. Woodward and his first wife then, I guess it must have been, when she was still out and about. No, it couldn't have been. It must have been his second wife. It was his second wife, I'm pretty sure.

GORTLER: Woodward's second wife?

BERSON: Woodward's second wife; Doering's first wife. Doering was living up there on the estate at Katonah where Hickrill was. In fact, it was called Hickrill—that's the name of the estate. So he had a party. He threw a party for Woodward and Woodward's wife at his home at Hickrill, and he invited two other people whose names I should have mentioned—Marshall Beringer, who was a student at that time, and Harold Zeiss, who was also a student at that time, and myself. So the three of us, and our wives, were invited to the party and this was a nice social occasion. He introduced all of us, of course, to the guests, and so I met Woodward, then, for the first time. I think now it was pretty clear that what Doering was trying to do was to cement my credentials with Woodward. Well, it didn't quite work because after the party, the next day or so when I saw Doering in the lab, he said, "Well, you should write to Woodward now and ask him about where you stand on the post-doc." Woodward wrote back saying that, well, he was very interested but he really didn't have any funds at that time—the usual excuse you give to somebody when you're not that interested—but that he would be happy to take me into the lab if I could get a fellowship. So that left it up to me. Doering, then, took over and somehow finagled a fellowship, a National Research Council [NRC] fellowship, for me. I had to apply for it. As I remember there was some kind of a local committee. There was some kind of screening that took place at Columbia. This was the days before the general advertisements of openings where these things would be called to people's attention. I think that they must have had a flyer go around soliciting applications from students, but apparently not all the students knew about this. I certainly didn't. The first thing I knew was, I don't know, within that month sometime, I was told that I had been recommended for an NRC fellowship, and very soon after that the fellowship came through. Those were real plums at the time, very rare, and a great privilege to have, and there were no strings attached. It was a portable thing, so you could go wherever you want.

In the meantime, but before this had happened, there was something else I should tell you about. And that is, again, this is in accord with this tradition of everything being done under the table, you know, it's who you know. I was called into Doering's office sometime during my third year of graduate school. He introduced me to a man whose name I won't mention to you who was the chairman of a department at a well-known university, who asked me whether I would mind coming up to his department with the possibility of receiving an offer for an academic job. This was while the Woodward thing was still in abeyance and I didn't know about the fellowship. So I went to this interview. I spent all day there. They made me the offer. I was mulling this over and then almost immediately after that, on the heels of that, came this thing from the NRC fellowship. So I decided, you know, in retrospect perhaps unwisely, although probably wisely, to turn down the offer of an academic job. Now this was a pretty good place. In those days, or even now, people don't do that very often, which just goes to show you how naïve I was. But I talked to Doering about it and he said, "Well, if that's what you want to do, I think you really should." I felt very diffident about taking a job at that stage. I was really pretty darn ignorant. I wanted to do natural products chemistry and I was not prepared for it. I hadn't been immersed in that atmosphere.

So I went to Woodward and I stayed there for a year and I worked on a problem in the alkaloid field. I was surrounded by all these hot shots who knew all about natural products. Not only was Woodward there, but [Louis F.] Fieser was there, very active in natural products. Gilbert Stork was there. Marshall Gates was immersed in the total synthesis of morphine at that time. Dick [Richard] Turner was working on steroids. I mean it was a hotbed. It was the place to do natural products in this whole country, in the world probably. So I soaked up that atmosphere for a year.

WEININGER: None of your work with Woodward was published?

BERSON: No, it never was published, along with a lot of other Woodward post-docs and theses. I mean, the Harvard chemistry library is full of Woodward students' theses that consist of a very long, very detailed, beautifully-concise, imaginative, creative, brilliant introductions. That's the problem. [laughter] Then the results, which really, frequently, didn't work out.

WEININGER: Let me interject at this point. One of the things that Woodward I think was justly famous for was really to have brought mechanistic thinking to natural product synthesis.

BERSON: Yes.

WEININGER: Was that evident at that time when you were there? I mean, did you have some sense of that? You know, aside from the amazing intuition that this guy had. Did you sense any other way that he went about thinking about synthesis planning that was unusual? In other words, could you detect this?

[END OF TAPE, SIDE 3]

BERSON: The question about Woodward and the role that mechanism played in his thinking about synthesis and about natural products generally, I think that was a very important component in Woodward's intellectual bag of tricks. That's an almost derogatory way of putting it, but he had a very good feeling for mechanism and it was not the Hammett type of thing. It was not based upon the kind of quantitative understanding of thermodynamics and kinetics that Hammett had, but it was an intuitive feeling about how reactions go. It was sort of the Robinsonian arrow pushing, raised to a higher level, and tied in, in a much more formal way, with resonance theory. It was almost entirely resonance theory.

I should say this also about the Doering experience that I had: despite the fact that in 1951, two years after I left Columbia, Doering had already synthesized tropone, which was the first compound in which the existence of a non-benzenoid, aromatic sextet was recognized—the first existing compound. It was an extremely important paper and was published simultaneously with a paper by Hyp Dauben who was then at Washington, who also synthesized tropone. Now that was the first place that anybody ever mentioned Erich Hückel to my knowledge, in the whole field of organic chemistry. This guy was totally ignored until Doering put him on the map in 1951. Yet the strange thing was that in 1946-1947, when I took Doering's course in advanced organic chemistry at Columbia, he did not mention Erich Hückel, he did not mention molecular orbital theory. The whole course was based upon resonance theory. So somewhere in there, Doering saw the light, and where that came from, I don't know. So if you ever have occasion to interview Bill Doering about that period in his life, that's a very interesting period.

So, in any case, the message that I'm trying to convey is that at some point around the late 1940s to early 1950s, Doering was already at a changeover point in which he was beginning to recognize the importance of speaking from the point of view of molecular orbital chemistry. Now where that came from in his thinking, I don't know. I wanted to find out, but I still really don't know. That's something to explore.

So I'm getting pretty far afield from Woodward now. We were talking about Woodward's use of mechanistic thinking, and it was based largely on resonance theory. The same was true of Stork. In fact, most people in organic chemistry argued theoretical points, electronic points, in terms of resonance theory. This was certainly true of [Saul] Winstein, it was certainly true of Herbert C. Brown. It was true of [Donald J.] Cram. [John D.] Roberts. All the people that were at the forefront of the field in those days. Now it's true that Roberts, somewhere around the middle 1950s, became sufficiently familiar with molecular orbital theory so that he wrote this very nice book on notes on molecular orbital calculations, which was very influential (3 (a)).

GORTLER: Jack Roberts and Andy Streitwieser were doing molecular orbital calculations on all the molecules they could handle. I mean, they were teaching themselves.

BERSON: They were teaching themselves, that's right, with a lot of help from Bill [William G.] McMillan whom Jack Roberts quotes in his memoir (4). McMillan was a buddy of his from his undergraduate days at UCLA [University of California at Los Angeles].

So, in any case, yes, it's true that Roberts and Streitwieser were doing this, but it's very interesting that Hückel's work tends to get lost in the shuffle. This is something that I wanted to talk to you [Weininger] about in your paper (5), because when you talk about the development of molecular orbital theory in this country, you don't really talk about Hückel very much. You talk about Streitwieser and Roberts, and I would say that's true as far as their influence is concerned. But there is a gap there of more than something like thirty years between the time Hückel did his work and the time this thing came to the general attention of the chemical public.

GORTLER: Hückel published when? In the early 1930s?

BERSON: The first paper was 1931.

GORTLER: But nobody was trained in that area. I mean, I came much later. I wasn't trained in that area.

BERSON: It's all his, Hückel's, fault. His career, his laufbahn, the tragedy of Hückel is his own fault, and I try to make that clear in my book (6). Well, it's a long story, but fundamentally he was left on the outside and all of this stuff had to be rediscovered essentially.

GORTLER: He got interested in some other things.

BERSON: Well, he was rejected. He was a physicist. He never was a chemist. And he was just trying to make it with the physicists and the physicists looked at this stuff and they curled their lip and they said, "Rranghh, organic chemistry!" So he was rejected by the physicists. The German organic chemists certainly didn't understand what the hell the guy was talking about. And he didn't have the ability to sell his work, to bring it into a form where a chemist could understand it and use it. And that's a big talent. That's a very important thing to be able to do.

WEININGER: Roberts makes this point about [Linus C.] Pauling that I wrote in my paper. He said, if [Robert] Mulliken had Pauling's personality, [laughter] we would have perhaps been using MO theory a lot sooner.

BERSON: Maybe so.

WEININGER: Roberts talks about spending some time in Cambridge and Mulliken was there. I remember his saying that he sat for an afternoon at St. John's College [listening to Mulliken] and coming away like he wasn't sure what was going on. Whereas Pauling, was not only brilliant but was a brilliant salesman.

BERSON: Oh, he was. He was a terrific salesman. In effect, he sold us a bill of goods with his resonance theory because it didn't work. [laughter] It didn't work on two of the biggest problems in organic chemistry of our century, namely aromaticity and another aromaticity problem, which is the orbital symmetry theory, which is really kind of a branch of aromaticity. It's the aromaticity of transition states, but it's the same problem. And resonance theory does not give you a clue. Simple resonance theory does not give you a clue to how to talk about those problems. So in a sense that was a cul-de-sac that people were charmed into by Pauling's enormous influence on the field. He was just dazzling. Just dynamic and everybody wanted to follow him and emulate him. But this thing wasn't going anywhere as long as people were doing valence bond theory the way he was doing it. Now ultimately, by the 1980s or so, people like Oosterhauf figured out what was missing in valence bond theory that would allow it to be applicable to the kind of problems that people were really interested in organic chemistry. And it turns out that you can't truncate the basis set, which is what Pauling did. You can't truncate it as severely as he did with all these nearest neighbor interactions and single perturbations. You have to do multiple perturbations, and when you do that, you get all the Hückel results. You get the magic numbers and all of the aromaticity things from valence bond theory.

So valence bond theory and molecular orbital theory are not that disparate. They both are approximations—approximate solutions of the Schrödinger equation, and at some point they must converge if quantum mechanics is at all correct. But it took a long time for people to recognize that, and the fortunate thing about Hückel was, Hückel did both of these at first. Hückel's theory is just as approximate as Pauling's—maybe more so. But Hückel did his original approximations in the 1930s. He could see. He had in front of him the idea that you have to account for the aromatic sextet, and that valence bond theory, if you truncate it in the way that Pauling subsequently did, was not going to lead you there. There were just too many functions that had to be permuted. It was too big a problem mathematically. The molecular orbital thing could be truncated quite severely, but nevertheless it gave you immediately, just automatically, like that, all these energy levels fell out. You fill them up two electrons at a time, and boom, there's aromaticity. So that's what convinced Hückel, at the time, to reject the simplified valence bond method of doing the problem and concentrate on molecular orbital theory, and he was absolutely correct until the advent of digital computers, which then, much later in the game, allowed you to do either problem to much higher levels of approximation. When you do the valence bond problem correctly, you get the same answer.

WEININGER: But he must have been one of the very few, really early theoreticians who had any interest in organic molecules. I mean, these guys would do hydrogen or the $H+H_2$ reaction.

BERSON: They went on to lithium hydride. [laughter]

WEININGER: Right.

BERSON: And they really worked very hard on that.

WEININGER: Exactly.

BERSON: They thought that the comparison with the experiment was to get the bond length of lithium hydride to within a gnat's eyebrow. Wow! That's theory!

But Hückel got this idea about organic chemistry from two sources. One was from [Niels] Bohr, of all people. He'd been a post-doc with Bohr, and Bohr told him, well, you might want to take a look at double bonds. Carbon-carbon double bonds and other kinds of double bonds in organic chemistry—a very interesting problem. And the other thing was that Hückel's brother, Walter, was an organic chemist. So he had, in a sense, a special kind of background that other theoreticians simply didn't have, and Pauling certainly didn't have.

GORTLER: At some point we have to talk about when you got interested in physical organic chemistry. First, lets finish your post-doctoral work. Did you interact with any of the other chemists. I mean, there were a lot of people there. Whom did you interact with in Woodward's group? Did you have any contact with Paul Bartlett?

BERSON: Some, but very small. I was working so hard in Woodward's lab that I didn't really take time to go to Bartlett's seminars, and that was a mistake. I should have done that. It wasn't until I came back on sabbatical ten years later when I did that. [laughter] But Bartlett's influence was pervasive around the department and I knew several of his students at that time. I'm trying to remember some of the names.

GORTLER: I'm mainly interested not so much in who was there but who did you interact with? Who did you talk with?

BERSON: I spent a lot of time, of course, with Woodward.

GORTLER: You actually did spend time with Woodward?

BERSON: Oh yes, a lot of time with Woodward. Woodward was accessible at that time. He'd come into the lab and people in the lab would tremble a little bit because he was kind of a loose cannon. [laughter] My lab partner, Flash Georgian, this was before the days of recycling, would pour ether residues down the sink. Woodward would come into the lab, smoking, and he'd sit down at my desk, facing me, and then he'd be five feet away from the sink. When he was finished with his cigarette, he'd flip it into the sink every once in a while. [laughter] But he came in and he was very interested in what I was doing. He had lots of ideas and I tried my best to follow them. His seminars, of course, went on until all hours, so everybody interacted with him then. He was very close to his students then. I think the stage of large-scale natural product synthesis was just beginning about the time I was leaving Harvard, because that's when the steroid synthesis project began. The people on that project were people like Franz Sondheimer, Dave Taub. This is really shameful, I can't remember. There was a Swiss or German by the name of H. (Hans or Henrik) Heusler.

I spent some time with Gilbert Stork and he was very helpful. He was still an assistant professor, but it was clear that he was brilliant and had a great future ahead of him. He was very accessible and very open. You know, Gilbert, he's a nice guy. And I knew Dick Turner. I knew Marshall Gates. At that time they were available, and, you know, we spent time discussing chemistry with them. Derek Barton was there that year and gave lectures on the conformational analysis, so that's the first time I ever heard that thing exposed in so much detail. I didn't spend much time with [Louis] Fieser who was kind of remote.

GORTLER: It was just as well.

BERSON: Yes, probably so. But Woodward was at a stage, then, when he had a lot of individual problems being done. Gurbaksh Singh was working on patulin. McLemore was working on an alkaloid problem. Ernie Wenkert was working on some alkaloid problem. Jerry Meinwald, I think, was also working on an alkaloid problem. I mean, these were not massive teams of researchers, but when that began was just about the time I was leaving. Franz Sondheimer came in sort of in the middle of the year. We overlapped for a while. Dave Taub was there as was H. Heusler and they were part of a large team that worked on steroid synthesis. And then things became more and more, sort of, institutionalized. The massive teams of people that he [Woodward] brought together to work on problems like strychnine synthesis, reserpine synthesis, chlorophyll synthesis, all of that, came much after my time. So I didn't really get to experience that way of doing chemistry. It's just as well that I didn't because, as we'll discuss in a moment, resources available to me at USC were not—I mean, it was just laughable for me to try to do that kind of chemistry there. So the answer to your question is, I did not interact strongly with the physical organic people at that time, in Bartlett's group or any of the other groups. Well, [Frank] Westheimer's group didn't get started until later.

WEININGER: Westheimer wasn't there yet.

BERSON: Wasn't even there yet. So I'm trying to think of who were the other physical organic—there may not have been any. No tenured faculty, certainly. Maybe an assistant professor, I'm not sure. But in any case, there was no one who made a big impression on me. I mean, Bartlett made a big impression, but just because of who he was. Not because of any strong interaction I had with him.

WEININGER: Did you interact with anybody down at MIT?

BERSON: No. [Arthur C.] Cope was around at that time, but, you know, I wouldn't have seen those people unless they came to the Woodward seminars. I mean, my interaction with the MIT people began a decade later when I was back on sabbatical. Then I got to know George Buchi and some of the other people—Fred Greene.

WEININGER: C. Gardiner Swain?

BERSON: Gardiner Swain, yes. So those people I got to know then.

GORTLER: Just one interjection. Tell me a bit about your math background.

BERSON: Well, it was spotty. I was always very interested in it, but I was never very good at it. I had the misfortune of testing out rather strongly on the math placement test when I entered City College, so they put me into an advanced class. I really wasn't ready for that. This, again, has to do with the fact that I went through high school like a breeze. I mean, somebody should have just slowed me down and said look, you've got to take this, this and this. There's stuff you just don't know. So I kind of floundered in that advanced calculus course. I never really developed any mathematical savoir-faire or know-how after that. So my formal training in mathematics stopped with calculus. You know, we did things like multiple integration and so on, but I've had very little formal mathematics. I never had a course in differential equations, for example, although subsequently, when I started doing kinetic work, I obviously had to learn something about that. One had to do that then because this was long before the days of canned computer programs that allowed you to simulate all these things and get the rate constants out without knowing any mathematics whatsoever. [laughter] You had to derive all this stuff. And it also, just to jump the gun a little bit, it imposed upon us a kind of formality in the style with which we designed problems in physical organic chemistry. That is that we frequently designed problems to have closed mathematical solutions—solutions that gave you integrable equations.

