CHEMICAL HERITAGE FOUNDATION

GILBERT STORK

Transcript of an Interview
Conducted by

James J. Bohning and Leonard Fine

at

Columbia University

on

6 August 1991

(With Subsequent Corrections and Additions)

THE CHEMICAL HERITAGE FOUNDATION
Oral History Program

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Gilbert T. Stork

(Date) November 26, 1997

(Revised 17 March 1993)

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

GILBERT STORK

1921 Born in Brussels, Belgium on 31 December

Education

1942 B.S., chemistry, University of Florida
1945 Ph.D., organic chemistry, University of Wisconsin

Professional Experience

Lakeside Laboratories, Milwaukee, Wisconsin
1945-1946 Senior Research Chemist

Harvard University
1946-1948 Instructor
1948-1953 Assistant Professor

Columbia University
1953-1955 Associate Professor
1955-1967 Professor
1967- Eugene Higgins Professor of Chemistry

Honors

1957 Award in Pure Chemistry, American Chemical Society
1959 Guggenheim Foundation Fellow
1961 D.Sc. (honorary), Lawrence University
1961 Baekeland Medal, North Jersey Section, ACS
1962 Harrison Howe Award
1966 Edward Curtis Franklin Memorial Award, Stanford University
1967 Award for Creative Work in Synthetic Organic Chemistry, American Chemical Society
1971 Gold Medal, Synthetic Organic Chemical Manuufacturers Association
1973 Nebraska Award
1978 Roussel Prize, Paris
1979 D.Sc. (honorary), Université Pierre et Marie Curie
1980 Nichols Medal, New York Section, ACS

1982	Edgar Fahs Smith Award, Philadelphia Section, ACS
1982	Willard Gibbs Medal, Chicago Section, ACS
1982	Award in Chemical Sciences, National Academy of Sciences
1982	D.Sc. (honorary), University of Rochester
1983	National Medal of Science
1983	Pauling Award
1985	Tetrahedron Prize
1986	Remsen Award, Maryland Section, ACS
1986	Cliff S. Hamilton Award, Nebraska
1987	Monie A. Ferst Award and Medal, Georgia Tech
1988	D.Sc. (honorary), Emory University
1991	Roger Adams Award
1992	George Kenner Award, Liverpool
1992	Robert Robinson Lectureship Award, U. K.
1992	D.Sc. (honorary), Columbia University
1993	Robert A. Welch Award
1996	Wolf Prize, Israel
1997	D.Sc. (honorary), University of Wisconsin

ABSTRACT

Gilbert Stork begins his interview with a description of his childhood and family background in Paris. Stork and his family moved to the United States in 1939. He decided to begin his graduate studies in chemistry at the University of Florida in 1940. There, Stork earned his B.S. in 1942, and in 1945 he received his Ph.D. in organic chemistry from the University of Wisconsin. While earning his Ph.D. at Wisconsin, he taught a section of the Army Special Training Program. Synthesis related to quinine, and stereochemical control in synthesis highlighted Stork's graduate work and early career. His first employment after receiving his Ph.D. was with Lakeside Laboratories, working on estrone synthesis. There, Stork also began work on hydrogenation techniques. Stork left Lakeside in 1946 and began an instructorship at Harvard University. While at Harvard, he also consulted for the Syntex Corporation. In 1953, Stork left Harvard and joined the faculty of Columbia University as an associate professor, where he continued his organic synthesis research. Next, Stork worked on polyene cyclization and enamine alkylation while continuing his synthesis work. Stork concludes the interview with a discussion of various developments in organic chemistry, the future of university research funding, and memorable students and co-workers.

INTERVIEWERS

James J. Bohning is currently a professor at Lehigh University. He has served as Professor of Chemistry Emeritus at Wilkes University, where he was a faculty member from 1959 to 1990. He served there as chemistry department chair from 1970 to 1986 and environmental science department chair from 1987 to 1990. He was chair of the American Chemical Society's Division of the History of Chemistry in 1986, received the Division's outstanding paper award in 1989, and presented more than twenty-five papers before the Division at national meetings of the Society. He has written for the American Chemical Society News Service, and He has been on the advisory committee of the Society's National Historic Chemical Landmarks committee since its inception in 1992. He developed the oral history program of the Chemical Heritage Foundation beginning in 1985, and was the Foundation's Director of Oral History from 1990 to 1995.

Leonard Fine is Professor of Chemistry and Director of Undergraduate Studies in Chemistry at Columbia University. His special interests include polymer chemistry and materials science, industrial inorganic and organic chemistry, engineering plastics, problems in solid waste management, and the recovery and recycling of post-consumer plastics. Among his recent publications are two practical manuals on principles and practices of infrared spectroscopy and a general chemistry textbook for engineers and scientists. He holds a B.S. in chemistry from Marietta College and a Ph.D. in chemistry from the University of Maryland at College Park.

TABLE OF CONTENTS

INTERVIEWEE: Gilbert Stork

INTERVIEWERS: James J. Bohning and Leonard Fine

LOCATION: Columbia University

DATE: 6 August 1991

BOHNING: What I'd like to do is go right back to the beginning. I know you were born on New Year's Eve, 1921, in Brussels.

STORK: That's what they say. [laughter]

BOHNING: Could you tell me something about your parents and your family background?

STORK: Sure. I was born in Brussels, but we lived there for only about nine months. My mother was French, from the Lorraine part of France, and my father's family was from Brussels. But we lived in Paris afterwards, so I was brought up in Paris.

BOHNING: What did your father do?

STORK: My father was a jeweler. He and his three brothers inherited the business of their father, who had a jewelry store. Actually, they had three of them. One of them was in Brussels and one in Ostend, which is a summer resort. My father was concerned with buying things, so they had an office in Paris, as far as I remember.

When he eventually came to this country he survived on extremely careful handling of money that he had saved over the years, because he did not work here again. I could presumably calculate how old he was when he showed up here. He was not that old; he probably was fifty, or some number like that. His older brother was already in the States.

BOHNING: Why did he move to Paris?

STORK: I don't think my mother had any interest in living in Belgium. [laughter] The Belgians

don't have all that great a reputation in Europe. The Belgians, to some western Europeans, are sort of the Poles of Western Europe. That is, as you would expect the Polish jokes in this country, the Belgian joke is a joke about someone who is somewhat slower, and perhaps sort of dense. Especially in France, there are likely to be Belgian jokes.

BOHNING: So you grew up in Paris. What was it like and what kind of schooling did you have there?

STORK: Elementary school is a very dim memory for me. I learned to read and write, so far as I know, at home, probably mostly with my mother. I remember vaguely that eventually I went to the lower school of the Lycée Janson de Sailly. There are various lycées in France; they are essentially preparatory schools for universities. It is a little bit like elementary school and high school here; that is, at a certain point you switch over. So there was first this lower school. Let's see, what would it be—ten, nine, eight? They count in reverse there. Here you start with one and go up. There it's in reverse. You start with eleven, then ten, nine, eight, and so on and finally first.

In those days there was a terminal secondary school exam, a baccalauréat, which was a two-part thing. You first had one, and then you had one more year where you could divert to either mathematics or what they called philosophy, which, I guess, would be the arts. Then you'd have another exam, the second part of your so-called baccalauréat, which in France was essentially the entrance exam to university. That is, if you pass this exam, you automatically could go to the university. I don't know whether the system has changed, but I know that now it's only one baccalauréat at the end.

So I was at the lycée called Janson de Sailly. These schools were extremely good schools. They were just simply quite different, I'm sure, from what they are today, and very different from the American operation. The American operation is essentially opposite to the European one; that is, you do essentially nothing in the high school years, and then work very hard in college. The French and probably Central European system was the reverse. You killed yourself in high school, and then it was pppfffffff. [laughter] It was essentially nothing much. Which is why you could spend your time on the terrace of a cafe with no great damage, once you got to college. But in high school, it would be a rare day that you didn't have at least three hours of homework, and weekends that you didn't spend memorizing history books, possibly without the slightest understanding.

I have very mixed feelings about the European education system. There's no question that on paper it's infinitely superior. But there is serious doubt about the extent to which one learns anything other than rote knowledge. That's a different question, but it's not clear. It can be suspect: if you're taking twelve subjects, there can be some suspicion about how much time you can devote to understanding any one of them. But you do learn to survive the pain of

studying. That much you learn, that this is a normal sort of thing. You are trained to do that, so then you don't mind it so much.

BOHNING: Were there any athletics?

STORK: Yes. Gym was compulsory. We had some of that. We ran around the courtyard. I guess we probably played some volleyball and things like that.

BOHNING: But there were no organized sports of any kind?

STORK: There were things you could join. There was an athletic association, but it was nothing that was required. But drawing was required.

FINE: Tennis must have been required. [laughter]

STORK: No, no. [laughter] I was born in Paris and went to school there until what would here be the ninth grade or tenth grade. The last three years, which included both baccalauréats, were in the south of France in Nice, where I did in fact play tennis, but that was just because it's nice weather. It's not a bad thing to do, but that had nothing to do with the school.

BOHNING: What was the science education like?