Now this was the kind of thing that, for me, was epitomized in the work of [E. D.] Hughes on the Sn2 Reaction. The reason that thing made such an enormous impact was that here was a problem that had been set up so that the solution came only from a deep understanding of what the kinetics were all about. Hughes had to derive those kinetics, but it was a very ticklish kind of derivation because, superimposed upon the kinetic changes in the reacting system itself was the decay of the iodide isotope which was a non-trivial thing because it was going on at a pretty fast rate. It was going on competitively with the reaction itself, so you had to compensate for that. This made the kinetic equations very complicated. So I sweated through that. Everybody, I think, was conditioned to avoid setting up a physical organic problem that had a kind of open-ended solution, which would require—if you were going to integrate the equations, if you were going follow the reaction as a function of time using rate constants—you to be able to integrate those things and there was no way of doing that in most instances. But when the machine [computer] integration came in with, you know, just matrix inversion and that whole business of just turning the thing over to a canned program, all of this became kind of trivial. Everybody was doing simulations then. So that was another thing in a way that led to the demise of the peculiar expertise of the old-fashioned physical organic chemist. That is, those who were in the know could solve kinetic problems and devise experiments that required kinetic solutions. But later on, anybody could do it because you didn't have to be able to do that. So we lost a lot of cachet then—our priestly position, as it were, was undermined. [laughter]

GORTLER: That's an interesting point.

BERSON: But that's a diversion. Well, the parallel is in natural-products chemistry. The old-fashioned natural products chemists—somebody like Leuchs or Robinson—who hammered away at the strychnine molecule for decades, chipping off pieces and reconstructing little bits of the structure only by chemical transformations. Not one single spectroscopic tool, and yet they put the whole structure together pretty much. Of course, the problem was solved in the end by Woodward with the aid of infrared spectroscopy, but fundamentally they did the bulk of the work without doing that. But when instrumentation came in, particularly NMR [nuclear magnetic resonance], all those people were back numbers, and particularly x-ray crystallography. There isn't even a field now of organic chemistry that is called "the structure of natural products." It's a branch of analytical chemistry. If you can get the stuff as crystals, you send it out and you know what the structure is in a couple of days. So that's sort of technological unemployment, you see, and the parallel thing came in in physical organic chemistry with these computers, to some extent.

So anyway, how did I get to be a physical organic chemist? Well, it didn't happen at Harvard, I can tell you that. I left Harvard thinking I was going to be a synthetic and natural products organic chemist. And I went through hell before I finally got an academic job and I did it. I was there for a couple of years and then I began to switch to physical organic chemistry. I'll tell you why on the next tape.

[END OF TAPE, SIDE 4]

BERSON: A couple of other people I should mention from that time that I interacted with—one was Harry Conroy who was a student of Gilbert Stork's, and we used to spend a lot of time together arguing about chemistry.

GORTLER: He ended up doing a lot of theoretical chemistry later in his career. He really kind of left the field of natural products. He was a very good structure person.

BERSON: He got into very formal aspects of quantum mechanics and was very good at it from my understanding. But yes, he left structural chemistry of natural products and I think he did that because a lot of the romance and glamour was going out of the field with the advent of the x-ray crystallographers. So he didn't find that terribly challenging anymore and he drifted off into this other area.

GORTLER: What did you say you used to argue with him about?

BERSON: About chemistry. I mean, he had very strong ideas about things that, in some instances, he knew a lot more about than I did. But it took me a while to realize that. [laughter] He was trying to convince me of these things and I was resisting. In fact, he was a very smart guy and I enjoyed being with him because I learned a lot from him. Other people from that era that I remember—Gene [Eugene] Van Tamelen was around and I guess I knew him slightly. He was in Stork's group, and another fellow, Al Burgststahler, who was with Stork at that time.

WEININGER: He went to Kansas, right?

BERSON: He went to Kansas. All of these people became professors.

So it was a very good experience, and in an area where, as I say, I started out knowing very little. I learned a tremendous amount there about natural products, and so on. Well, you want to talk about how I got the job at USC [University of Southern California]? Well, that's an interesting story too. In those days, the jobs were not announced. They were almost entirely done by the "old-boy" network. So sometimes belatedly I would hear about them. Sometimes I didn't hear about them at all. Then it would come to my attention that so and so got a job at such and such a place. I'd say, "What? I didn't even know there was a job there." So I got into the mode of writing letters, you know. Somebody told me I should write letters to the department chair at these places or to famous chemists at these places and offer my services. I did that. I wrote about sixty letters that year.

GORTLER: So by then you had decided that you wanted to be an academic.

BERSON: Absolutely. But we'll come back to that point in a minute. But it was clear that if I wanted to do work like Woodward and Stork and those people, and have a lab of my own and work on ideas of my own, that I would only be able to do that in academic work and an industrial place was not a good venue for that kind of lifestyle. So I began to write these letters. I wrote sixty letters and I got back a uniform response when they answered. Most of them did answer. They answered very politely. Nowadays you probably might not get an answer, but they answered very politely and they all said, in one way or another, no. Some of them even offered excuses. So what I came away with was a collection of approximately sixty, maybe fewer, letters from some very significant—famous, in some instances—chemists. I have autographed signatures of all these wonderful people—Linus Pauling, for example—telling me that they didn't have a job for me. [laughter]

GORTLER: By that time, did you think that there was, well, maybe not in academia, anti-Semitic problems?

BERSON: Yes, I wondered about that.

GORTLER: There certainly was in industry.

BERSON: Oh yes, there certainly was. And there certainly was in academic life too. I mean there's absolutely no question about that. But, the more important point is whether I felt discriminated against because of my background, and I have to say honestly that I did not then. In retrospect, people have told me I was naïve, but I don't think so. Because, I mean, there were guys—I mean, Ernie Wenkert got a job. Jerry Meinwald got a job. I'm trying to think of some of the other people who were of Jewish background who got jobs. Now Jerry tells me that his job was really kind of a back door thing because he was not appointed. He was appointed as some kind of a visiting instructor and then an opening opened up and he was there and they saw his quality and they kept him on.

GORTLER: Did Ernie go to Iowa State at that time?

BERSON: Yes, I think so.

WEININGER: Because he used to attend our synagogue in Des Moines on holidays. I think he closed down his laboratory on Friday afternoon and he'd teach his courses on Sunday morning. This is the middle of Iowa, you know. He obviously was serious about his religion.

BERSON: Yes, he was quite serious. So I found it very difficult to accept the idea that I was being discriminated against. I mean, I think you're going to have other excuses—that I was not as experienced as these people in natural products chemistry and Woodward probably thought of me as a little naïve about this and maybe not ready. So, I guess I was aware of this at the time. He never told me that and I had no external reason.

GORTLER: He knew you were looking for a job?

BERSON: Certainly he knew. He wrote letters for me, and Bill Doering did. So things got pretty late in the recruiting season and I was not having any luck, and I heard again through the rumor mill that there was a job in Max Tishler's lab at Merck. I said, well, okay, it's not an academic job, but it's a good group. They're doing basic research. Why don't I try to see whether I can get a job there. So I applied. I asked Woodward to write a letter for me, which he did, and I received an offer for an interview from Max Tishler. I went down to Merck and I spent the day there. And at the end of the day, Max called me in. Max was really, you know, the word is a mensch. He was a straightforward guy and no nonsense. He was very blunt with me. He said, "Look, you made a good impression here. I don't want you to think that we're rejecting you for cause. But the thing that worries me is the same thing that worried Woodward when he wrote his letter on your behalf, and that is, he thinks that you want an academic job. And I think you do too. I think that's what you really would be happiest doing. I'm just not going to make you an offer now until I have evidence that you are convinced and dedicated to a career in industrial research," which was a very straightforward answer. And it did not surprise me at all.

So I really had come to the end of my rope. I didn't know what to do then. I was pondering about whether I should start writing letters to industrial companies since I had covered the waterfront of the academic field—every department in the country. Well, I hadn't written to some places that, you know, I would not think of going to, but I'd covered pretty much every substantial chemistry department in the country. So I was about to get started on my campaign for an industrial job and I got a call from Bill Doering in the lab. We didn't have a phone in the lab, so I had to go out in the hall to answer him. And he started to chew me out. He said, "How could you even think of taking an industrial job?! Don't you have any pride? Don't you have any sense?" I mean, it was really a tongue-lashing. So I said, "Well, I really don't have any alternatives. I've tried all the places and nobody wants me, and so I have to do something. How am I going to eat next year?" [laughter] He said, "Well, I think you should try to get an academic job again next year." I said, "Well, that's fine except that my fellowship runs out this year."  And he says, "Well, I'm going to talk to Woodward.  Why don't you talk to Woodward first about this and see if he can't keep you on for another year."  So I did, and Woodward didn't make any promises.  He obviously was very reluctant to do this.  Finally, then, I heard from Doering that Woodward had changed his mind, I think because Doering twisted his arm.  So Woodward made me an offer for another year's post-doc on his funds, since my NRC fellowship had expired.  Well, this was around March or April, I guess it was.  Now, what I had forgotten completely about was that there had been one advertised job that year. [laughter]  It was at the University of Southern California [USC].  They were advertising for an organic chemist who wanted to carry out a research program in natural products chemistry and organic synthesis.  So I presumed to try to pass myself off as a natural products chemist.  I applied for this job.  I had completely forgotten about it because so much time had gone by and I hadn't heard from these people.

GORTLER:  I mean, you weren't passing yourself off.  You really were a natural-products chemist.

BERSON:  Well, I was trying to be, let's put it that way.

GORTLER:  That's what your degree was in.

BERSON:  Of sorts.  Yes, that was my claim.  I was either that or nothing. [laughter]  Anyway, so I had applied for this job rather not hoping very much that I would get it, but I got a telegram from Anton Burg who was the chairman at that time.  I'd never had an interview.  I'd never met any of those people.  But offering me a job!  The telegram had the salary they wanted to pay me, when they wanted me to report to work, and that I had to let them know immediately.  So, that was my academic offer for the year, and instead of staying on for another year with Woodward, I mulled this over for a long time.  I talked to Doering about it, and he said, "Well, you probably should take it.  It's a chance at an academic job.  You'll get started and see how it goes."  So that's where I ended up, and I was there for thirteen years.  It wasn't so bad.

GORTLER:  What was it like when you got there?  I mean, you'd never seen the department?  Of course, I took a job exactly the same way.  I didn't have an interview.  I was on the West Coast.  They hired me on the East Coast.

WEININGER:  I was in England when I got hired to teach in Worcester.

BERSON:  So it was sight unseen.  That's the way they used to do it, and okay, so fine.  I did have to send them a photograph.  I remember that. [laughter]  They wanted to make sure that I was human, I guess. But in any case, I got out there and it was a very interesting situation. I was allowed to have a lab-office combination for myself. Now that meant a small, basement lab, below ground level, with a desk in it. The desk was my office, and there was a hood in there and that was my lab. I would say it was about 10 feet by 10 feet altogether, maybe. But by the time you got the desk in there, there wasn't a hell of a lot of room, let's put it that way. I could have one other lab down in the basement or, if I wanted more space, I was free to go down the street two blocks outside the chemistry building to an old, converted, wooden barracks building, which was where they taught the undergraduate organic labs and where I was supposed to be supervising those labs as part of my teaching obligation the first time I was there. I could have a bigger office and I could have a lot more lab space. Well, that office and lab was two blocks away from the main chemistry building, from the stockroom, from the library, from other chemists, you know. What was I going to do out there? So I decided to stay in the main building in the basement. Within about two years, the fire department condemned all the barracks buildings at USC, all the ones that had chemistry labs in them, and said you've got to have a building to put these in because these are a terrible fire hazard. So they built what was then called the organic wing that was a small concrete and brick building where I was allowed to have an office and more like a real office with an adjoining lab, a separate lab, and space for a few students. I don't remember how many I was given space for, but I didn't have many anyway so it didn't make much difference. So that was the beginning, really, of serious research at USC.

GORTLER: Your first couple of publications were, in fact, on structure, but within two or three years you published a number of papers on mechanisms—*cis*-bromination of bicyclic olefins. A lot of work with somebody by the name of R. Swidler (7).

BERSON: Ron Swidler. He was my first graduate student. A very good man.

So time went on and what became the straw that broke the camel's back was that I was trying to synthesize the alkaloid emetine at that time. That had been a project that was related to the project that I worked on with Woodward. When I came to Woodward, I wanted to work on emetine. I wanted to work on the structure of emetine, which then had not been fully elucidated. But I didn't have any very good ideas about it and I look back and marvel about how Woodward was able to euchre me out of that crazy project because I would have botched it and it wouldn't have come to anything. He put me into this other thing that he thought was a more achievable objective in the time that I had there. But the total synthesis of emetine itself was something that I had not considered undertaking until after I'd been in Woodward's lab. By then I thought that, well, perhaps I had some ideas about how this could be approached. So the first person in my lab who worked on that was Ted Cohen who is now a professor at Pittsburgh. Ted worked on the preliminary stages of this plan for putting together the structure of emetine. In the meantime, several other labs were working on it and midway through the work of successor students to Ted, we got scooped two or three times. So, you know, you can't do this kind of work one graduate student at a time, which is what I had. But Ted did some very nice work in the preliminary stages of this (8(a), 8(b)) and really set the whole thing up and it was ready to be continued by another student (8(c)). We published several papers on this, including some mechanistic work (8(a)) because that was very interesting.

WEININGER: Who was funding this at this time, USC?

BERSON: Basically. I didn't have any money. The National Science Foundation didn't begin until 1951.

WEININGER: There was other government money.

BERSON: There was Navy money. I wasn't able to get any of that. I wasn't able to get NIH [National Institutes of Health] money either until later. But at the very beginning, I mean, the pharmaceutical companies were nowhere in sight. They were not out there funding. Not me, anyway.

GORTLER: It probably didn't cost a lot to do this research.

BERSON: I had some chemicals. We didn't get an infrared spectrometer until about 1953. But then we didn't get an NMR until 1962, which was the year before I left. So there was an instrumental lag there.

GORTLER: How big was the department? Who were the other organic chemists?

BERSON: The department was, I don't know, it must have been a faculty of somewhere in the twenties. There were four organic chemists—myself, Norman Kharasch, Ronald Brown and Milton Kloetzel. Those were the four organic chemists. Nobody else was doing natural products work, and nobody in the whole southern California area was really doing natural products work of the Woodward-Stork style. I mean, there was [Laszlo] Zechmeister at Caltech [California Institute of Technology], but he was very narrowly focused on plant pigments and chromatography.

GORTLER: That's true. That was one of the real centers of physical organic chemistry.

BERSON: Absolutely. It was the Mecca.

GORTLER: Were you going to seminars at UCLA?

BERSON: That's a very good point, which I'll come back to.

So time went on and it was clear that I was getting my head bloodied, and in this total synthesis game, I couldn't compete with the big research groups. One of the groups that scooped me was Arnold Brossi's group at Hoffmann-LaRoche. He published a paper with, I don't know, a half a dozen authors on it that cleaned this whole thing up and we hadn't even gotten off first base. So it gradually became clear to me that this was not the way that I was going to be able to do chemical research. I could not, with the manpower resources at my disposal, do natural products research. I mean, I had something like seven PhDs in the thirteen years I was at USC. That's all the students I had. So I was always manpower-deprived.

I began to try to recruit post-docs and to some extent I was able to. Some of them were good; some were lousy; some were worse than lousy. It was not a successful enterprise, largely because of the student problem, and the student problem was exacerbated by the fact that there were already two major centers of organic chemical research in the area—at Caltech and particularly at UCLA. Anybody who wanted to do physical organic chemistry was going to go to UCLA, not USC. I had some good students. I don't deny that. I mean, Swidler was very good. Ted Cohen was very good. Earlene Brown was a very good student. Bill Jones. You know, I really shouldn't complain too much, but there weren't very many of them.

So I gradually began to sort of realize that the people whose work I admired in natural products were also good physical organic chemists. They used this kind of discipline in their own work and Woodward is a prime example, but also Stork and Derek Barton. There were a number of people of that type who clearly were at home in the subject and could make profitable use of it in their own research. I began to wonder whether I couldn't begin to handle physical organic problems with the resources that I realistically had at my disposal. That is, one student, one problem or maybe some very small number of students on a problem. So I began to shift over to that style and although I had sporadically attended the UCLA seminars from very early on, I began to attend them religiously. In fact, I was sort of a nuisance over there. Every Thursday night we had this knockdown, drag-out, very intense seminar and Saul Winstein was in the leadership of that and, gosh, he was a very strong influence on me. It was like having a thirteen-year post-doc to be around that guy. He was so deep. He just would not let you get away with anything. I would say that if I learned anything about physical organic chemistry, he certainly was at the heart of it. The approach to the subject, the way you had to let your mind work, the kinds of things that you had to always be concerned about, were really for the first time made clear to me in Saul's seminars and in personal discussions with him. He was not an easy guy to get to know, but I will flatter myself to say that before I left the southern California area, I was almost a friend of his. You know, we spoke the same language and he took me seriously, well, for one reason, because I sided with him in this non-classical ion controversy, but not only because of that. I don't think he sought my opinion, but he took the trouble to explain to me where his opinion came from, and that was really a tremendous experience for me, so I will always be grateful to Saul. Don Cram was also a very receptive, very open, very warm guy and I had good relations with him. So that was where I gravitated.

GORTLER: Any other participants? Jack Roberts?

BERSON: Jack Roberts came over occasionally. George Hammond came occasionally, especially later on, you know, when he came to Caltech he would come, not every week, but frequently, I would say. So it was a good, lively group and there were lots of pretty intense discussions, and some people came out kind of bloodied after a seminar [laughter], I'll tell you, given that group.

WEININGER: Were you there when Herb Brown visited?

BERSON: Oh yes, but that was not at the Thursday night seminar. That was a special seminar they had, and this was the time when Herb was going around the country propagandizing for his view of those observations on "non-classical ions." His seminar got to be very rancorous because it was soon after this fiasco which took place, I guess it was at an ACS meeting in Houston in which Herb presented data which Saul and Jack Roberts subsequently accused him of knowing was incorrect. Saul stood up and accused him of that right at the meeting and said, "Those data are incorrect and you know it, Herb!" And then Herb Brown shortly after that came out to the southern California area and he spoke at Caltech, and he said the same thing at Caltech. And that part is written up in Jack's autobiography. But he came to UCLA, and I'm trying to remember, I think he did not say that at UCLA because I'm not sure he was certain of getting out of there alive. But it was a very rancorous discussion period.

WEININGER: I talked to a guy who had been a grad student there at UCLA who was at that seminar, and he said he was kind of shocked.

BERSON: Well, it was. Don Cram brought in a collection of his reprints, and he was leafing through them, and you could see his ears getting redder and redder because of what Herb had said about Don's work and Don's interpretation of these things. At the end of the seminar, Don stood up in a trembling voice and he opened up this book and he said, "You are insulting the work of my students. Years of effort went into this! How can you say what you're saying?" And he was in tears. It was really a shocking thing! So, well, you know, you could argue the pros and cons of the scientific aspects of this, but there's no doubt that there were very, very deep feelings involved. And the reasons for that, well, I think that it would take a psychiatrist to figure that out.

[END OF TAPE, SIDE 5]

BERSON: Paul Bartlett was very reticent to take an open stand on this, and everything he said that was negative about Herb's points of view was muted and you had to read between the lines to understand what he was saying.

WEININGER: I never knew him but I've heard about him and I've read, of course, a lot of the stuff, and it seemed to me that he was desperate to avoid getting into these *ad hominem* aspects. He always wanted to keep it on a kind of detached, scientific level.

GORTLER: In fact, he never wanted to use the term non-classical.

WEININGER: Right. Also, everybody talks about him as being a real gentleman.

BERSON: Well he was, I think, and he really felt very uncomfortable with this combative aspect of things and he didn't appreciate the name calling, I mean, really flat-out name calling; the business with a gun on the table. You know, a joke is a joke but you can only go so far. No, I think that a very deep antagonism grew up between Herb Brown and Saul Winstein, and that was the motor that kept this thing going and which caused a lot of smoke. I have very strong opinions about this. I think that Herb's influence in this field was basically negative. I think that the case for a non-classical structure was pretty sound. I think that Saul pushed this about as far as it could go based on indirect evidence, and he had as strong a case as could be mounted. You could adhere to the Brown point of view only by the invocation of epicycles and various ad hoc hypotheses, which did not flow from the internal structure of the subject. So I was convinced about this long before Herb was, if he ever was. It seemed to me that by prolonging this, he was creating a point of contention that was like a vortex. It sucked large portions of the physical organic community into it. Whereas, there were many, many other problems out there that needed to be addressed, so all this talent went into solving what, in my opinion, was an already solved problem.

GORTLER: Westheimer commented to me about that. It hurt him to see all of this brainpower wasted on this. He said there were really important problems out there. Just take the problem of oxidation or almost anything else [laughter] that was more useful.

BERSON: Sure, there were just massive numbers of problems, and so it was kind of a drain on the whole field. In a way, I have to plead guilty because I was part of it. I was a participant. I got very involved in it and I saw the point of diminishing returns and I faded out of the picture long before a lot of other people did, but nevertheless, I made my little contribution to it and I don't feel that I totally regret that in the sense that I learned a lot about how to do research from the work that I did in the non-classical ion field. I think the methylnorbornyl work, for example, was a case in point (9). You mentioned that.

GORTLER: Yes. That was one of the papers that you recommended that I look at, so why don't we talk about that.

WEININGER: What led you into it? I mean, it was 1967 already.

GORTLER: But by then you were at Wisconsin.

BERSON: Yes, that started at Wisconsin long before 1967.

WEININGER: Yes. You had forty pages in the journal dedicated to that problem

BERSON: Yes, it was a culmination of a lot of work. Well, let's see, how do we get into it? The objective of that study and of another study, which we did with Phil Grubb (10) was to study the stereochemistry of these shifts. The vicinal and the transannular shifts in norbornyl cation. Now, I must say that Paul Bartlett had been working somewhat along this line, but he'd been studying a system in which the migrating group was an aryl group. I don't know whether he ever published that, but if he did, he didn't make a big deal out of it. But I think he came to the conclusion that at least he thought that the vicinal shift should be on the exo-side because it was going to a place where there was a de-localized cation and the bottom side, the endo-side, was being occupied in this partial valence with the bridging carbon atom, so that the migrant group should come over from the other side. So our thought was, well, let's investigate this, but let's simplify the system a lot, and so we took the aryl group off and we made the migrant group a hydrogen. In order to provide a thermodynamic driving force for that, we wanted a methyl group on the origin of migration so that after it migrated you would have a tertiary cation left. So we studied this in the case of the 2-norbornyl-3-methyl cation and there are two isomers of that. In one of them the methyl is endo- and the hydrogen is exo-, and then the other one just the reverse. So the prediction would have been, following up on this idea of Bartlett's which we then fleshed out more, the idea would have been that in the hydrogen migration, to give the tertiary cation, the hydrogen should migrate from the exo-side rather than from the endo-side. So the thought was that if you start out with the leaving group—p-bromobenzene sulfonate or tosylate—at the 2-position and a methyl group at the 3-position; if the methyl group is endo-, then the hydrogen will be exo-. That [hydrogen] should migrate very readily to the 2-position because it's stereoelectronically favorable and it gives a tertiary cation. On the other hand, if you start out with the exo-methyl group, the hydrogen will be endo-. Then the migration will be stereoelectronically unfavorable. And what would it do then? Well, the first thing we did was to try that reaction. What we thought was, if this prohibition against the migration is really a strong prohibition, you shouldn't get that tertiary product or if you do get it, it should come from some completely different mechanism.

Now, what we found was that in the case where the methyl group was endo- and the hydrogen in the 3-position was exo-, it went very cleanly to the tertiary cation. And we showed by essentially stereochemical labeling, by using enantiomerically enriched reactants, that that was a direct hydrogen shift. It was just going by an exo- to exo- shift and it was producing the rearranged cation with no monkey business, no fancy mechanism, just as you would expect for the migration of a hydrogen to a secondary center in order to produce a tertiary center.

But then we changed those two things; we put the hydrogen in the endo- position and the methyl in the exo- position. Now this hydrogen that wants to migrate ultimately can't do it because of this stereochemical prohibition. So what does it do? Well, it turns out that it goes through this circuitous mechanism of successive 6-2, 3-2, 6-2 shifts and it goes all the way around Robin Hood's barn, and it ends up giving you the enantiomerically opposite isomer of the same tertiary cation. So these two epimers of the labeled starting material produce with complete stereochemical specificity, the opposite enantiomers. So this convinced us that there must be a very strong prohibition against endo-migration. And that was, to us, a very powerful piece of evidence in favor of the non-classical cation.

Now, who told me this? Winstein never said he agreed with me about this. I think the best he said was, "Oh, that's very interesting," or something like that. [laughter] But someone recently wrote me that he had had a conversation with Winstein around 1967 or thereabouts, and Winstein said to this person (and I can't remember who the hell it was) that you know that this non-classical thing is correct for a lot of reasons, not least of which is the observation that these migrations are exo- exo. So, whether he would admit it to me or not—[laughter]

GORTLER: He wasn't about to give you the satisfaction. [laughter]

BERSON: It made an impact on him.

WEININGER: All right. I think Bartlett published a different paper of yours in his "Nonclassical Ions" book (11). It was one of your papers with with Allen Remanick (12).

BERSON: Yes, that's a different one. That's on a deamination. Yes, Bartlett smoothed that one over too. We got into a big fight with [Elias J.] Corey there, which is a story I don't particularly want to go into. I mean, we won the fight, but there's more to it than that, which I don't choose to talk about.

WEININGER: All right. I have a few questions. One is, in that methylnorbornyl paper (9). At the end of that you go into this LCAO argument, when you're talking about the linear versus the bent geometry of the system. When did you start using that kind of analysis? This is something, again, where resonance is not going to tell you anything, right? It's basically got to come out of some kind of MO-type theory.

BERSON: Absolutely.

WEININGER: So I really would like to hear about when you started to use these MO arguments.

BERSON: Well, I mean, the line there is very clear. What got me going on this was the Woodward-Hoffmann papers starting in 1965, but I had heard [Roald] Hoffmann lecture on orbital symmetry as early as 1963 or 1964, and it was like somebody turning a light on in a dark room. In fact, you know, Michael Dewar was saying this kind of stuff long before, but he, again, couched it in this very lapidary, mathematical style, which was very off-putting to organic chemists! Nobody could read those damn papers. What does this all mean? How can we use it? Well, Hoffmann was just sort of a homebody and he put this in our language. I picked up on that and I began trying to use that type of argument—the orbitals interacting with each other, and so on.

WEININGER: Did you ever take a course in quantum mechanics?

BERSON: No, I never did that.

WEININGER: Had you seen Jack Roberts' book (3) at that time? That came out just about then.

BERSON: Oh sure, yes. It came out before then. I mean, I had been working through Jack Roberts's book (3(a)) and, you know, I was working through Streitwieser's book (3(b)). I was already teaching this stuff in my courses, a little bit. That was as early as 1963 or thereabouts, although I didn't do much of it because [Howard] Howie Zimmerman was far ahead of me in this and we split the course and I let him concentrate on that. But I was already starting to think about that then. But that would not have sufficed.

When I first started to do molecular orbital calculations of sorts was earlier, about 1959 or so, 1958, in work with Earl Evleth. We had made a nitrogen analog of sesquifulvalene (13 (a)). What you have there is a fulvene unit in a fulvalenoid arrangement with a pyridine ring with the nitrogen of the pyridine in the 2-position [See II, below]. So if you count the two formal electron-paired bonds that are in the pi-orbitals of the pyridine ring plus the nitrogen lone

[insert figure 2]

pair, then you have an electron sextet, and so it's electronically analogous to sesquifulvalene in which you have a fulvene bonded to a cycloheptatrienyl unit. So this is a nitrogen analog of that, and in order to understand something about the molecular spectroscopy of that and the dipole moment, and so on, we tried to do some molecular orbital calculations. We did these in connection with a fellow named Stan Manatt who was then working at Jet Propulsion Laboratory. So we published some papers with Stan and Earl Evleth and myself (13 (b)). Earl, incidentally, subsequently became a professor of theoretical chemistry at one of the branches The University of Paris; Paris V, I think it is.

So that was the first time we really began to do that, but that was in connection with kind of an old problem. It was in connection with a problem of a kind of statics problem—how do you describe the structure of this thing? Whereas what I was trying to do in that paper in 1967 was to treat a dynamics problem, a kinetics problem. Why does the reaction go this way? And that's the essence of the orbital symmetry thing. You want to talk about transition states. Now what I was totally unaware of at that time, and this is to be blamed on Woodward and Hoffmann themselves, was that [Kenichi] Fukui had figured all this out earlier, but again, he didn't put it into terms that we could really use. He did not have interesting organic problems that were begging for a solution. All he had was explanations for well-known phenomena—things like, "Why does chlorobenzene undergo electrophilic aromatic substitution ortho-para? That kind of old, classical problem in classical chemistry.

WEININGER: So, in other words, let me ask you if this is the case here. What you're saying, or this is what I take you to be saying, "People could have still explained that with resonance theory." I mean, you know, it's the same thing we teach in organic chemistry. You can give a resonance explanation.

BERSON: Yes, that's right.

WEININGER: So even if MO was better in some way, from the point of view of the organic chemists, you're not necessarily getting anywhere. So what you're saying here is that the

Woodward-Hoffmann orbital symmetry rules could be applied to something where resonance theory just couldn't offer an explanation.

BERSON: Failed. Totally failed.

WEININGER: Is that right?

BERSON: Exactly right.

WEININGER: That's an important point.

BERSON: Exactly right. Now, I want to make clear also that in Roald Hoffmann's—going back to this thing we were talking about at lunch which was the [M. G.] Evans so-called application to transition state theory of the idea of aromaticity, he did that by a valence bond—an old, really, a resonance theory kind of argument, and it's false. It doesn't give the right answer because it doesn't tell you how many electrons you have to have. In other words, by Evans's line of argument, ethylene plus ethylene, face-to-face cycloaddition should have been an allowed reaction. It should have been a resonance allowed reaction. So what he was talking about was the Diels-Alder reaction, four plus two, which he likened to a cycle of benzene. But if you extend his argument, which was that the more electrons you have, the more stable the transition state is going to be, then four plus four should have been even better. So two butadienes going to cyclooctadiene should have been better.

WEININGER: So it's really the Woodward stuff, the orbital symmetry that really, in a sense, begins to, as you say, open the window.

BERSON: For me it certainly did. Now I put myself at fault because it should have opened up long before then. But so should it have for a hundred other people out there. You know, we all saw that stuff and our jaws dropped. We said, why the hell didn't I think of that? It was all out there. You know what I mean? They didn't invent quantum mechanics.

But let me just follow up on this business about M. G. Evans. Dewar claimed that Evans discovered the essence of orbital symmetry theory, and I take the opposite position. The one thing he did not do was to discover the essence of orbital symmetry theory. He talked about stabilizing transition states aromatically. That was a new idea, and I certainly don't derogate that. I wouldn't want to belittle that. But what he did not have was an understanding of what constitutes aromaticity because he was thinking in terms of resonance theory. That is, it seems to me, a very important point. It lies at the heart of the conflict between Pauling and Hückel and the whole development of theoretical organic chemistry at that time. This whole process was delayed twenty-five to thirty years at least by Pauling's dominance of that argument.

WEININGER: Right. You asked me why I didn't refer to Hückel in my paper (5). There were several reasons, but one is, I mean, I'm reporting on what people said, and they did not talk about him. I'm not trying to rewrite history.

BERSON: Absolutely. I understand. But what I'm saying is that it astounds me every time, over and over again.

GORTLER: You act as though you're surprised. The fact is, this happens in science continuously.

BERSON: I know. It's very discouraging. [laughter]

GORTLER: Well, of course, [Gregor] Mendel's paper was published in some obscure journal someplace that nobody ever saw, so how long did biologists just ignore that? This just repeats itself.

WEININGER: Yes, I mean, there is something about the necessity of a context for a discovery, right?

BERSON: Absolutely. The time has to be right.

WEININGER: The time has to be right. And sometimes, I mean, the insight comes in a context that's not prepared for it. The ground's hard and stony and won't absorb the seed.

BERSON: Absolutely. That's exactly right. That's a very good metaphor. And that's exactly what happened in this case. But what Roald Hoffmann points out is, with respect to this M. G. Evans business, that the one who really had the insight about what constitutes an aromatic transition state and how important the number of electrons in the cycle is, was this fellow [N.] Syrkin. He published a paper as early as 1956 in which he pointed out that there are a whole bunch of reactions—he had a number of examples, including things that we would call today 1-5 hydrogen shifts, Cope rearrangements, and things like that, which he recognized as being six-electron cyclic transition states and therefore having aromatic properties. But he never followed up on that. It was just, again, one of these explanatory things which was published in obscurity in a Russian journal. Nobody knew about it. And Roald subsequently learned about it and, in fact, refers to it in the book that he and Woodward wrote. So there's another case in which people were looking the other way and they didn't know what Syrkin was talking about.

WEININGER: I want to ask you another question about this period, now switching to something different. It's something I'm very interested in. It was interesting in one of the little potted biographies in one of the papers that you recommended we read. You mentioned that they always ask you, "What are your interests?" And it says, well, Professor Berson is interested in blah, blah, blah. And one of them says, "and funding."

BERSON: [laughter] Yes.

WEININGER: So, one of my questions was, is this like a flip remark because we're all interested in finding money for our work, or did you have something else in mind?

GORTLER: No, he spent half his time—

BERSON: Maybe more than half.

WEININGER: But I am very interested in the funding question here, because one of the things I'm particularly interested in, and I'm going to be working on this in the fall, is the support aspect. You know, things on proving the correctness of orbital symmetry in these polycyclic ring systems that have no application to anything, getting supported by the AFOSR [Air Force Office of Scientific Research], right, and with other people the ONR [Office of Naval Research] as well. From having dug around in the Winstein Archives, I know that Winstein and Roberts both had advisory positions for AFOSR. So I'm interested in how you got onto that kind of funding and what did you have to write to get funded? I mean, what kind of arguments did you make to get money from these people to support this very "pure" research?