STORK: I remember a chemistry teacher—and in fact those who claim that there's a relationship between teacher and eventual avocation may have a point. I remember the chemistry teacher, but science education was mostly pretty dogmatic, as it would have to be. You did two hours a week of physics and chemistry, or whatever it was called. There was some sort of a lab where we did awfully elementary things. Maybe we had a Bunsen burner and warmed up something, although I don't really remember any details. This was in Nice, not in Paris. I don't remember anything about science education in Paris. I don't think there was any experimental science there. There was, of course, mathematics.

But in Nice the personality of this chemistry teacher was quite different from that of the other teachers. He was actually a very strong, no-nonsense person, which was quite extraordinary. His class was probably the only one where I had a certain amount of discipline. Discipline was a peculiar thing in the French system. It was both brutally enforced and missing.

It became a point of honor to try to screw up the system because the system was so tight. The penalty for twisting the cap of your fountain pen while the teacher was speaking was four hours of copying history books on the day off. The days off in these days were not Saturday and Sunday, but Thursday and Sunday. (This has now changed, I believe, to Saturday and Sunday.) So you spent Thursday in there, copying pages. And if you accumulated enough of these penalty hours, which I think was some number like thirty, in three months' time, then your parents had to come and plead that you were not as bad as it appeared. So my main aim was to keep it down to twenty. [laughter]

But it became essentially the system versus the individual. Presumably, all these things have changed a lot. But this chemistry teacher was able to maintain discipline in his classroom without resorting to such nonsense. To me, he was an impressive person when you listened to him. I'm sure that made some sort of impression on me. I really didn't take serious chemistry until I came to this country, when I entered the University of Florida, in February 1940.

BOHNING: At the time you had taken the chemistry, you hadn't given any thought to making it a career.

STORK: Well, it was sort of by default. I mean, I was limited by how I had studied English. I had studied English in high school, as a required subject. It was required to study either English or German. So I studied English, which was a couple of hours a week. You covered two pages of some Shakespeare play in about a semester's time, and you dissected the hell out of it; you really didn't have very much of anything useful. But the French were very strong, both in English and in French, in what they call *explication de texte*, which is the dissection of everything there is to know about the sentence structure, how the words relate to something, and so on. So you really didn't learn to speak that much. When I came here, it took me a long time to understand what people were talking about. I could write some English, and I could actually understand it to a considerable extent if it was written. But it was several years before I could understand what was going on in a movie. I could see the things moving around, but I didn't understand the dialog in a movie. I didn't know what was going on.

The truth is, when you don't know a language it's easy for people to say, "Well, you can learn it." It's obviously true. At one extreme, you say, "If one billion little Chinese can learn Chinese it mustn't be that hard." That's one point of view. On the other hand, you're not convinced if you can't speak Chinese that, in fact, it's something that you can learn. So that eliminated things like law and business, that sort of thing, where you'd have to talk to people. Something in which you would presumably deal with inanimate matter sounded very attractive. [laughter]

So it was sort of by elimination. Actually, I've wondered about it once in a while, "Why did I do that?" Well, when everything else sounded really pretty uninteresting, chemistry was

interesting. I still remember exactly the day, because it was sort of a revelation. Because of the language problem, because I really did not relate to the American adolescent culture at that time, I was really quite isolated. What did I do socially? Socially, I mostly stuck myself in the library and looked around it. In those days, the library at the University of Florida was about half the size of this room, and it had very little of anything. But it was nice because there was essentially no one in there when there was a football game going on.

Then, for some reason, which I don't remember, I had become interested in quinine. This became a thread. A lot of psychological trauma came from that one thing—quinine. Why I became interested in quinine, I cannot imagine. But whatever the reason was, I was looking around, and I was looking into quinine. That probably was the second year that I was at the University of Florida. I was there two and a half years, and the second year I was taking organic chemistry. Maybe there was some formula of some alkaloids in the book that we used at the time; I don't know what it was. Anyway, in *Chemical Abstracts* I came upon a paper by Paul Rabe (1), a great German chemist who has more or less been ignored since. Rabe had in fact done something that was unbelievable. That is, in the early 1930s, which was fifteen years before anybody else did anything much on alkaloid structures, he had first of all found out what the structure of quinine was, which is no mean feat, including, eventually, its three-dimensional structure. He also had managed to synthesize hydroquinine, which is the same thing as quinine except that it has an ethyl group instead of a vinyl group, an accomplishment that was really quite amazing for the time.

This was really attractive to me. You can see why, because I am not mathematically inclined, I really doubted I could pass, even with effort, some sort of elementary mathematics test. I had calculus and did quite well. But the fact is, I was not mathematical. Now chemical synthesis was something, which was not mathematical at all. There's absolutely no mathematics in synthetic organic chemistry; it's fantastic, whatever the science people say with respect to the mathematical basis of science. There's a lot of science, which still has absolutely nothing to do with it. Well, it may have something to do with mathematics. If you say the world would not exist except in mathematical terms, that's possible, for all I know. But that's a different thing. When I drive my car there's a lot of mathematics involved there, but I'm not doing it. And in organic chemistry, in synthesis at least, you don't really have mathematics at the operational level. So that was quite attractive. It was something I could actually follow and understand and get excited about. Also, there's the art part of it, which is really a very nice feature. Now, why society tolerates it is something else. [laughter] But so long as society does, it is really quite nice. At that time the question of whether society tolerated it didn't come up. It's more of a problem now.

So I became extremely interested in organic synthesis and decided I should synthesize quinine itself, the substance with the vinyl group. At that time I became more and more interested in it. You don't know why you start collecting stamps, but some people get fascinated by that, or playing chess, or whatever. There's an initial event, and then you get caught up by this and it excludes other things; the other things don't get a fair chance. If somebody had

shown me what oceanography was all about, maybe I would have liked that, I don't know. So it happened that way.

BOHNING: I'd like to back up if I could and go back to Europe. I wanted to ask you why your family came to the United States. Of course, the war and the political situation was pretty grim at that time. Was it 1939 when you came? Why did they come here then, rather than some other country?

STORK: Well, what other country? People go to the United States because the United States represented, and still does represent, freedom. That was one reason for it. Another reason is that the older brother of my father was already here at the time. He had been here for maybe a couple of years. I have no doubt he was motivated by events in Europe. So there was somebody here. But then again, the fundamental thing was that the United States was the United States. America was freedom at that time, and probably still is.

BOHNING: You had just finished the second baccalauréat.

STORK: That's right. I passed it in Nice, in the south of France. The baccalauréat is a uniform degree, a uniform exam, all over France. That is, the exams are sent from Paris to the various parts, all opened simultaneously, and everybody took the exam at the same time. A crazy French operation. When that was finished, my parents came and, obviously, I came with them. And that's it.

BOHNING: Frances Hoffman has a number of your childhood stories in the Aldrich article (2).

STORK: Yes, I brought this along just in case I needed to refer to it. [laughter] I actually was conned into reading this thing and correcting some of it, and on the whole this is pretty much true, what's in there.

BOHNING: Do you have any other memories of growing up in Paris, unrelated to schoolwork? What it was like growing up there, as a young boy?

STORK: It was highly structured. You walked to school (Janson de Sailly) which was about a mile from where we lived in an apartment in Paris. You walked there early in the morning (sometimes it was dark when you left) and came back home for lunch, which was interesting.

There was a couple hours' break for lunch and then you had to come back to school. Come back home in the evening, do your homework, go to sleep, go back there. Go there on Thursday to copy pages out of a history book. [laughter] And on Sunday, French society (and I suspect Indian society must be that way even more so) was extremely structured in the sense that there was really not much intergroup visiting. The idea of dropping in on some friends to play checkers or whatever wasn't done by most people of that particular social group. You didn't do that; you just went home. Even the telephone was not something that you really used. We really didn't do very much socially.

There was one time when I transgressed that sort of thing. A friend of mine had a bicycle, and I wasn't allowed to ride my bicycle in Paris. But we would race against the clock on his bicycle; we'd just go up to a point, come back, and clock it. That was not good, especially when I was knocked over by a taxicab. I couldn't hide the fact that I was out there bicycling because the police brought me home kind of bloody. This was bad. The reaction was clearly an emotional one, but there was also considerable unhappiness when they heard that I was racing around on a bicycle. There were a great many reasons for my parents' concern, including the fact that this was not something we "did."

I still remember one time when we were playing in the schoolyard, at a place where you could play sort of handball. I don't think people play that here. It's with a leather ball, about that big, and you hit it against some sort of a wall and it has to hit the wall above a certain point. It doesn't bounce much; it only bounces about that much. I don't think that's what American handball is, because handball is a bouncing ball that bounces a lot; this doesn't bounce much. But we were playing happily enough when school was over. Maybe school was over at 5:00 p.m., so it was 5:15 or something like that; there was nobody there at the time. The head of the school ran into us and was indignant, and was going to tell our parents. [laughter] It was simply just not part of the structure. I had four hours punishment once for being in a classroom reading a book instead of being outside, during recess, kicking balls when you were supposed to be kicking balls. It cost me four hours because of it. [laughter]