BERSON: That's a very interesting point. Now, let me just try to reconstruct in my mind the climate of that time. I can tell you that this was in the 1960s, the beginning of the 1960s. I was getting funding not only from NSF but also from NIH and from AFOSR. And, I believe, also from the Army Research Office. There were two—there was Air Force and there was Army. I was getting money from both of them. I don't remember making any special concessions to application. I wrote a straight, flat-out research proposal because I knew who was on those advisory boards. I had served on advisory boards to the advisory boards. I remember there was a meeting [laughter] that I attended in which a question came up, "Well, how can we persuade these mission agencies to continue funding basic research?" I was quite outspoken about it then and it was clear that for a time, at least, they were going to do that. In fact, there was a time when it was either AFOSR or ARO (Army Research Office) that wanted to fund all of a person's research. I remember being approached by an officer—I'll say it was ARO—asking me whether I would accept such an arrangement. And this was a time, you may recall, when this whole business about the Mansfield Amendment came up in which Mansfield wanted all of the federal research funds to be put under a single agency rather than having multiple agencies. I don't remember what the arguments in favor of that were, but it struck me at the time as a very bad idea, and I'm still convinced of that, because one thing you do not want to have is a target. If you have a political upheaval that makes research vulnerable, if it's all concentrated in one place it can be obliterated by one bad guy in congress. It's much better, it seemed to me, to have it scattered around. The science community got into such an uproar over it at the time that that idea was shot down—the idea of consolidating it, which I think was all for the good. But I was definitely approached by the ARO or AFOSR, one of those Army/Air Force mission oriented agencies, to let them fund my whole program and I didn't do that. So I kept going with grants on one cycle to the next with them and at the same time keeping up my grant applications to other agencies.

GORTLER: Was it the same reason? You were afraid that if they withdrew your research, everything would kind of fall apart?

BERSON: Yes, that was fundamentally it at the beginning, but later on it got to be another reason and I stopped even applying for those partial support grants. That was a political thing. That came in the mid-1960s. I was very upset about the Vietnam War. I had a son who was approaching draft age. I had another son who was two years behind. I did not know when the hell this thing was ever going to end, and I decided that somehow I could not put myself in the position of, even indirectly, associating myself with what we were doing in Vietnam. So one year I simply did not apply, and I received communications from the officers of the agency essentially urging me to apply. I didn't apply and I essentially stopped asking for money from those agencies for—I'm going to call it—reasons of conscience or whatever you want. But I severed my ties with that kind of activity. I didn't want, even indirectly, anything that I did to facilitate what we as a power were doing in Vietnam. I was so opposed to that whole thing. So, you know, for whatever it's worth. Now at that time one could afford to do things for principle because there was a lot of other money out there. I had NIH pre-docs, I had NIH and NSF post-docs, NSF pre-docs. I mean I had all the money. I had twenty-five or thirty students hanging around and I really couldn't keep track of them. So what was the point of just collecting all this money?

[END OF TAPE, SIDE 6]

WEININGER: It’s a very interesting subject. Now there's been a lot written about physics, particularly. I mean, the amount of money they poured into chemistry was trivial compared to what they poured into physics. The military got convinced, by the end of World War II, that science had played a very big role in winning the War and that a lot of that science was what could be classified as basic science. After all, they had assembled all these tremendous teams of people, right? Out in Chicago, you know, all the nuclear stuff and the radar lab at MIT, and they did not want this to fall apart. They did not want these people to just kind of dissipate. The ONR was the biggest and the most ahead on this. They decided that they were going to have to sustain this research enterprise themselves until some other arrangement came along, and so they did.

BERSON: Yes. Well, as I say, that played a very, very important role. I never had ONR money, and I had the impression that most of that went into the physical side of chemistry. Colleagues of mine had ONR money.

WEININGER: Swain had ONR money.

BERSON: Yes, but I think that was not a usual kind of thing. I don't think I ever even applied for ONR money. But these other things were just out there, you know, like ripe apples sitting on a tree. If you needed money, you could get it from the AFOSR or what have you.

WEININGER: And you didn't have to claim any particular application? In other words, you could send the same grant application to NSF and to AFOSR?

BERSON: Oh, maybe one or two sentences. With thought of a fig leaf or a concession to their mission orientation and to indicate solidarity, let's put it that way. That, of course, was one of the things that turned me off; that I really couldn't any longer continue to do that. So that's all I have to say about that. I think they did a fine thing and I don't know where that stands at the moment. I have the impression that there's less and less of it now and maybe not much at all.

WEININGER: That the agencies are all mission oriented?

BERSON: Yes, and I think this is true for all the agencies, and we could spend a lot of time talking about that subject if you want to, about what's happened to other aspects of funding.

GORTLER: If you could back up just a little. You had a paper in 1959 that dealt with the resolution and stereochemical correlation of norbornane- and norbornene carboxylic acid (14).

I guess the important part of the paper was the use of the isotopic labeling. Could you say a word about that. That was very clever, and I wondered whether very many people picked that up afterwards. You were doing the isotope dilution as an aid to the determination of optical purity. I take it that was the importance.

BERSON: It was exactly. That was, I think, that may have been in the title of the paper.

GORTLER: Yes, it was, but it was sort of an addendum. "We were doing this project and here we did this, but the "this" may have been the key element in the paper.

BERSON: Well, isotopic dilution, of course, was a known technique, and, in fact, as we cited in the paper, the use of isotopic dilution to determine the enantiomeric purity had been used. We were not the originators of that. That was originated by Graff, Rittenberg and Foster, three biochemists at Columbia P&S. There had been a claim in the literature that in certain forms of malignant tumors, the growths contained cells that were very rich in d-amino acids. So the question became, "how do you determine whether there are d-amino acids in these tumors?" The point was that if you analyze using paper chromatography or some chromatographic technique like that, that doesn't distinguish d from l. So there's a long, tedious process that would have to be used in order to determine, for each amino acid, what the enatiomeric purity was and whether, in fact, the d form was dominant. Rittenberg had been a student of [Harold] Urey, I guess, at Columbia, and then he had gone to P&S to work with Schoenheimer. He had set up Schoenheimer's isotopic analysis lab which at that time was based upon deuterium, mostly. And Rittenberg and these other two fellows, Graff and Foster, worked out a method for direct analysis. The amino acid they were interested in was glutamic acid, and they did this by isotopic dilution. But they never took it any further. They certainly never applied it to any organic system, so it was buried in the biochemical literature.

Now, what happened was, at the time that we had to do this, I thought, well, why can't we do this by isotopic dilution? We had been doing some other experiments in which we had used isotopes, and so I sat down and I wrote out all the equations for doing this that allowed us to do that analysis by this means of isotopic dilution. We were writing this paper up, and then I said, wait a minute, I've seen this before. Our paper was published in 1959. Probably fifteen years before that, I had given a seminar, when I was an undergraduate, on that paper of Rittenberg. So it all came back to me and essentially I had reinvented the wheel. [laughter]

GORTLER: Oh, you didn't even realize it?

BERSON: I didn't realize it until we were ready to publish the paper, and it fortunately came into my head because if we had published it as an original thing, we would have made a much bigger story out of it and then it would have been very embarrassing for somebody to say hey, look, this was done a hell of a long time ago. [laughter] So it worked out very well, but I think the importance of this was not so much the use of isotopes. If I may say so, the importance was that this was the first time that I'm aware of that anybody used a method for direct analysis of enatiomers other than optical rotation. That was followed, of course, by other methods using NMR which are much more convenient. So this thing fell pretty much into limbo since nobody was going to take the trouble to do an isotopic dilution if you could do it with a simple NMR experiment using a chiral shift reagent or something like that.

WEININGER: Now you can just put it through a chiral column.

BERSON: Yes, you can put it through a chiral column. It's trivial now. But this was the first, really, so that was an important paper, I think.

GORTLER: I guess it's already clear from how you described USC why you went to Wisconsin, but can you tell us what actually happened? The year before you left for Wisconsin, you were at UCLA, I think.

BERSON: Before I left USC?

GORTLER: Before you left USC, you were at UCLA and I wondered if you were being considered for a position there.

BERSON: I didn't spend a whole year there. I spent part-time. I was teaching a course. Saul [Winstein] wanted me to come and teach a course, and I would go over, I think, three mornings a week or something like that, but I didn't spend much time there. I don't think I even had an office there. I just came and gave the lectures and if students wanted to talk, we would go to their lab or something like that. So I wasn't really at UCLA. I just traveled across town on the freeway, you know, the usual thing.

GORTLER: How did the offer from Wisconsin pop up?

BERSON: Well, you know, you asked me about whether UCLA was considering me at that time. They never asked me directly. If they had, I would have jumped—no question. But they didn't, and I subsequently learned that they had talked about it, but they decided that it was carrying coals to Newcastle. By then I was too, too strongly in that area and they already had that covered very thoroughly.

GORTLER: And then right afterwards they hired Chris Foote, but maybe they didn't think he was a physical organic chemist.

BERSON: Well, he came out of Woodward's lab, you know, and he was doing I don't know what, but very different things from what he ended up doing. So, his history was sort of parallel to mine actually.

WEININGER So you didn't go across town, but you went from one of the warmer spots of the country to one of the coldest.

BERSON: Yes, to one of the coldest, right. So Wisconsin was really a glorious opportunity for me and it was six of the happiest years of my life because for the first time I really felt that the impediments had been removed from me. The resources were available, not only in terms of students, but also in terms of excellent new lab space and very active colleagues. A thriving department with a great tradition in all fields of chemistry and some very active people whom I learned a lot from and interacted with very strongly. It was just a different world. I got into the major leagues, basically. I mean, I don't want to say anything derogatory about USC, but that was backwater as far as chemical research was concerned. There was very little going on there.

GORTLER: Did they come and recruit you?

BERSON: Yes, I got a phone call from Harlan Goering and in his usual way he said, "Hey, what are you doing?" [laughter] So we moved, then, in the summer of 1963, and almost immediately I began to attract a large number of students, many of them outstanding students.

GORTLER: I'm going down this list and I see that there's a “Berson School of Physical Organic Chemistry” out there.

BERSON: Well, a lot of students went on to do their own work. If you say a school—

GORTLER: Well, I meant they were your students.

BERSON: They were my students, but, by gosh, a lot of them didn't work on problems that they were working on with me. They went off in all directions. At first, I guess, I felt a little bit, hey, what are you guys doing? [laughter] But I learned to love it. I think it was great. So we did a lot of interesting things. It was a very lively group. It was a fruitful time and we discovered some things that I thought were interesting and probably, at least we thought, they were important. There is a kind of an autocatalytic effect. That is, if you have a certain amount of momentum going, and the students are being accreted to this pile, their energy and their determination and their intellect just drives and adds to the ferment of the whole thing. So I was floating on a running stream of bubbling ideas and accomplishment that these people were turning out.

GORTLER: They were sort of pushing you.

BERSON: They were pushing me all the time. I had to work like a beast to keep up with them. [laughter] And, you know, we kept changing. The problems we were working on kept evolving and shifting completely, dramatically into new areas. So that was a very seminal time in my career.

GORTLER: Actually, it's sort of interesting and now I'm beginning to understand some of this. One of the first papers you suggested I look at was one with Maitland Jones on the stepwise mechanism of the oxy-Cope rearrangement (15). I guess that must have been one of your early forays into thermal rearrangements, and trying to understand that kind of reaction. Yet, in this particular case, your final suggestion was that it was, in fact, a stepwise mechanism as opposed to a concerted mechanism.

BERSON: What we were trying to show was that there really were two pathways, one of which starts out with the two ene groups syn to each other. You may remember that there were two stereoisomers of the starting material, and the vinyl group, in one instance, was pendant over the double bond that it had to become attached to to make the Cope rearrangement occur and in the other case it was pointed away. We agreed that the ordinary Cope rearrangement was a concerted reaction, but what we found was that even when the vinyl group was pointed away and therefore there was no hope of it being concerted, that one also gave the Cope product. So that was the origin of the title of that paper, that we had found a non-concerted Cope rearrangement. Now the other significance of that, of course, is that it became a synthetically very important kind of transformation, and we pointed that out in the paper, in one of those papers anyway (15 (b)), that you could make unsaturated cyclohexanones by the Cope rearrangement. Of course it became very popular when Evans found that you could accelerate this reaction many orders of magnitude by using the anionic version of it, by putting in potassium hydride or something like that. As a result you didn't have to heat it up and it made it compatible with all kinds of tender functional groups on big molecules that people were trying to synthesize. So there are many, many references to the oxy-Cope rearrangement in organic synthesis—very few of them to our paper, by the way. [laughter]

I met a fellow in Taiwan, whose name I won't mention, a very kind and nice fellow, who told me that he was very disappointed. He always admired the oxy-Cope rearrangement, and it had turned out to be such an important component in organic synthesis and that he was a synthetic organic chemist and he was very upset that most people don't recognize that it was really developed in our lab. This fellow then somewhat later in the day made me a present of a book that he had written called *The Tactics of Organic Synthesis*, or something like that. In leafing through the book I looked up the oxy-Cope rearrangement, and sure enough he discusses it at great length, but he doesn't mention us. [laughter]

WEININGER: Now, is this the origin of your interest in sigmatropic rearrangements, because it certainly takes over as a big theme in your research.

BERSON: Yes, well, that and the work that we did also at Wisconsin. George Nelson's work, was a culmination of a series of papers, on the thermal 1,3-sigmatropic rearrangements (16). The one that he worked on was the bicyclo[3.2.0]heptene rearrangement, but we were working on other thermal rearrangements. Well, somewhat after that we started working on the stereo-isomerization of cyclopropanes in about 1968, but the Nelson paper came out in 1967.
This really goes back to an early interest in the Diels-Alder reaction. Sid [Sidney] Benson and I had written a couple of papers on the use of pressure effects on liquid phase reactions (17), and one of the key examples of that was some work that Cheves Walling did on the Diels-Alder reaction- the dimerization of cyclopentadiene. From "measuring" the volume of activation, which you could get from the pressure dependence of the rate constant, at least that's what was thought at the time, he came to the conclusion that this was a stepwise reaction because the transition state was very large. It was much larger than the product. So that you went to, in his view, a very loose kind of transition state, and that, to him, meant you were making only one bond so it was occupying much more volume and it was going through a diradical intermediate rather than a tight transition state, which you would have from a concerted reaction. So Sid and I wrote two papers. We were both criticizing this work of Walling's and our papers were, subsequently, criticized by other people.

GORTLER: Where was Benson?

BERSON: Benson was at USC. So this was in the USC days.

GORTLER: That was an interesting collaboration because Benson was a physical chemist.

BERSON: Yes, absolutely.

GORTLER:  So you were readying yourself, in a sense.

BERSON:  Oh, sure.

GORTLER:  This was back in the 1950s.

BERSON:  This work was done in the early 1960s.  Anyway, I became very interested then because here was a thermal reaction.  I was getting very interested in thermal reactions, and there was clearly a whole category of thermal reactions that could be formulated with biradical intermediates, or as concerted reactions, and this became one of the big problems of the next couple of decades in physical organic chemistry—how do you tell the difference between these two?

So we segued from there into really studying biradicals directly, not necessarily as components, not as points of transition states or intermediates, but as actual, observable species. So that's how we got into that area.  But all through that period, starting at USC and going to Wisconsin and continuing here, we were working on thermal rearrangements and the idea of investigating the role of biradicals in those reactions was the center of our attention during that whole period.  And it was during that time that you saw a couple of papers in which you said that I was saying something negative about Bill Doering or something that Bill had said. Actually, I never mentioned him.  I mentioned what he had said and I was arguing against it. I'm not sure which paper you're thinking of.  Oh, it may have been in the cyclopropane paper.

GORTLER:  Yes, it was the cyclopropane paper (18).

You said that "Doering and Sachdev had concluded that these distributions were excellent and in agreement with the 35/65 ratio of diastereomerization to enantiomerization," and then you pointed out that his results were, in fact, directly opposite from the ratio that had been predicted.  And, you wrote, "Since the predicted order of preference is the reverse of that reported experimentally, the nature of the alleged agreement is not clear."  I thought that was a rather pointed swipe at your old mentor. [laughter]  Was he [Doering] still here [at Yale]?

BERSON:  No, he was at Harvard then.

First of all, he never believed what we published.  And I couldn't get him to discuss it, really.  I tried.  I sent him pre-print copies of the paper, you know, in manuscript form, and I said well, you know, I'd really like to talk to you about this, but I never could generate a discussion with him.  He just brushed it aside.

GORTLER: That was one difficult paper though. That's the one that has this very complicated kinetic analysis, and it occurred to me as I went through it, I said, gee, did he really expect some reviewer to actually read this?

BERSON: Well, you know, it's a very interesting point you raise, because seventeen years later, John Baldwin submitted a paper to *JACS [Journal of the American Chemical Society]* in which he claimed to have found an error in that kinetic analysis. [laughter]

GORTLER: It took him that long?

BERSON: So, somebody did review it. [laughter] Unfortunately, his correction was wrong. [laughter] So his paper never got published. I think that everybody should be pleased that it worked out that way because I didn't want to get into a public shouting match. But, I mean, he had found something in the Bigeleisen equation about isotope effects and we had to make some corrections for isotope effects there, and he felt that invalidated the whole derivation. It was a factor of two that we had gotten wrong. Well, it could easily have been the case because there are lots of factors of two there, and if you're not very careful, it's easy to make a mistake. But, as luck would have it, we hadn't made a mistake and he had made a mistake. [laughter]

I mean, this thing was quite confusing that he had there, that you just quoted, because that was simply contradictory to what had been predicted. But another thing that he had done in there, which was just flat-out incorrect was, he had combined two rate constants and calculated an activation energy from the sum of two rate constants. Now, in transition state theory, you're not supposed to do that because there is one rate constant per transition state. I mean, it's a no-no. It's like having a bifurcation at the transition state. You may have it if transition state theory doesn't apply, but he was calculating an activation energy. That means transition state theory. So that was simply an error, and we pointed out that his ratios for internal rotation versus ring closure were off because he had calculated these activation energies by that erroneous process. So there really were two criticisms there. Yes, that's one place where we disagreed where I mentioned him by name, but there are other places where I haven't mentioned him by name, but I put down arguments that he was putting forward at that time where we disagreed.

GORTLER: I just wondered whether you were arguing now over times that he had admonished you as a graduate students?

BERSON: Well, let's hope that wasn't true. I tried to keep it on a scientific basis.

GORTLER: You probably looked at the Cope rearrangement many times, but there was a 1990 paper that you suggested I read (19). That was the acetelynic Cope rearrangement, and in that particular case you were actually looking for biradicals and didn't find them.

BERSON: Exactly.

GORTLER: And I wondered what made that important?

[END OF TAPE, SIDE 7]

WEININGER: I wanted to ask Jerry whether he feels he has a style of doing research because, at least I get a sense of looking over the papers you gave us, that there are certain kinds of elements that one would see—there's a kind of intricacy—in the work you do, I mean both in terms of the experimental stuff itself and then the kinetic analyses which are, I think, intricate is the word I would use. I'm wondering whether that's conscious.

GORTLER: The use of stereochemistry in a very sophisticated way. You're right. And also your use of isotopes.

WEININGER: Right. I mean, there are certain kinds of motifs I think you'll see.

BERSON: Yes. There's no doubt about that. I think that's true. I'm not sure that it adds up to a style, but it's pretty clear, at least in that phase of physical organic chemistry, that a lot of information was available to be had. Now the downside of that was that some of these things were not available from Aldrich Chemical [fine organic chemicals supplier] and they involved major synthetic undertakings. The work we did on the homodienyl hydrogen shift is a case in point. It's described in a set of papers that came out in about 1990, I think. Work with Parziale and Getty. There may have been a review article on it in *Accounts of Chemical Research* (20).

GORTLER: Yes. You wrote a review article, "The Overlap Component of the Stereo-electronic Factor."

BERSON: Right, yes.

GORTLER: Do you usually ask your students to do at least one synthesis during their research?

BERSON: No. That's not a priority. In other words, I have been very selfish about that. There have been a lot of complaints about that style of doing research over the years—particularly some of the industrial companies have complained that the students are working too much on one thing and they'd like them to work on a variety of different things. I've always taken the position, probably selfishly, that what the student learns the most from is confronting a difficult, substantial problem and actually solving it or at least getting it to the point where it can be solved. A student learns much more about the real life of research from that than from having a series of broken up, small problems each of which is more or less guaranteed to work. So I've had to worry during my time a lot about making sure that a student doesn't get bogged down.

I have an understanding with the student at the beginning that, look, I don't know that this is going to work. It's really kind of blue-sky stuff. If it works, it will be great and we'll learn something new, but if I see that we're getting into trouble here and we're not getting anywhere with it, I may just advise you to get off. Some students will shy away from tackling a problem like that; others plunge in and they are gung ho. In some cases, they are so gung ho that they refuse to admit that they've been beaten, that they are not going to solve this problem. It's like pulling teeth to get them to switch over onto something else. So I've always had that worry because the problem itself has been the objective. All these other things feed into it, they support it, but I don't choose problems as illustrative of the technique of isotopic labeling or of stereochemical labeling or of synthesis or anything like that. What I try to do is to identify a problem by its intellectual content. If we knew the answer to this, would there be other things that we would know the answers to? So that's the driving force.

I don't think that's a style, but if it is a style then the way it has manifested itself is that it frequently turns out, as you point out, that these techniques that we have been using at least in that aspect of our research have been very powerful. Now when we got further into the real non-Kekulé compounds and high spin compounds, we had to use other techniques of course. But again the idea there was in pursuit of a defined intellectual problem. It's not to say that we always got the answer we were looking for. Many times we got complete surprises. We had no idea what was really going on, so these things were kind of accidental discoveries, but at least we started out with that kind of thing in mind.

GORTLER: What about that acetylenic Cope rearrangement that we started to talk about earlier?

BERSON: Okay, let's get that out of the way. Now the idea was that the Cope rearrangement at that stage of the game was said to be a concerted reaction, but Bill Doering was still taking the position that it might be going by a biradical mechanism. This was based upon some arguments that go back to Sid Benson. Sid was arguing that you could determine the heat of formation of a biradical on the basis of a small number of assumptions. One of them was if you start with cyclopropane, for example, and you ask yourself, what does it take to break a carbon-carbon bond in cyclopropane and make the propane-1,3-diyl biradical? So Sid Benson said that, well, we ought to be able to get an estimate of the heat of formation of that biradical from the activation energy for carrying out the cis to trans isomerization of dideuteriocyclopropane, which [Benton Seymour] Rabinovitch and [Edward William] Schlag and, in fact, Ken Wiberg, were involved in back in the 1950s. They showed that you could get the cis to trans isomerization thermally and they postulated, as [George] Kistiakowsky had, that this went through a biradical. So Benson said, well I can estimate the heat of formation of the transition state for that and I can estimate the heat of formation of propyl biradical, a 1,3- biradical. We can get the heat of formation of propane-1,3-diyl by creating it (mentally) from 1-propyl radical. So think of the heat of reaction for propane going to 1-propyl + H• and assume that the heat for 1-propyl to 1,3-propane diyl + H• is just the same. Now that's a big assumption.

In any case, if you put those two things together, then you can get the energy for the back reaction, which is the energy of cyclization of propyl biradical back to cyclopropane. Now, if you go through the calculation using Sid's argument, it turns out that there is a barrier of something like 9 or 10 kilocalories per mole, just to cyclize, that is, to make cyclopropane from the biradical. We are talking about two radicals in the same molecule just going boom and forming a single bond. Why should that cost 9 or 10 kilocalories of energy? So, it's called the Benson Barrier and there's been a lot of argument in the literature about whether it really exists, and if it doesn't exist, then what's wrong? Well, one of the things that Bill Doering points out, and I think correctly, is that people have been using the wrong energy for the dissociation of propane to 1-propyl + H•. Sid was using an earlier value for the bond dissociation energy of propane. If you use the more modern energies, the value of the Benson Barrier drops to something like 5 kilocalories. And then Bill wanted to get rid of the remaining 4 or 5 kilocalories by saying, well, the 65 kilocalories that Benson used was based upon Rabinovitch's observation of the activation energy for the cis-trans isomerization of dideuteriocyclopropane. But Bill says, "Rabinovitch has now redone this and it's no longer 65, it's 61 which will bring the energy down so there's practically no Benson Barrier. That's the end of the Benson Barrier and we can write 'finished' to that story."

I wasn't aware of this for a long time until somebody else tried to use it in an argument. They tried to use the later Rabinovitch activation energy that Bill had quoted in an argument, and I went back and actually read Rabinovitch's paper, and that's not what Rabinovitch was talking about at all. It was a completely different thing. [laughter] He was talking about the activation energy for the reaction in the low-pressure limit. In other words, what Rabinovitch was talking about was the problem of energy transfer. How fast does the energy get transferred by collisions with other molecules? So that activation energy did not apply at all to what Benson was talking about and so we still are faced with this 5 kilocalorie barrier. Who knows what the answer is, whether it's real or not?

In any case, getting back now to this acetylenic-Cope rearrangement, and I'm sorry to make this such a long story, but this is where this argument came from. Doering was now arguing that the Cope rearrangement—if you used the Benson-type of argument and calculated the heat of formation of the hypothetical cyclohexane-1,4-diyl biradical that you would get by just taking 1,5-hexadiene and closing it without any breaking of the other bond, in other words, a stepwise reaction going through a cyclohexane-1,4-diyl intermediate, if you calculate the heat of formation by Benson's method, the additivity method, then you get the heat of formation for that biradical which is very close to the measured energy of the transition state of the Cope rearrangement. The activation energy for the rearrangement was measured by Doering and other people. So Bill still wanted to float the idea that maybe this is a rearrangement that takes place through a biradical intermediate, which is very close in energy to the transition state.

So our thought was, well, why can't we investigate this? The point was that if you have a cyclohexane-1,4-diyl intermediate, then if the cleavage of the second bond is not very fast on the time scale of an internal conformational isomerization, then you could build in stereochemical labels, and then the rearrangment product should have some scrambling of the stereochemistry depending upon the relative rate of those internal rotations with respect to the rate of bond cleavage of the second bond. We wanted to try to measure or estimate the rate of that internal bond rotation and compare it to the actual, overall rate of reaction and see whether there was any chance that that would happen. Well, it turns out, in the case of the acetelynic-Cope rearrangement, the intermediate would be a cyclohexene-1,4-diyl, and that intermediate should have a much lower barrier for rotation because it's not really a chair-to-chair isomerization. It's a half-chair to another half-chair, which is a very low-barrier kind of process.

In fact, we went ahead and made a precursor of cyclohexenyl monoradical—3-cyclohexene-1-yl -- and we sent that to Dan Wayner up at Ottawa (21). They measured the rate of stereomutation of that monoradical and we used that as a model for what could be expected for the rate of stereomutation of a biradical. There's still an assumption, and that is that having the other radical center there doesn't slow down the rate of isomerization to the point where the experiment is inconclusive. Well, it turns out to be a very low barrier for the isomerization, which was measured by time-dependent ESR [electron spin resonance] spectroscopy, so we went ahead then and did the stereochemical experiment. The idea was that if there was a biradical intermediate in the acetylenic-Cope rearrangement it should destroy the stereochemistry. In other words, we should lose stereochemical integrity during the rearrangement because of that internal isomerization that was going to be competitive with the bond cleavage.

Now what we determined was that the rearrangement took place with complete retention of stereochemical integrity. There was no racemization whatsoever. That meant that the rate of cleavage of the second bond in the Cope rearrangement had to be at least some orders of magnitude faster than the rate of isomerization of the alleged biradical intermediate. Since that alleged biradical intermediate was modeled on a monoradical that already had a rate constant for conformational isomerization in the range of 1011 or 1012 per second, which meant that the bond cleavage rate has to be at least a hundred times faster than that. So it puts it in the realm of almost faster than a molecular vibration, so it's not an intermediate anymore. So that was the rationale of that experiment.

But it all goes back to this very early stuff about biradicals, and Sid Benson and I sitting around in the barracks talking. [laughter] I just seem to remember this, talking about this, because his lab had not been moved out of the barracks. He stayed in there. He was a physical chemist. [laughter]

WEININGER: They weren't worried about fires with his stuff? [laughter]

BERSON: That's right. [laughter] So, as I say, this experiment is vulnerable to criticism. I mean, I don't think there's anything wrong with the experimental work, but I think the criticism is that there are some assumptions here. This is a model. We haven't actually measured that rate of isomerization for the biradical. We've only measured for the monoradical. And we've said, "Well, we're going to use that rate as if it were the same as the rate for this hypothetical biradical." But the idea of designing the experiment so that in order to match the result one has to push the biradical off of any conventional scale of rate constants so that it's like a form of logical elimination by *reductio ad absurdum* is really what it boils down to. [laughter]

GORTLER: I wanted to talk about some of the papers in between but it’s getting late, so let's talk about the biradical work. We can come back and talk about these other things as well if time permits. That work seems to be an outgrowth of a lot of things, that is, some things you did before, so why don't you tell us, in your own words, what were the origins of the biradical work.

BERSON: The work with the directly observable biradicals?

GORTLER: Yes, the non-[August] Kekulé structures.

BERSON: Yes, well, that had its origin in another aspect of the work on orbital symmetry. During the middle to late 1960s all the way through the 1970s, we had been designing a number of systems to test orbital symmetry rules and we had found a number of, I think, interesting things. All of the work that Woodward and Hoffmann had done was related to kinds of systems in which there was no problem about the change in multiplicity. In other words, the biradicals that people had been postulating were always sort of implicitly assumed to be singlet biradicals. Nobody really wanted to talk about triplet biradicals. We began to worry about the question of whether triplet biradicals ever can play a role in these reactions, and if so, to what extent can one apply orbital symmetry theory to such systems because the orbital symmetry theory, if you think about it, depends, in a way, at least in its simplest and most primitive form, upon electron pairs. It depends upon double occupation of orbitals by pairs of electrons. So what we were worried about was what would happen if you have degeneracy, or near degeneracy of orbitals. Then the possibility now becomes quite prominent that it could slip over into the triplet manifold. The triplet, generally speaking, one might think would tend to be more stable or at least accessible. How would one recognize the intervention of that kind of a biradical? So we set out to study some biradical systems in which we would be generating a species that was known to have a triplet biradical ground state. Now, sometime before that, in the middle 1960s, Paul Dowd had made trimethylenemethane, and so we thought, well, what happens if we involve a trimethylenemethane unit in a thermal rearrangement? Will the reaction retain the stereo-specificity that we see in other thermal reactions that are associated with orbital symmetry concerted reactions or will everything break down and just degenerate into a kind of stereo-random thing?

So Wolfgang Bauer, a very nice German post-doc in my group, did the crucial early work (22). We started out with a system that he showed still retained a lot of orbital symmetry characteristics in it. If you think about the ring opening of cyclobutene to 1,3 butadiene, what we did was to replace the double bond of the cyclobutene with a three-membered ring. So we fused on a cyclopropane ring. The first thing we wanted to see was how well our orbital symmetry effects transmitted through a three-membered ring sort of homo-conjugating that whole system. So we made those molecules stereochemically labeled with appropriate substituents on the breaking bond and we examined the stereochemistry of those, and lo-and-behold, they were, to a considerable extent, stereospecific in the same sense that the thermal ring opening of cyclobutene is, namely conrotatory. So we said, ah hah, well here's a thing in which you might have expected, in which people, in fact, had postulated the existence of a biradical. The thermolysis of bicyclo[2.1.0]pentane is really what we were looking at. There's an exo-endo isomerization there if you have the appropriate substituents and people had postulated a biradical intermediate there for that exo-endo transformation.

So, having shown that that ring opening is stereospecific, we then said, well, what would happen if we put a methylene group at the 2-carbon of that cyclopropane ring? That would mean, then, that this hypothetical biradical intermediate would be a trimethylenemethane. So Richard Bushby undertook the synthesis of the diazene precursor (Figure 3) of that bi-radical and that's how we got started in this whole thing (23).

[insert figure 3]

He made the corresponding trimethylenemethane, showed by ESR spectroscopy that it had a triplet ground state. Later, in work primarily, or at least originally, by Dale McDaniel, we went ahead and examined the chemistry of that species (24). Now the advantage of having incorporated that trimethylenemethane into a five-membered ring was that it opened up a rich chemistry, particularly cycloaddition chemistry, which one cannot observe, apparently, with trimethylenemethane itself. If you look in the literature for reactions of trimethylenemethane itself, about the only thing you'll find is that it closes to methylenecyclopropane, but the other reactions are essentially unknown. The reason has to be, I think, that it ring-closes so readily that you can never trap it with external trapping agents. But in this case we were able to trap its derivative, 2-methylenecyclopentane-1,3-diyl.

WEININGER: There's no barrier to re-closing it?

BERSON: There's no barrier to re-closing trimethylenemethane itself, I think. It must be a very low barrier. I'm talking about singlet now, singlet trimethylenemethane. Nobody has ever observed that. But even the triplet has a barrier of only 7 kilocalories, so if you consider that that's a lower energy species, the barrier for the singlet must be miniscule.

WEININGER: But of course there is no torsional barrier is there, as there is in the propane-1,3-diyl?

BERSON: No. In the propane-1,3-diyl itself, there are all kinds of other things that come into the picture. Yes, definitely. But, in any case, the main point about our trimethylenemethane, if I can call it that, it's actually 2-methylenecyclopentane-1,3-diyl, is that it is trappable. And it's trappable both as the singlet and the triplet, so we've been able to separate out the chemistry of those two entirely different species. It's sort of like carbene chemistry. There are a few cases in carbene chemistry where for a given carbene you can see both the singlet and the triplet chemistry, and that's the case here with, now, a whole range of these biradicals. So we got really intrigued with this and we began to investigate this in some detail. That led us into all kinds of other things with biradicals and we became particularly interested in this spin problem.

Now, I worked in the field of chemistry for something like forty years before realizing that the guiding spirit of everything that I've done, at least in physical organic chemistry, has been Erich Hückel. I did not realize this until very, very recently. You know how that happened? We were wondering-this is the period around 1976-1978—how does one know that Hund's Rule applies to biradicals and what is Hund's Rule after all? Where does it come from? So, we began to study this in some detail and to try to learn something about the origin of the separation in energy between multiplet states of a given species. And we came to the conclusion that we didn't know beans about this. Moreover, it turns out that Hund didn't know beans about it either. And people have been throwing this idea around as kind of a shibboleth or a rubber stamp. As long as you have a triplet, that must be the ground state. And it had been confirmed for some carbenes, people had found that to be true. Dowd had found it to be the case for trimethylenemethane and for tetramethyleneethane, he thought, although that's not clear right now. There's some experimental evidence that points in the other direction, that at least in the gas phase it seems to be singlet. So we became very sensitized to this problem because this was the material we were working with. We were working with biradicals derived from so-called meta-quinonoid substances. We were the first to synthesize a metaquinone, and we synthesized from that the corresponding biradical, or meta-quinonoid, really. So we became conscious of our ignorance and we became very sensitized to how does one decide about this issue of what's the ground state, or what should be the ground state?

[END OF TAPE, SIDE 8]

WEININGER: What got you into your interest in the history of chemistry enough so that you actually wanted to go ahead and do research and write about it? I'm wondering if it's connected. I mean, you talked about realizing there's a deep obligation to Hückel, and now you're talking about digging into the origin of Hund's Rule, which, you know, we all just accept without thinking about it. Is this connected or does it have another origin?