Life was highly structured in a peculiar way, so that there was not all that much social interaction. Interaction was with family on Sundays. We had a house about six miles outside of Paris, where eventually we moved to from the Paris apartment and lived there, in a place called Garches. On Sunday, the Paris family would come out there, eat cookies and who knows what, play croquet. [laughter]

Here is another example from which you can get an idea of the structure of this stratified society. I had a bicycle when we moved to Garches. I was allowed to go around Garches with my bicycle and do various things with it. The French are very high on cycling. It's the national sport; there's the Tour de France and things like that. So I had visions of becoming a cycling champion of some sort, even though my bicycle was an extremely heavy toy bicycle. There was a race every year in Garches in which you went around the town x times and then somebody eventually won. And I did whatever it is that one has to do to enter that race! I had no time to

get from the place where you registered, which was I think the plumbing supply place, to my house before my parents had been contacted by the plumber who thought that they should know that their son was thinking of entering. This was considered definitely a working class sort of event. The funny thing was that it was this plumber, who was part of the working class, who alerted them to the fact that there was something bizarre there. [laughter] He was a strange character. So there was not all that much interaction other than with family, and sort of in school, to the extent that you had to be involved with school.

BOHNING: I was going to ask about your family. Do you have any brothers and sisters?

STORK: I have a sister who lives in the south of France in Carcassonne. She's five years younger than I am. We eventually became quite close when she was probably in her late forties, after she lost her husband. Before that, we considered each other only a nuisance. [laughter] She taught English in a French high school.

I had a brother who was younger; there was about a year and a half difference between the two of us. He died when I was five or six. This affected my mother very much. This was in the days before antibiotics; he had a middle ear infection and died. My mother always believed that the doctor was clearly responsible. The good part of this was that she had absolutely no use for doctors, which probably saved the lives of several of her relatives, and beyond that had no particular awe of them. The idea of second opinion must have originated with my mother from that event. [laughter] The other thing is that she had great ups and downs in mood, which also contributed to my being even more set apart from society than the normal French system would do, because her moods were sort of inexplicable to me as a young child. So the only thing was to withdraw from this. My father was a sort of a mythical figure. I had enormous respect for my father, but we had almost no contact. I knew my father, I saw my father, I loved my father; so far as I knew he loved me, but he was really very much dominated by my mother, except in important decisions. He really made important decisions, such as coming to this country, which was a very major decision in the context of Europe back then. She would go along with that. But the day-to-day tornado was under her control. [laughter]

[END OF TAPE, SIDE 1]

STORK: That continued after she was in this country. She was a very remarkable person. She could be absolutely charming, and absolutely incomprehensible. Very, very difficult.

BOHNING: It sounds like you did a lot of reading.

STORK: Yes.

BOHNING: What types of things did you read?

STORK: Mostly chemistry things having to do with synthesis.

BOHNING: But I meant other than chemistry.

STORK: Not that much. Literary reading I did under forced conditions; that's actually quite an interesting thing. I would guess that ninety-eight percent of the population in this country of any educational level reads more than I do of any of the things that normal educated people read, such as novels or even detective stories. I was lucky with detective stories. The first and probably next to last detective story I ever read was *Murder on the Orient Express* by Agatha Christie, which is really not bad. I really didn't read all that much. When I came here, it was at the time that you probably would read the most, but the language was a problem. I had to be made to read. I took one course that was required, some sort of elementary English, whatever they called it. I had to read something about Queen Victoria. I forget what else. I had to read various things like that. So I read that, but it was slow. Mostly I would read maybe a couple pages in the beginning, a couple pages in the middle, and a couple pages at the end. I was sometimes fascinated by how they end these things and how they start them. But I don't really get that much about the story itself. So I really don't read all that much of anything. Some historical things I read.

BOHNING: What about when you were younger in France?

STORK: Yes, then I did. At that time I was very much interested in poetry. I spent time putting what I considered to be poetry on paper. I can't say that I wrote poetry because that's much too exalted for what I did. But that was actually a fairly serious effort. I can just say that this was part of the normal growing turmoil. To a large part, it was, especially as a fair number of these poems were dedicated to girls even younger than I. But I cared about it and I knew a fair amount about it.

I was actually quite good in French literature. I had a feel for French writing at that time, enough so that I even represented my school: in secondary schools they selected three people to represent the school in a national competition. I did not win anything. But nevertheless, that was something that I cared about.

French books are actually marvelous. I never understood the English language literature with respect to the number of words that people use to tell you something. It's really incredible compared to the French. The French novel is a flimsy two hundred and thirty little pages like that with large character, which you can easily read on the train from Paris to Le Mans, which is less than a two-hour ride. I think it's just great. My feeling has always been that if you can't say what you want to say in that many pages, you probably don't know what you want to say. It's really quite bothersome; it takes too much time. Even after I was in this country I would read French novels once in a while, mostly for that reason. It was the standard sort of thing that you would read—[Jean Paul] Sartre, [Albert] Camus; that sort of thing.

Or they would be historical things. The person that is nominally in charge of the film department here (whose name I forget at the moment) is a very well known movie writer (Amadeus) who should do a movie of my favorite historical figure. He definitely must make a movie of [Pierre Augustin] Beaumarchais. Beaumarchais was a fantastic figure. There is a boulevard in Paris called Boulevard Beaumarchais, so somebody would recognize it. Everybody knows Beaumarchais because he wrote the libretto for *The Marriage of Figaro*. Most people don't realize it, but you can actually make a case that the American Revolution might not have succeeded were it not for Beaumarchais. Which is a remarkable statement, and I'll let it go at that. But let's say that figure, which is really not that well-known, started life making the thinnest watch that had ever been made. He was a watchmaker. The thinnest watch in the world, which brought him to the attention of the court, and that started an unbelievable career, which included supplying the American Revolution with arms under some Spanish false name. It was really quite a fantastic operation. Things like that, I like. But they're short—fascinating, but short. I don't care for books like *Gone With the Wind* or things like that. [laughter] Some of it I just plain don't understand. Some of it I've tried to read, but often it's just trivial. I'm not reading that much science either anymore, except current stuff that you need to read, like the journals.

BOHNING: When you came to this country in 1939, how long did it take before you decided you wanted to go to a higher educational program here?

STORK: I don't think it ever was a thought. That was something that I was obviously going to do, without any thought being given to it. I mean, you did that. In those days, the people who were in our particular social group knew about the lycées (secondary school), (there was another parallel system which you had a sort of dim awareness of, some sort of vocational school system). And these people went to the lycées, which terminated in the baccalauréat. If you passed the baccalauréat, that almost made it sure that you would go to a university simply because why else would you want to follow that course? The system said: now you can go to the university. So you just did that.

So I don't think I ever gave it a thought. Then, eventually, I became fascinated by this quinine business. I had my own lab at the University of Florida when I was there for about two and a half years. There was nobody there. (Actually, it's a very good place today.) It was really a very peculiar place, but I had my own lab and I could do what I wanted. I could easily have killed myself; there's no question about that.

BOHNING: The story by Frances Hoffman tells how you got to the University of Florida (2). You had intended to go to UNC [University of North Carolina] originally.

STORK: Yes, this actually is quite right because I told her that. When we came here, I didn't know anything. The first thing I wanted to find out was about the universities. I was extremely withdrawn and I couldn't speak English very well. So what do you do? You go to the library. The library is one thing that I understood. So I went to The New York Public Library. I spent most every day in The New York Public Library. I haven't been there since. [laughter] That's not true; I was once there to try to find a patent. I think it's almost impossible to find a patent at The New York Public Library.

FINE: Did you come into Ellis Island?

STORK: No. I think even in those days Ellis Island didn't function anymore. I don't know when they stopped.

So I just studied the books relating to U.S. educational operation and eventually got some fantastic conclusions out of this. There were some requirements that were pretty serious. I was aware that money was going to be a problem and so, obviously, I wasn't going to go to a place where I had to pay. Now, in the European system you essentially didn't pay anything in those days. You paid maybe twenty dollars a year to register, or something like that. It's probably changed, but not much. It's more like the New York City system. So it obviously had to be a non-private institution. I thought the possibility of a fellowship or scholarship was null. But I did check schools here because we were in New York. I stopped somewhere within the confines of Low Library, at Columbia, where they made it clear that they would never in a million years consider my application. [laughter] But I didn't go any further because I'm not sure I understood; there was a nice gray-haired lady who I talked to. Then I went to the New York Public Library, researched these things, and concluded that North Carolina was where I should go.

BOHNING: Why did you conclude that North Carolina was the place?

STORK: It just came out of these damn pamphlets from the U.S. Office of Education. They had tables showing what fields they were very good in; they indicated that chemistry was one of them at North Columbia. And you didn't have to pay anything—it was free; et cetera, et cetera. And it was reasonable timing, because it sounded to me that it was less cold in North Carolina than here in New York. You have to remember that before that I was in the south of France in Nice, where I could play tennis every day.