BERSON: Well, the general answer to the question is that I got old and I began to wonder, what have I been doing all this time? Does it make any sense? So that began to turn my mind toward how do we do science and what is it that makes some science accepted and stimulates a lot of additional findings and progress and other science just sort of falls by the wayside and one doesn't hear much about it anymore? What are the key elements that distinguish between those two categories? But beyond that, now I'm becoming very interested in the philosophy of science because I've begun to wonder about, "Is there a logical component to what we do?" These things are obviously very closely tied up with the history of science. Well, I could go on about this, but in the forthcoming issue of *Angewandte Chemie* it's going to be in No. 7, I believe, of the International Edition, you'll find an exchange of views, let's put it politely that way, between myself and a man named [W. Martin] Wallau (25(a)). I don't know what his background is, but he lives in Brazil and he has written a critique of a paper that I wrote. My paper was entitled "Kekulé Escapes, Popper Notwithstanding" (25(b)). That was published last year in *Angewandte*. So this guy has written a critique and I've got a rebuttal to that critique and they're going to be published side by side (25(a)). But he maintains that philosophy of science has nothing to do with history of science. It's not a methodology. It's not supposed to tell people how to do research. Well, if that's not what it's for, then what is it for? You better believe that [Karl] Popper thought that what he said was what scientists should be doing. But then I had been asking myself for a number of years, well, "Who is Popper to tell us what to do?" Do all the philosophers agree with him? It turns out that they don't. It's a terrible fight among these people. So what is the philosophy of science? What is scientific methodology and what is its relationship to the development of our subject and to science as a whole? Now, the answer is, I think, that there is a connection but it's not a normative connection. Science is not reducible. I mean, you can reduce the philosophy to a set of rules, but science, by and large, ignores those rules. It proceeds by its own internal dynamic. It's just in total ignorance of what the philosophers of science tell us.

GORTLER: But surely you don't know any scientist or chemist who ever, considering a problem, says, "Gee, how would I approach this?"

BERSON: Exactly, but we are criticized because we neglect that. We are criticized, by some philosophers, for failing to follow their recommendations on how we should do science.

WEININGER: But, if I may interject this here, that's because a lot of philosophy of science, at least in the traditional form, I think is changing. It's based on a certain type of physics, all right, and that's become the template.

BERSON: Exactly.

WEININGER: And so, in fact, I think history and sociology of science have a lot to tell us because they tell us about the uniqueness.

BERSON: Absolutely. About how it's really done.

WEININGER: And the internal, sort of, unwritten norms of different paths of science.

BERSON: I agree. I'm absolutely with you, 100 percent. That's exactly right. So basically what these people are doing is imposing upon us their own grid, a kind of Procrustean bed that we're being pressed down on, saying that these are the rules you have to follow. We can't work that way. That's not the way we work. We're not smart enough, in a sense, to do it that way.

WEININGER: No, our system is too complicated.

BERSON: Too complicated.

WEININGER: I mean, it's a big difference—a molecule is so much more complex than an isolated electron.

BERSON: Fantastically. Absolutely.

WEININGER: You can't operate the same way.

BERSON: Absolutely. So that is the interface that I'm trying to explore now. So whether this book will ever get finished, God only knows, but this Kekulé and Popper article was kind of a preliminary shot across the bow of the philosophers, and by gosh, they answered back with all guns ablazing! [laughter]

WEININGER: At least you know someone's reading it! [laughter]

BERSON: Somebody's out there reading that stuff! [laughter]

GORTLER: Had you finished talking about the Hund's Rule?

BERSON: Well, I was coming back to that. This is in connection with Hückel, it turns out, oddly enough. Hückel, you know, had been an associate of Hund at Göttingen, just after his Ph.D. I guess he was sort of a post-doc.

Well, let me tell you this story. I was talking about what we were talking about in the lab [in 1976, 1977], that is, how do we know that Hund's Rule is right, and when do we apply it and when don't we apply it? Well, in 1977, two papers appeared, one by [Alexander] Ovchinnikov in the then Soviet Union, and one by [Weston] Borden and [Ernest] Davidson in the United States. Both of them gave a set of rules for recognizing in which classes of biradicals does Hund's Rule apply and in which should it not apply. In the latter cases, you could have violations of Hund's Rule, that is to say, you could have singlet ground states. Now the reasoning behind these two papers was very different. Ovchinnikov was arguing from a valence bond point of view using a Heisenberg Hamiltonian. We looked at those papers and we decided we didn't know what a Heisenberg Hamiltonian was and valence bond theory, forget it, we didn't know anything about that. So we took his results, which he did, bless him, couch in a very easy formalism for a chemist to understand and it was a very predictive kind of theory. It predicted that certain connectivity patterns of the centers in a pi-electron system would allow you to tell whether that molecule, if it was a biradical, was going to be a high spin or a low spin ground state.

Borden and Davidson derived a very similar set of results by using molecular orbital theory. Their argument was based upon a set of physical principles that one could understand. It turns out, for reasons I don't want to go into too much, that if you have a biradical or a multiradical in which the orbitals in which the unpaired electrons are circulating have zero overlap or close to zero overlap, it's as if they were totally unaware of each other's existence. An over-simplified way of thinking about the physical basis of Hund's Rule boils down to an electron repulsion argument. It has to do with the fact that in the singlet state those two orbitals are taken with a positive sign in the space part of the wave function, and in the triplet state they are taken with a negative sign. This means that any time in the triplet state that two electrons spatially get close to each other, they automatically recoil, so you have perfect electron correlation, they stay away from each other, and that minimizes the electron-electron repulsion. Whereas in the singlet ground state, they circulate through the entire combined wave function and therefore they can't get out of each other's way. That's a higher energy state because of electron repulsion. That's a simple argument. Now, Borden and Davidson called the group of biradicals, which have this property of having spatially separate orbitals, "disjoint." They coined a word, and so we've used that word. I don't particularly like it, but it conveys the idea that they're not talking to each other. But basically it boils down to making the same kinds of predictions that Ovchinnikov's rules did.

At that time, there was no example in the literature of a molecule, a biradical or a higher multiplet state, that violated Hund's Rule, let alone a direct test of this idea of theirs that it intimately depended upon the structure. In other words, they were saying you can't consider a biradical just to be two electrons on a blob of just some sphere. You know what I'm saying? This is the way a physicist would look at it. You just have two electrons and you have to worry about how do they interact with each other. Not so. It depends very much on the nature of the thing around which they are circulating. The connectivity. It's a very deeply chemical idea. The physicists never tumbled to that. These were chemists that came up with this.

So we were just thrilled in the lab! We said, “My God, look at all these molecules that they make predictions about or that are implied by those theories! You can just write them down on a piece of paper.” You can spend the next twenty-five years doing nothing but testing these rules, and that's basically what we did. So between 1977 and the time I retired, about 1997, that was the main focus of our research. But now here's where Hückel comes into this. So we were sitting around the lab congratulating ourselves that here these theoreticians had come to our rescue just in the nick of time. We were ready. We were really pumped. We had our low temperature helium cryostat set up. We had our low-temperature FTIR [Fourier Transform Infrared Spectroscopy]**.** We were contracting with Kurt Zilm to do low temperature, solid state, magic-angle spinning NMR on our biradicals. And, boom, we weren't just going to be fumbling around in a vacuum now. This was a focused set of objectives that we could concentrate on. Well, a couple of days later, one of the students in my lab, Ed Helinski, a very smart guy who's now a professor at Florida State [University], came into the office. He had some papers in his hand and his face was pale. He looked ashen. I said, "Ed, are you alright?" [laughter] He said, "Yes, I'm okay. But I want you to look at this paper." He had made a copy of a 1936 paper by Erich Hückel in which Hückel had pointed out, in the case of the first pair of biradicals to which these ideas could be applied—in 1936! This is work of Eugen Müller who had consulted Hund, by the way, and Hund told him that his molecules should both be triplets. These were molecules that had been made originally by Schlenck and Brauns in 1915. Those were the first biradicals ever made. Müller had an ambiguous result with one of them and the other one he found was a triplet. He got some magnetic data which showed that it was a paramagnetic molecule and therefore he said it's a triplet and therefore Hund is right. The following year or maybe even later the same year, Hückel published a paper, which was completely lost between 1936 and 1977 when Ed Helinski rediscovered it. What Hückel was saying was exactly the same thing that Borden and Davidson were saying. They had rediscovered Hückel's work. They had never heard of it when I called it to their attention. They had rediscovered Hückel's argument, *in toto*, of course at a much more sophisticated level because they had all kinds of computational backup now. Hückel had made the argument in more qualitative terms, but fundamentally it was the same argument that if the nominal NBMO [non-bonding molecular orbital] wave functions have zero overlap, that isn't necessarily a triplet. Hund's Rule does not apply and that has to be tested by experiment. That's not predictable. In 1936 this guy had this idea! The guy was just a genius.

Now, the sobering thing to this story is that in 1950, the seminal paper on biradical chemistry, the theoretical paper on biradical chemistry, was written by Christopher Longuet-Higgins. It was published in the *Journal of Chemical Physics* (26). It was based upon simple Hückel calculations, and what he did was to calculate the properties, the energy levels, of a whole bunch of monoradicals and biradicals, and he showed that a number of biradicals that are now known—tetramethyleneethane was one of them and I believe meta-quinodimethane was one of the ones in his group—should all be triplet species. Now tetramethyleneethane is a very interesting case from the Borden and Davidson point of view because that's disjoint, and that's exactly the kind of molecule that Hückel was saying we don't know what the ground state should be. But Longuet- Higgins apparently was unaware of Hückel's paper. He doesn't cite it and he simply goes ahead and blithely applies Hund's Rule. So from 1950 all the way through to 1977, everybody was assuming that if you make a biradical, it's going to follow Hund's Rule. It's going to be a triplet ground state. All this stuff was buried and this is stuff that Hückel had worked out and which now came out of left field and we now realized what the significance of that was. So we pointed this out, that Hückel's paper had been overlooked, and I included this in my book (6) and in my article on Hückel (27). Still a lot of people ignore it. Longuet-Higgins, for one, has ignored it. He's never said anything about it. [laughter] So this guy, he had been sort of a ghost or an angel, if you want, looking over my shoulder. All this orbital symmetry stuff and the biradical stuff goes back to work that, in some sense, he anticipated. He was a genius. That's the only word I can use for him.

WEININGER: What led an American graduate student, in 1976-1977, to go look back?

BERSON: Yes, I asked Ed that, and a French chemist, I've forgotten his name, had a passing reference to that paper in a different context. Ed is a very thorough guy and he was, I think at that time, in the stage of preliminary work for his thesis and he was gathering all kinds of references. He said, well, I better go read that Hückel reference [laughter], and boom, there it was.

WEININGER: [laughter] Isn't that something? [Weininger leaves the interview at this point.]

GORTLER: You published a lot of reviews. Obviously it's been a lot of work to do that. Why do you choose to publish that way?

BERSON: Well, let's put it this way. I don't think I publish reviews instead of papers.

GORTLER: No.

BERSON: But in addition to papers.

GORTLER: Yes, exactly.

BERSON: The reviews are not always just of our work. I put a lot of work into a review for Paul de Mayo's book (28) on molecular rearrangements, the first version of that, and that was a review on Wagner-Meerwein rearrangements in bicyclic systems. And that review, I think, dated from a period of time when we were beginning to get into that area. I started working on that in probably about 1959. It didn't get published until 1963, but most of it was written in 1959 and 1960. But the stimulus for that was that I just had to become familiar with the literature. There was an enormous amount of it out there, and I somehow had to organize it and the stuff that was coming out had very little in the way of historical background. Winstein, particularly, and also Roberts were publishing papers in that area. I was following that work. [Christopher] Wilson, of course, many years before had proposed non-classical ions. So I felt that I owed it to myself and to my students to organize that stuff, and I used the occasion to do that. In the later stages anyway, I taught a course. The course at UCLA was based largely on that chapter that I wrote. Again, we are talking about "coals to Newcastle." So Saul and I used to have some pretty hot arguments. [laughter] He came to every one of my lectures. It was great! It was just terrific. The students loved it. But I learned a lot and he straightened me out on a lot of points. So that was really the motivation for that review.

Now a number of the other reviews were in *Accounts of Chemical Research*. Those were our own work. The first *Accounts* article that I remember was probably in 1967 or 1968. It was in the first volume of *Accounts* (29). It was one of the first issues.

GORTLER: Yes, that was one we were going to talk about briefly. That's the one on the stereochemistry of sigmatropic rearrangements.

BERSON: Right. So that was very hot at the time. The Woodward Hoffmann stuff was at its height.

GORTLER: And you had already done some work in this area.

BERSON: We had done some work on that. The Nelson observations were part of history then (16) and we'd worked on the tropilidene rearrangement, the circumambulatory 1,5-sigmatropic shift of cycloheptatrienes. That work with Bob Willcott (30) was also in the same review article. The Willcott work was also reviewed in the *Record of Chemical Progress* in 1966 (30 (d)). The full paper of the Willcott work appeared in JACS in 1966 (30(c)).

GORTLER: And then there was a review on the memory effects in multiple carbonium ion rearrangements (31).

BERSON: Yes, that's right. That one was in *Angewandte Chemie*.

GORTLER: In the review on the sigmatropic rearrangements (29), you suggest an additional experiment where if you took that bicyclo[3.2.0]heptene and you put very large substituents underneath [in the *endo* position], it should not go by a concerted rearrangement. Did you ever build those molecules?

BERSON: Yes, we made the one with the methyl group on the inside, and that was what happened (32). The stereochemistry was lost completely. It was randomized. Well, we had some rate measurements, which showed that when the methyl group was up the rearrangement still went with inversion, just like the deuterium case. But if the methyl group was down, you lost that stereochemistry and it didn't go that way. What we could tell was that the rate of the rearrangement with the methyl group starting up, namely the inversion pathway, was at least fifty times faster than the rate of rearrangement starting with the methyl group down, which told us that in order for the methyl group to turn in when it starts out down it's sterically impeded. And that means not only do we know that the overall result is an inversion of configuration, but to a very high degree of probability, we thought, that it means that the direction of rotation is inward. That in the concerted sigmatropic rearrangement, that that thing must turn over with a forward somersault and not with a backward somersault overall, because if it were turning with a backward somersault, the methyl group being down would not impede the reaction. It would be turning away from the point of steric hindrance, if I make that clear.

GORTLER: I'll have to think about that a little bit. [laughter]

BERSON: The idea is that by putting the methyl group in the endo position, you force the inversion pathway to be hindered. If the inversion pathway really does involve a forward somersault, which orbital symmetry tells you that it should, then that would be sterically impeded. If it involves a backward somersault, that would not be true. So the fact that it is impeded by a very substantial amount, a factor of at least fifty fold, that tells us that not only is the overall result inversion, but also that the inversion somersault takes place according to the orbital symmetry predicted pathway. So that's a refinement, really, of the original experiment, the deuterium experiment.

GORTLER: Tell me a little about the memory work, where you were looking for shallow minima on the reaction pathway (31).

BERSON: That's right. Now that work started out with some work by Pat Warnhoff—Patricia Reynolds-Warnhoff is her publication name (33). The objective there was to compare the behavior of a carbonium ion generated by different pathways and see whether they produced the same results. In other words, you try to generate a common carbonium ion from two different precursors. Does it make any difference which one you start with? Does it make any difference in the product distribution?

GORTLER: Essentially, does it remember it's origin?

BERSON: Exactly. Does it remember where it came from?

GORTLER: Yes, what made you think that there would be that recollection? I mean, just observations of other carbonium ion systems? Were there systems where there were multiple rearrangements?

BERSON: Well, we thought that the systems that we investigated might have conformational, local minima that they could fall into, and that the sequence of encountering those minima would be different depending upon which precursor you started from. Therefore, if reaction could take place before conformational equilibration, there ought to be some memory effect. That's fundamentally what we were looking for.

[END OF TAPE, SIDE 9]

BERSON: We then did some further work in that area by Joe Gajewski in a different kind of system (34). David Willner did some work (35). The Willner and Warnhoff work was done at USC, and then the Gajewski work and some work by [M. S.] Poonian and by a very large number of other people was continued at Wisconsin during a large part of the time we were there.

The general answer to the question is that there are memory effects. Then the question became why are there memory effects? Now our feeling was that these were differences in the structure of the carbocations themselves. Other people wanted to ascribe them to counter-ion effects or solvent effects, you know, differential solvation and so on. We tested that out to the best of our ability by starting with different leaving groups, for example. We observed the same effect, quantitatively the same effects, in deamination that we observed in solvolysis of arene sulphonates. They were independent of solvent. We changed solvents. We could start out with starting materials with the leaving groups in different locations so that the instantaneous location of the counter-ion would be different in the two. The results from the two pathways were identical. That is to say, you got memory effects but they were the same memory effects, regardless of where you started out. So our long-range conclusion was that this was probably not an example of a counter-ion effect or a solvent effect, rather it had to do with the structure of the cations themselves. Now, I have to say that Herb Brown intimidated me during this period because we wanted to broach the idea that some of this could be due to non-classical bonding because if you start out from two different precursors, the bonds that are being delocalized in the course of generating the carbocation are different, and so there's going to be some time lag before the initial cation organizes itself into the final target cation or the cation that it's destined to become. Non-classical bonding would be one way of preserving that memory. Now, we never used that word, but it's sort of implied in what we wrote. We made a much more general kind of suggestion that it had to do with conformational differences, that is, actually the location of atoms without specifying what kind of bonding we were looking at.