So then I was on my way to North Carolina. It turned out they had a quarter system, which meant I was too early for one and too late for another. I think the story that Frances Hoffman wrote (2) is slightly exaggerated. It was not quite that I stayed on the bus until it became warm enough that I thought it worthwhile and got off. [laughter] I'm not sure whether that's what she said, but maybe.

BOHNING: It's close.

STORK: No, it's more of a caricature of reality. What happened is that I'd looked at it and thought North Carolina, but then it turned out it didn't seem suitable to me. Then I said, "Well, what else is near there?" and it turned out to be the University of Florida, so then I went there. By that time my parents had decided to settle in St. Petersburg, Florida. That was another good reason. I really don't know why they moved there. Probably there was some motivation that it was not too expensive to live, and it was warmer than New York. Or, maybe, there was somebody whom they met or whom they knew who lived there. When I got to St. Petersburg, I said, "Well, what universities are around here?" It turned out to be the University of Florida.

In February of 1940, I entered the University of Florida. I got some advanced standing of a very bizarre nature. I didn't care what credits they gave me, but the extraordinary thing was that they gave me three credits for French but twelve for Greek, which was fabulous and difficult to explain, but unimportant. [laughter] I had taken what the French call Greek for four years. Classical Greek. I can read the signs on sorority houses, and that's about it. [laughter] But nevertheless I had four years of Greek. I can read it; I can read it without understanding it. I can read it about as fast as I can read French. Noise-wise, with the sound of it, there's no problem. But the fact is that I don't know what it means. And I got twelve credits out of it.

The net result of it is that I could get out of there in two and a half years, especially because the chemistry course was not divisible. If you entered in February, you had to take the final exam for the whole year. This was a good thing, which almost cost me my first year. (I don't know whether Hoffman goes into this or not.) I was doing very well on the chemistry exams, which were a multiple choice thing, where I could test my hypothesis that the longest answer is statistically much more likely to be the correct one than the shortest one simply because it's harder to phrase correct things than incorrect things. I'm not sure if it's still true. I

wouldn't be surprised, but it probably has been adjusted by this time. Possibly for that reason I was doing extremely well on these tests.

But I never went to the lab. I went to check out the equipment. I thought that you went to the lab if you didn't know the answer to the question and then you tried to find out. But I knew the answers to these questions, so I thought I didn't have to go to the lab. I never went. The next time I went was to check in. I remember there was a little porcelain spatula that had a little cup at one end and a little flat thing at the other end. It's about that long [three inches]. There was a slight chip on the flat part; they charged me twenty cents or something for it. I was outraged; I'd never been there! I'd never touched the thing! [laughter] It turned out that it was serious because although I got very good grades on the tests, no one had ever mentioned I was supposed to go to that lab. So they flunked me, because I didn't go to the lab. I learned afterwards that, once in a while, they would give tests in that lab, and I was never there. But they never said anything about it!

That was pretty serious. I thought it was very serious because you had to pay. They had a system, which was an interesting system. Although the school was free, if you flunked the course you had to pay sixteen dollars. That was the time when a hamburger was ten cents and a Coke was five cents. That's like one hundred or two hundred bucks today. Two hundred dollars is a lot of money to pay. So that was much more serious so far as I was concerned, than the fact that I'd gotten an "incomplete." But an incomplete would have been murder because I would have wasted a year; I would have to take this damn thing over again. So I carefully studied the rules and regulations of the university and found out that if somebody is not doing satisfactorily, he has to be told. And if he pays no attention then he has to receive some sort of a letter. But I had never received anything. So I raised all hell about it, that I didn't want to pay that sixteen dollars. Eventually they compromised and gave me a C for the year. But that C was okay because that's passing. [laughter]

So then I could go on to the next thing, which was organic. I took organic chemistry and I passed my physical chemistry. I was very lucky because I think it was the end of the old, essentially non-mathematical physical chemistry. I think the textbook was by Farrington Daniels (3).

BOHNING: What about organic? Do you remember what you used for organic?

STORK: It was a big red book and the last name started with a W. I could find out easily enough. At the moment I don't remember and I don't have that book anymore. It had photographs every so often of people like Emil Fischer and other well-known organic chemists.

FINE: Was it Frank Whitmore?

STORK: No, Whitmore was a serious sort of thing that I got later. The other text was the College Outline Series, which in those days was only that size [four inches in length] (now it's expanded to be eight inches in length) and had some nutshells of things which our chemistry professor was very fond of. His name was Cash Blair Pollard. He was very fond of it because he was one of the editors. We had to buy this book, and he presumably got some sort of royalty out of it. So that was one book that we had.