GORTLER: Do you think the reason you hedged like that was because of Herb Brown?

BERSON: Absolutely. Herb Brown was going around the country giving lectures saying that there was no such thing as non-classical bonding and that people were making too much out of this, and he was shooting people down left and right and citing people from the literature who were invoking non-classical ions, sometimes admittedly with insufficient evidence, and we didn't have any evidence that this really was non-classical bonding. But this was like throwing a red flag in front of a charging bull, you know? I didn't want to get into that argument. So we soft-pedaled that aspect of it. [laughter]

GORTLER: Do you think that he had something to do with Saul's [Winstein] early demise?

BERSON: Well, a lot of people say that. I think that one has to keep in mind the fact that Saul had a long history of heart trouble, so he was kind of a ticking time bomb, and I don't think people realized how serious it was.

GORTLER: He probably worked very hard no matter what or who was pushing him.

BERSON: Oh, he was an enormously driven individual. But let's put it this way, those encounters with Herb didn't help.

GORTLER: You said earlier that the years at Wisconsin were enormously productive and yet you spent only six years there. In fact, I noticed on your resume that part of that time you were in Cologne and part of that time you were in western Ontario, so you weren't even there for six years.

BERSON: Yes, well, the sojourns in Cologne and in western Ontario were a matter of a few weeks each time, not for whole semesters or years. So I really didn't leave.

GORTLER: So you weren't running away from Wisconsin right from the beginning?

BERSON: No, I was in contact with the group and I never left for very long.

GORTLER: But they were extremely productive. At that point, were people starting to leave? A group of people went to Stanford [University] as I remember, or maybe just a few people went to Stanford.

BERSON: Yes, I came to Wisconsin just after that. They had gone. Gene Van Tamelen and Bill [William] Johnson had already left. A number of other people had left to go other places. Wisconsin, in fact, is one of the key farm clubs for other departments. [laughter] You could put together a pretty darn good department from people who have left Wisconsin, which is probably not exactly what they want to be known for, but it was a powerhouse group. There's no question about it.

GORTLER: So why did you leave?

BERSON: Why'd I leave Wisconsin?

GORTLER: Yes. I can imagine, you know, that it had to be a great lure to come here [Yale].

BERSON: Yes, I think it was a combination of things. It was mostly personal, selfish things. This was not an obvious step up to come to Yale. The department was in a pretty run down condition, as I became aware when I became chairman a year after I got here.

GORTLER: I was going to say, did they hire you to become chairman?

BERSON: No, that was not in the deal. They sprung that trap after I got here. But I think it was the location. It was the feeling that Yale was a smaller place and I'd feel more comfortable with it. I didn't really enjoy teaching classes of three or four hundred people which I had to do at Wisconsin. I had virtually no interaction with the undergraduate students. It just was not done; it was not expected. There was something too big about it. There were also some other things. Well, I'll say this at the risk of possibly offending some people. There was too big a cleavage between the various branches of chemistry at Wisconsin, probably because of size. But there was a very strong separation into subsections, or whatever you want to call them. Sections: there was an organic section, a physical section, a theoretical section, and the groups were kind of orthogonal to each other. There was very little interaction.

GORTLER: You seem to have interacted with people all along the line. I mean, you did so with Benson. Of course, the USC department was small. And here you seem to both interact with people within the department and outside the department.

BERSON: That's right. It was much easier to do here, I found. I don't know exactly the reason for that, but there was an insularity about the way the Wisconsin department operated that I didn't like. I felt ultimately it was going to be a handicap to me because the deeper I got into this stuff, the more I realized that I didn't know, and I had to have colleagues in areas that I was unfamiliar with who were willing to spend some time with me and just teach me or lead me, you know? I found it very difficult to do at Wisconsin. I tried very hard.

GORTLER: Who did you find here that did that sort of thing? Wes Borden. Is he still at Washington?

BERSON: Yes, he's still at Washington, but I sought him out, you know, when he was still at Harvard. So we made contact there. It was clear that he had a lot to teach me, so I've depended on him a great deal over the years. But over time, you know, I've interacted with Mike McBride, with Ken Wiberg, with Kurt Zilm in the department here. Zilm's a physical chemist; a low temperature NMR guy. Our collaboration led to the first NMR spectra of biradicals (36). So that was very important work for us. That was sometime in the 1980s, the middle 1980s.

GORTLER: There was another paper where you had collaborators in Canada and Switzerland (37).

BERSON: Yes, there was a group at the Ottawa laboratory—Tito [J. C.] Scaiano who we collaborated with on some fast kinetics work. We had several papers with Tito. That was on the nanosecond time-resolved kinetics. I tried very hard to, well, first of all, look into the possibility of setting that up here by ourselves. I was discouraged from doing that because people I talked to, Chris Foote for example, said it took him five years to get his system up and running. Well, ugh, five years. [laughter] Then we tried to make contact with Nick Turro. That didn't work out because he had the hardware but it hadn't been used for a number of years and it had fallen into decay and it had been cannibalized.

GORTLER: You did do some work with Nick [Turro] on a trimethylenemethane intermediate (38).

BERSON: Yes, that was just some static spectroscopy. But then we finally made this contact with Tito [J. C. Scaiano] who had unparalleled capacity to do that stuff at Ottawa. The first of those papers must have been in the late 1980s (39). That was a very important collaboration.

Then the work we did on tetramethylenebenzene [TMB] (37). We had collaborators all over the place. We had again Tito's group. We had Zilm's group here at Yale. That must have been 1993. A full paper was published. And we collaborated on that work with Pierre Vogel's group in Lausanne, Switzerland. These people were all sort of coming from different points of the compass, focused on this one problem. The reason that we did that was, to reproduce all that technology would have been just very time-consuming and probably foolish. This way all we do is share the credit but the science gets done, you know?

GORTLER: As long as you can convince those people to take on a problem.

BERSON: Well, I think they were really interested in this.

GORTLER: It presents a challenge for them.

BERSON: Sure, and they had techniques that could be applied, so it's kind of a showcase for what they are capable of doing.

GORTLER: The last paper you suggested to me was also a review and it reviewed a lot of your earlier work (40). "Tunable singlet and triplet energy spacings." That's really kind of cute stuff.

BERSON:  That's pretty far out stuff, yes.

GORTLER:  Of course, you suggested where it might go in terms of conductors and anti-conductors.  Do you want to say anything about that particular article, or does it speak for itself?

BERSON:  Well, let's say that this was an idea that was sort of an off-spring of the work on the violations of Hund's Rule.  So we began to think that, well, there are other ways that one could have biradicals that had singlet ground states that didn't depend on this lack of spatial overlap of orbitals, the kind of Borden-Davidson consideration.  So what we thought was that if you start out with a typical, sort of, an idealized biradical, the frontier orbitals are degenerate.  They have exactly the same energy, and that's what leads to all this confusion about signlets versus triplets.  So if you want to get away from that and get into the realm where you begin to favor singlets, you can put in some perturbation in which you separate these two orbitals, and eventually you'll get to a point where the gap between those two orbitals is larger than the repulsion energy of the two electrons, for putting two electrons in one orbital.  So that's the strategy that we followed, and we did that with that set of papers that was reviewed there (40).  We did that by tuning that frontier orbital separation by changing the hetero atom from oxygen to sulfur to nitrogen, and the prediction would be that one should increase the singlet-triplet separation, and that's true at the calculational level, but experimentally it's very difficult to prove because you usually don't have both the singlet and triplet in hand as observable entities.  So the final note in that symphony, as it were, was struck by leaving the nitrogen invariant but changing the substituents on the nitrogen.  You see, the nitrogen is a functional element because you have either NH or some NR, some substituent.  Now that substituent allows you to change the electron demand on the nitrogen, and thereby to change the perturbation of the biradical orbitals.  So in the last case, we were able to switch over a series of those 3,4-dimethylenepyrrole biradicals from being robust singlets to being robust triplets by changing the nature of the substituent on the nitrogen.

GORTLER:  Also by changing the wavelength in which you generated the biradicals.

BERSON:  Yes, that's an experimental ripple, which was a purely serendipitous finding.  We did not know that that was going to work that way.  At first, in fact, it didn't work that way because when we used the same wavelength of light we had used to generate all the singlet biradicals, we got the singlet form, but when we switched over to a different wavelength, we generated the triplet form.  Now, exactly what the reason for that is, is buried in the mysteries of the excited states of these precursor molecules, and we don't really understand why that is.  We have some speculations, but no solid evidence on that point.

GORTLER:  How did you happen to change wavelengths?  I mean, normally you wouldn't.

BERSON: It was a stubborn graduate student, Linda Bush, who came in (41). She had put in years of work making these precursors—very hard molecules to make, at least the first time around. [laughter] We subsequently discovered a much easier way of doing it, but it's always the case that the first time through was really hell on wheels. But she finally got some of the stuff and she did this experiment and she found a molecule that was a singlet molecule that had no ESR spectrum and it had all the properties of a singlet. I said, "Well, Linda, it looks as though our prediction is not going to hold up. What do we do next? You know, should we just publish this?" And she said, "Wait a minute. I want to try another wavelength." I said, "Well, what makes you think that's going to work? Why should that make any difference?" She said, "I just have a hunch." So, who knows, she had probably seen something in the literature that gave her the thought that perhaps one could enter an excited state manifold from a different spin point by using different wavelengths of light. So she went ahead and tried it and it worked. I can't tell you how big a lesson that was for me. [laughter] I was supposed to be her mentor, but if I had had my way, I would have talked her out of trying it.

GORTLER: I remember, Frank Westheimer once said to me, "sometimes you just know too much, and that's when you don't do things."

BERSON: That's right. That's exactly right.

GORTLER: Why did you do the tetramethylenebenzene (37)? It had already been done. You just redid it because theory and the experiment didn't agree? And you did find some things wrong with the earlier work?

BERSON: Two reasons. It's more complicated than that. You see, we had published a theoretical paper. Paul Lahti, Angelo Rossi, and I, in 1985 I believe it was, had applied some rather approximate semi-empircal methods to calculating that molecule (42 (a)). That had an even bigger preference for the singlet state than tetramethyleneethane did. So it was sort of super-disjoint. And there's a good theoretical reason for that which has to do, I think, just with the fact that there's a larger number of pi-electrons so the correlation energy you recover by this dynamic spin correlation is greater the more of those you have. So that should favor the singlet more, and that's apparently what it does, at least according to our calculations. Also, Wes Borden had done some calculations, which predicted a singlet ground state (42 (b))

Then Wolfgang Roth published this paper in which he said that the diradical had a triplet ground state (43). He said these predictions are wrong and the whole idea of these disjoint molecules violating Hund's Rule must be wrong. This [diradical] is a triplet molecule and it agrees with Hund's Rule, he said. So at that point we had egg on our face. We had a calculation in the literature, which predicted an apparently wrong result.

GORTLER: There must be millions of calculations in the literature that predict the wrong result.

BERSON: All too many. This week, every week! [laughter]

Just follows very faithfully, whatever the experiment is. I don't mean to be cynical about calculations, but all these calculations are approximate and particularly in this field, the open shell field, that is not a well-explored area of quantum mechanics. I believe ultimately we're going to find something better than the way we're doing it now, because fundamentally, I would say, that one cannot predict with confidence which quantum mechanical method is going to give a reliable result in a completely new set of molecules. It's always been done by calibration, by this comparison with the experiment. And then you learn and you say, well, experience shows that this calculation is good for this kind of molecule. But if you have something completely new and has never been made before, it's a pig in a poke.

We had been trying to make tetramethylenebenzene ourselves, and basically the Roth group scooped us. They got there first. But what I did not know, or had forgotten about, was that sometime prior to that, Pierre Vogel had synthesized but had not yet published an independent synthesis of the Roth precursor of tetramethylenebenzene. It's a norbornane with a carbonyl group on the top and then four methylene groups elsewhere. This was even before the Roth paper appeared and before I knew that Vogel had done it, but I knew that we were trying to make TMB and we had failed. We were trying to make TMB from some other precursor. But he [Vogel] had seen our prediction in the literature that this should have a singlet ground state, and so he just wrote me. He said, "I have a sample of this ketone. Would you like to collaborate and we'll send you a sample and you can study the thing spectroscopically, using these matrix isolation techniques." So we made that arrangement, and in the course of our doing the preliminary work based upon a very small amount of sample of the precursor that we got from Pierre (it was a very hard compound to make), we got results that led us to think that the molecule did not have an ESR spectrum [i.e., it was not a triplet]. About that time, Roth's paper appeared. So this stimulated us because we were already involved in it when his paper appeared. We thought we understood what was wrong with his assignment of the structure. The difficulty was that the carrier of the triplet spectrum that was in the photolysis mixture that he had prepared, was not the same molecule as the carrier of the purple color. The purple color was one thing, we felt, (it was TMB singlet, it turned out), and the carrier of the triplet was something else. So that was the light that guided our work, and we proceeded on that basis.

Now ultimately what Jim Reynolds, the student who was leading this project, was able to do was to show that you could generate, the way Roth had done by photolysis, both the ESR spectrum and the purple color. But by irradiation at a different wavelength, you could selectively photolyze away the purple color, but in the course of doing that, the triplet spectrum remained unchanged. This was a clear indication that these were two separate things. So the carrier of the triplet, we still don't know what that was that Roth had. I mean, we confirmed the fact that it's in there.

GORTLER: You were able to see the triplet species?

BERSON: Oh yes, you can get it eventually, whatever it is. You have to go to a low temperature to see it. It's there, but it's not anything interesting in the context of tetramethylenebenzene, because we were able to show by NMR spectroscopy, in collaboration with Kurt Zilm, that the purple stuff is singlet tetramethylenebenzene. We, in collaboration with the Scaiano group, were also able to observe the purple transient in fluid solution by nanosecond spectroscopy and to get firm evidence of its actual structure. So that's absolutely nailed. [laughter] So that was really, if you wish, the first singlet, non-Kekulé, hydrocarbon. That's the significance of that work. It was not so much that Hund's Rule was violated but that we had demonstrated the correctness of a way of looking at the Hund's Rule problem, using a theory, the Hückel-Borden-Davidson-Ovchinnikov theory, that did lead to correct predictions. The violation of Hund's Rule itself, well, Hund's Rule is violated in certain atoms too, so it's a rule only approximately. That's not the point. The point is that we now understand under what conditions this type of molecule, biradicals or multiradicals, will violate it and will have low-spin ground states despite the fact that they're open shell.

[END OF TAPE, SIDE 10]

GORTLER: We had talked earlier about your beginning work in physical organic chemistry. It's clear who you were being fed by on the West Coast, but who were your heroes otherwise? Who were you reading?

BERSON: Well, Frank Westheimer was an absolute hero and I still think that he deserves a Nobel Prize. It's unlikely that he'll get one, but he was really a model of—what shall I call it—creativity. He had an instinct for the cutting edge and for doing new things and for the decisive experiment. I've admired him throughout his career. We never worked in areas that overlapped with each other, but from the outside I could see the quality of that work. Really extraordinary.

GORTLER: He once said to me, "You know, most people are granted perhaps one area where they've made a discovery in their lives," and he actually had made significant contributions in at least three different areas.

BERSON: Yes. That was one of the things that attracted me to him, that there was that creativity, that ability to get beyond just the things that he had grown up with and worked on all his life. So I was very impressed with him. Other people-well, certainly Hammett became more of a factor in my estimation as time went on because I became closer to physical organic chemistry and I could appreciate what he had done. Early on, when I was in graduate school, I was so dumb I didn't realize how important this stuff was.

GORTLER: You just didn't see the changes that were taking place at that time.

BERSON: No, I didn't really. I was out of it.

GORTLER: Most of us, when we're young, we're very focused.

BERSON: Very focused. You know, I could appreciate that there was something real and solid there, but the applicability of it, the broad scope of it, didn't hit me until considerably later. I'm thinking about people in other countries. I read a lot of [Christopher] Ingold in those days. He and Winstein were mortal enemies, although I don't think it ever got to the stage that Brown and Winstein did, and I found Ingold's way of crediting the work of other people to be a little bit self-serving and less than generous, but I think that was a common complaint. But his science, I think, was by and large seminal. I think that the recognition of the importance of the kinetic examination of substitution reactions—the nucleophilic and electrophilic substitution reactions—was tremendously important. I don't think he got everything right there. I think that there were some things about the stereochemistry, of what were essentially neighboring group reactions, which he refused to call that because he could see that Winstein had anticipated a lot of this stuff. So he went out of his way to devise a completely new set of nomenclature for that. I didn't find that very admirable. I thought it was kind of petty. But as a scientist I think he was a considerable guy, and one cannot overlook the importance of what he did.

GORTLER: It's interesting and it just occurred to me that, you know, he sort of painted these mechanisms with very broad strokes and wasn't worried about a lot of the detail. I mean, a lot of the work has been refined and refined many times, and it's probably a good thing that he didn't do the refining because people would have gotten bogged down in the details.

BERSON: That's right. Well, I think that's certainly true and you can see that even in a paper as early as the solvolysis reaction, the SN1 reaction, so-called, which really, if you look at it, doesn't have first order kinetics. It's not a unimolecular reaction. It's a very complicated process. It involves reverse reactions. And he recognized that. He worked out all the kinetics for that and he found ways for shutting off the back reactions so that it did become just first order. That was all, I thought, very well done, but he pushed the nomenclature. The categorizations, I think, offended a lot of people because it looked as though he was trying to, sort of, subsume the whole field for himself and make everyone else sort of working on his problems. The field was much bigger than that and I think that was a tactical mistake on his part; not so much a scientific mistake but a tactical mistake.

GORTLER: You did a fair amount of consulting work. You started consulting as early as 1957. Did you think the consulting had some value for your own research? Did it play an important role for academicians in general? I mean, not just your consulting, but do you think it is important? Did it do anything in terms of the academic-industrial interface as far as you are concerned or was it just a way to make a living?

BERSON: Yes, well, it was all of those things. I'd say, first of all, that I did learn something from these interactions, but I was always painfully aware of the fact that I wasn't being told everything there was to know. This was frustrating and ultimately I got very tired of being left on the outside. Whenever I got too close to encroaching on a sensitive area, a proprietary area that they didn't want me to know about, you could just feel everybody clam up.

GORTLER: Gee, I would think that they would trust their consultants.

BERSON: Only in certain areas, on a need to know basis. Do you know what I mean? They had very specific questions for the most part. How can I do this reaction? Or, how do I model these kinetics? Or whatever. So there was kind of a limited learning process there. I suppose that in some sense my connection with industry—my being known as having connections with industry—in the form of consultantships smoothed the way for my students to get jobs in industry. Now, I'm trying to remember. I don't know of any specific cases in which a company came to me and said, "Do you have any of your students that you want to recommend?" And then just followed my advice. It was always on the basis of a pretty open interview process that anybody could participate in and my recommendation carried whatever weight it carried, but it didn't go beyond that. I was not on the inside of their hiring practice. So I don't think it was terribly important from that point of view. But I think it did help me in advising students about what industrial life was like because I had been an industrial chemist only at a very junior level for a short period of time. So that was valuable to me, and many of my students went into industry. I think I counted, sometime in the not too distant past, that there were something like twenty former students from our lab working at DuPont at one time or another.

GORTLER: You've gotten a lot of awards and honors and so on. Now I'm not interested in those. I can read those off the list. What I wanted to know was, what did you think the real rewards were in your work? You've put a lot of time and energy into this.

BERSON: Yes, well, how can I put it? From the scientific point of view, most of the time I felt like a hack golfer. Have you ever played golf? It's a very humiliating game, and you can play an awful lot of holes before you hit one good shot. So I felt that I spent years fumbling around, doing things that didn't work out or that worked out sort of in an uncontrolled way where I wasn't really able to get a lot of satisfaction about the way they came out. We published the results but they weren't very influential and they were ultimately forgettable. But a few times things did work out, and those are just indescribable moments of joy because somehow you felt that you had made connections with the universe in some small way, that some little part of it you finally understood and you had nailed it down and it really did work that way. So there are a few of those cases, maybe half a dozen that I can think of. Also, we often got surprises, unexpected results that opened our eyes to something new. So we could not take much satisfaction in our foresight then, but we could feel good about finally understanding what was going on. Those too were occasions to treasure in our memory.

Now the rest of it, a lot of it had a teaching function. Students learned a lot from their problems. I learned an enormous amount from interacting with the students. Let's face it, the older I got, the tougher it was for me to keep up with the latest developments. These students were coming in, they were taking all these courses from my hot shot colleagues, and they would transmit that stuff to me, which was really about the only way I could possibly keep up. A lot of problems we worked on together, students and I, and big battles of learning spin quantum mechanics which was just an awful struggle for me, which a lot of it I've forgotten now, but I got to the point where I did understand it at one time. But this was in close collaboration with Dave Seeger and Ed Helinski, two very strong students of mine. None of that was in my background, you see. One of the most exhilarating parts of being a professor and trying to continue to evolve and to move into new areas of research is that you are forced to learn something new, so you remain a student all your life. You have no choice. You can stay in one area and continue to turn that crank and pump out lots and lots of papers, but that just really isn't a lot of fun. So the other way requires you just to suck up your gut and make the effort to learn something new. I had to do that two or three times during my life. One was the thing we've been talking about a lot this afternoon, switching from natural products chemistry to physical organic, but then within my physical organic work two or three times. All the biradical stuff and all the thermal rearrangement stuff, I had to learn that from the ground up. I didn't know any of that to start with. It was not in my background and one way or another, with the help of students and colleagues, I got into it enough so that we could do some work in those areas. That learning process is very exciting. It's very exhilarating. You feel your powers expanding somehow. So those are rewards. Those are out and out things that you can't get any place else but in academic work. You have the power. It's up to you. You have no boss. Nobody is telling you what to do. It's entirely up to you. And that independence, it's a very, very precious thing, and I'm just going to be eternally grateful for that as long as I live. It's just a tremendous privilege that is put at the disposal of people like us who have that freedom, that opportunity.

GORTLER: Where do you see the future of physical organic chemistry? Does it exist any longer? Has it been subsumed? The computer has certainly changed things drastically. Where's organic chemistry going? Where's physical organic chemistry going, if there is such a thing anymore?

BERSON: Well, I really shouldn't say much about organic chemistry because I've had run-ins with people who say dismissive and derogatory things about other people's work and dismiss whole fields as being sort of old-fashioned and irrelevant, and physical organic chemistry has gone through some cycles of that, by the way. I have some thoughts on this. I think that I'll make it more general without pinpointing any individuals. But I would say that one thing that I see about organic chemistry is the enormous role that is being exerted by the government granting agencies who, in turn, are responding to enormous pressures from the pharmaceutical industry. If you look at the funding patterns in organic chemistry today, you will find tremendous amounts of money being spent with the stated, ultimate objective of developing new drugs. Now I'm not saying that's an unworthy objective, but I'm saying that to essentially convert the whole field of organic chemistry to that goal is excessive. And the way we're going about it is not going to work. I mean, it's not going to work that we're going to provide larger quantities of a rare antibiotic or carcinostatic material by total synthesis, thirty-seven steps, that's not going to be a commercial process. So I think there's an over-emphasis there, but we have to keep in mind that people will follow the money. So I won't call it a switch, but certainly a diversion.

GORTLER: You think that this enormous over-emphasis on synthesis is actually money driven?

BERSON: That's the driving force. That's my analysis of it, for what it's worth. It has several aspects to it. It draws in lots of students because the pharmaceutical industry hires lots and lots of chemists, and when they hire chemists, they won't even look at physical organic chemists. They want people who are trained in synthesis. This disregards the fact that my work is 90 percent synthesis of some pretty hard molecules, but that doesn't cut any ice. They want people who are committed to that kind of lifestyle. And okay, that's fine. They need that, presumably. But that, taken simultaneously with the drying up of the heavy chemical industry in the United States, which simultaneously means the drying up of opportunities in industry for physical organic chemists, means that nobody wants to do physical organic chemistry anymore. Young kids don't want to go in that direction, and who can blame them, after all. It's a self-fulfilling prophecy.

GORTLER: You can't get a job?

BERSON: You can't get a job! I mean, why should I do that? I mean, these are very interesting problems you're working on, professor, but I can't get a job doing that! So that's the end of that. So the question of whether there is anything more to be done in physical organic chemistry is almost a moot point. There isn't anybody around to do it. There are still people working on it. I mean, I went to the mechanisms conference last summer and it was a beautiful conference. There was lots of very good work going on. A lot of it was in biological areas. So if you want to say does physical organic chemistry still exist? I would say, it exists, but to a considerable extent in its application to biological problems. What worries me about that is that because the field of research in physical organic chemistry is shrinking due to this decrease in funding patterns and the shift in the student interest, we are getting to the point where I worry that academic departments are not hiring professional physical organic chemists for their faculty anymore. It seems to me that it's only a matter of time before we reach the point where this kind of rigor in the physical organic way of thinking is going to be a thing of the past. So we will have more and more approximate ways of dealing with problems—even biological problems—and that's going to be a net loss to the progress, not only of physical organic chemistry, but to also biology, ultimately. So that would be a plea that I would make: we ought to try to save enough of physical organic chemistry as a separate, free-standing discipline to nurture the growth and contributions of a cadre, at least a small cadre, of people who are devoted to this subject and to its cultivation. We're not doing that and I'm very worried about that. So, you know, I don't know what else to say. This is kind of a selfish point of view about chemistry.

I don't see a big role for the development of academic departments in the direction of utility. In other words, I don't think that making devices in chemistry departments is a direction we ought to go in. I think that gets to be quickly very applied, and the component of real chemistry, of new chemistry, begins to diminish, and if you get people started in that direction, they start to be funded with that objective in mind and it's very difficult for them to explore the real academic underpinnings of what they're doing. The driving force to produce more and more utilitarian results is kind of irresistible. So I think there's a danger there for chemistry departments to become too focused on applications, on devices, on molecular materials. I mean, I think there is a point up to which chemists can make a chemical contribution, but beyond that point it gets to be problematical about whether that really is something that should be done in the chemistry department or whether our function should remain closer to the traditional function of nurturing chemistry for it's own sake. Not because we want to insulate ourselves from that, but that this is the seed corn of all these other disciplines—molecular biology, chemical biology, material science—all these things feed out from us, so we have to have some central core that has to continue. We can't just drop that and say we're going to hire faculty now to make devices, and we're not hiring anybody in physical organic chemistry. That's the kind of thing that's happening already at Yale, which was sort of an active place in physical organic chemistry for a while, but there's nothing on the horizon to nurture that field here. But, of course, what I'm saying is a little bit self-serving,. It's not totally objective. But I really think there is something to what I'm saying. It's not something that can be just casually tossed aside.

GORTLER: I keep thinking that well, perhaps, it's just been subsumed into the whole area of synthesis and all these guys who are doing synthesis are really thinking in physical organic terms.

BERSON: Dream on.

GORTLER: [laughter] I can be an eternal optimist.

BERSON: It's not true. I mean, you just look at the way they do things.

GORTLER: It seems like they've jumped back a whole century. I mean, it's the guys with the best memory or the best computerized knowledge.

BERSON: Yes, it is. Database is very important here. There's another place where instrumentation has made an enormous impact. What I see there is that it is now so easy for a chemist to determine the course of a reaction that the motivation for really investigating the mechanism of that and finding out why it went that way is very small if your long-range objective is to get to a particular target molecule. Everything points in the other direction. What you have to do is to change the conditions of that reaction so that this step is going to work or else to devise a different step and find out whether that works, essentially by empirical trial and error. No synthetic chemist that I know of worries an awful lot about mechanism. They can't. It's out of the question.

GORTLER: [laughter] I'm laughing because Ralph Hirschmann, who had gone from Merck to the University of Pennsylvania, did some collaborations with Amos Smith, and he said they were continually arguing, "because I'll find some reaction that doesn't go for some reason and I want to go and look and see why it doesn't go, and Amos just wants to try the next reagent. He says he just wants to push it."

BERSON: Exactly. And Amos has the realistic point of view because his constituency is the group of people who counts the number of total syntheses that you have actually finished. Not the bright ideas you've had, but how many syntheses, how many molecules have you made that somebody thinks are important molecules? So there's no motivation to go back and look at a mechanism. I can't blame these guys. That's the world they live in.

GORTLER: Two final questions, simple ones. Do you have any advice for young, aspiring chemists or people who are considering a career in chemistry? You may have just answered that question. [laughter]

BERSON: I don't know what to say. My personal feeling is that there are a lot of things to be known about how reactions take place. That's basically what physical organic chemistry is. I think it's a fascinating field. As we were saying earlier this afternoon, molecules, particularly organic molecules, are very complicated systems. We have not begun to scratch the surface of their behavior, of the things that control how reactions take place. So there is a big field there. And I think that it's unfortunate that there are so few people working in it. The people who are probably doing the most interesting work now are the chemical physicists. [Ahmed H.] Zewail, if I could get him to concentrate on what he should be doing, I think has a big contribution to make. I have the greatest admiration for that work and I would never say that he doesn't deserve a Nobel Prize for developing that stuff, but he has a powerful weapon in his hands, and in my opinion, that stuff that he does is at this moment a long way from solving a lot of problems in organic chemistry. It might ultimately, but he has got to make the effort to dig in and find out what those problems are and why his technique does not speak to those problems.

His Nobel Prize was for femto-second spectroscopy, in which he detects transient intermediates whose lifetimes are very short. It's very beautiful and important work. I think the technique potentially might be made very applicable to physical organic chemistry. I was very enthusiastic when he first got in touch with me about talking about how it might apply. But the point is that it has not yet spoken to a single problem in organic chemistry as it's carried out in the lab, and the reason is that the way he does the experiment, the way he generates these transient intermediates, puts him 45 or 50 kilocalories above the transition state for the reaction, and so it's a domain that is never explored in the laboratory. When you carry out the Diels-Alder reaction in the laboratory, you may have some of those molecules going through that have 2 kilocalories above the transition state, or 5 kilocalories, maybe. You know, there is a Boltzmann distribution, but you're not 50 kilocalories above the transition state. So the immediate question is, how are you going to relate what he is observing to the problems of organic chemistry itself? I don't see how to make that connection, and as far as I know, he has never made that connection. But there is an interface there at which, I think, something could conceivably be worked out.

There are other people working in other areas. There's some very interesting work going on in Barney Ellison's lab at Colorado and it was going on in the late Bob Squires' lab at Purdue [University] before he died tragically a couple of years ago, in the direct gas phase examination and spectroscopy of biradicals. Similar work is being done by Peter Chen at the ETH [Eidgenössische Technische Hochschule].

[END OF TAPE, SIDE 11]

BERSON: I think that if I were young and had the determination, I would try to learn enough about chemical physics so that I could either do some of that work myself or interact with those people. I mean, it's not something I'm going to do now, but I think that's where important new results are going to come from. Those people, some of them, were trained as basic physical organic chemists. Both Bob Squires and Barney Ellison were students of Ken Wiberg. Peter Chen was a student in my group. So these people, what they have shown is that it is possible to expand in that direction and to get new results there, and I think that is potentially a very fruitful direction for the field to go.

In something that you sent me or somebody sent me or maybe it was in the reprint that Steve sent me (5) or in Jack Roberts book (4). Jack Roberts said that, as far as he was concerned, what made physical organic chemistry different from physical chemistry was the creation of new molecules to test theory. Now my feeling is that that phase of physical organic chemistry is pretty much over, at least for now, and there are two reasons for it. One is that the thrust of these new instrumental techniques—fast kinetics, high resolution NMR, flowing afterglow spectrometry, photo-electron detachment spectrometry—all kinds of very fancy tools. Now it's going to be a rare physical organic chemist who is going to spend five years synthesizing a molecule to put in a machine like that. The ordinary physical organic chemist is going to want to have a molecule that he can put in there and then run a lot of other molecules through to make comparisons, to work up some patterns of behavior. So the motivation is not going to be coming from that direction for the most part. On the other level, the kind of thing that we used to do.

GORTLER: It sounds like the early days of physical organic chemistry when people would reach up and take compounds off the shelf for testing. We have come full cycle.

BERSON: Exactly, it was that way in the early stages and that's what we're doing now. And maybe we'll reach the point in this time around in the cycle where the synthetic aspect will become more important. But for the moment, the kind of thing that we did, which was to spend lots of our time synthesizing molecules for specific ad hoc purposes, nobody is doing now. For one thing, the kinds of molecules that you need to make are pretty hard to make, and the people that can make them by and large are doing synthesis because that's where the action is. They're not doing this stuff. So I think that Jack's definition is now kind of restrictive. I think the field is broader than that, and that's probably inevitable. I don't think it's bad. But I don't think we can hold onto one style of physical organic chemistry. I think it has to continue to evolve. And who knows, maybe it will come back again. Maybe there will be jobs again for students who are trained in those disciplines.

GORTLER: [laughter] But the fact is there won't be any students left. You're a dying breed.

BERSON: Yes, well, it will have to be built back up again, all over. Start from scratch. But maybe I'm too pessimistic. There are certain departments where there seems to be a certain stirring of activity, a certain interest in perpetuating this field, and maybe it will come back again. I certainly hope so because I think it's a worthwhile thing to do.

GORTLER: Last thing. What do you do for fun? You do work very hard.

BERSON: Oh, well, in the last few years, not much. I used to be physically very active. I used to do a lot of hiking. I used to play squash and racquetball. But all those activities are now in the past. I've got arthritis in a knee that makes it very difficult for me to do that, so I still do work out, but it's dull things—just aerobic workouts. I try to keep my body together one way or another. But I read a lot and go to the theatre. We like the opera and the ballet. We go to New York quite frequently for those. One of the motivations for coming to Yale was the proximity to New York, plus the fact that, of course, I have family in this area. My sister lives in Allentown, Pennsylvania and we have other relatives in the vicinity. So that was all kind of an attraction. We've traveled quite a bit. We've been abroad recently to France, Belgium, Switzerland, Germany, and Sicily.

GORTLER: This is no longer professional travel?

BERSON: Some of it is, but more and more not. Nowadays, it's mostly not. We enjoy that very much. So I'm getting to be, I won't say, incapacitated, but I recognize my physical limitations. I've got to draw the line at certain things that I used to like to do very much but I can't anymore. So it's a different phase of my life now and I have to learn how to deal with it. I think I'm trying very hard to do that.

GORTLER: Well, thank you very, very much. I really appreciate your spending all of this time.

BERSON: It has been a pleasure to talk to you.

[END OF TAPE, SIDE 12]

[END OF INTERVIEW]

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