He didn't know much organic chemistry. I think maybe it's mentioned in here (2), but I'm not sure. The main thing that I knew about him was that he was a former baseball coach at Purdue, and other than that, he raised police dogs. He was on good terms with the Gainesville police. There was one graduate student who was given to extracurricular activities of various types. Pollard always knew what he had been up to because he would get these reports from the police. [laughter] They were fairly innocuous sort of things, but rather colorful. But Pollard really didn't know very much about chemistry, and this was probably a very good thing, because then I could fool around. He probably had no idea what quinine was in the first place.

BOHNING: Who was chairman of the department and how many people were in the department?

STORK: There were four professors. There was one general chemistry teacher who knew strictly nothing, and lectured on general chemistry. In those days, general chemistry was extremely different from what it is today. General chemistry today is essentially physical chemistry, so far as I can see, and physical chemistry in the modern sense, not in the sense that I had it. [laughter] General chemistry was descriptive chemistry, so you did in fact learn the famous quote that "Silver chloride is not a green gas" (4). But you didn't really learn much of anything else. That person taught it, and it was a full-time job; I guess he was in charge of the general chemistry labs as well, which I didn't go to. The organic person was Pollard.

There was a physical chemistry professor, [John Erskine] Hawkins, who was a very nice man. I owe a lot to Hawkins, because I had decided I was going to stay at Florida. I had my lab and I was perfectly happy getting my Ph.D. there. All I had to do was continue doing things in the lab, and obviously I could make quinine within the next few weeks. [laughter] I could do that and get my Ph.D. What's wrong with that? Hawkins convinced me that I was out of my mind, and that I should go to a "decent" place, which he made perfectly clear he didn't think Florida was. But he was a very nice man. I still remember he had a place with high ceilings and there were distillation columns that went all the way up. They were filled with different kinds of things. He worked with turpentine, which was a great thing in Florida. There were pots full of turpentine, and he distilled and fractionated them and measured the efficiency of these columns. This is where I learned what an H.E.T.P. is, which is the height equivalent to a theoretical plate,

which measures the efficiency of these columns. This is about as far as physical chemistry could go; not quite, but pretty much so. The physical chemistry lab there was a reasonably serious lab. We did things; we tested things. I don't remember what it was, but we did and Hawkins oversaw them; he was himself in the lab. He was a pretty good teacher. I managed to get the highest grade in part of that course, at one time. But that is obviously a reflection on the technique of teaching, because I don't know the slightest thing about it. You could do a fair amount by memorizing. Anyway, he was a fine person.

And there was a fourth person who taught analytical chemistry. He was commissioner of public works in Gainesville. He was a very fine person. We did some electrochemistry experiments, plating copper on double platinum cylinders that were rotating some way or another, and finding out something about the current that was passing through. His main interest was the rate of growth of things that eventually plug up pipes. It was actually quite amazing. I don't know if you've ever seen a pipe that carries hard water or whatever; they get filled up with this solid chunk until eventually there's only that much of a hole left. That was really what he was very much interested in; he was a fine person. His name was [Alvin Percy] Black. Those were the four people that made up the chemistry department of the University of Florida.

BOHNING: Was it all-male at that time?

STORK: Yes. At that time it was roughly three thousand students. There was an agricultural experiment station. Blacks were not allowed in. It was the real South at the time. It was something that seemed sort of puzzling, so far as I was concerned, because that was something I did not know. In the summer, there were women, maybe schoolteachers, who would be there in the summertime. I became aware of this because I had a job as a waiter in a private establishment just outside of the college. In the summer, there was a lot of business there. I didn't understand English well enough. I remember when somebody in a crowded room full of these schoolteachers ordered what was probably beer of some kind and I thought they wanted watermelon. [laughter] I made my way with this big watermelon through this crowded room, and it was not the right thing. Eventually I got fired from that job. I actually got paid in meals; I got no cash for this. I got five dollars' worth of meal tickets per week. But five dollars was pretty good, because it was blue-plate specials, which were these plates where they had two vegetables and some meat. The blue-plate special was only twenty-five cents, which was not bad. We got paid that way. And then you could go back into the room where they stored stuff and steal some food here and there. [laughter] On the whole, Florida was not an unpleasant experience.

BOHNING: Who gave you the laboratory to work in on your own?

STORK: Well, there was space and it just happened. I'm reconstructing. I probably must have asked Pollard if it was all right. My dim recollection was that there was a person getting a Ph.D. working in that lab. I think his last name was Sugar, something like that. He was getting a Ph.D. making various piperazines. Pollard's research interest was making piperazines. You may or may not know that piperazine was not one of the most interesting compounds that people were interested in. It's a reduced pyridine with another nitrogen diametrically opposite the first nitrogen. It is a reduced thing. This chemistry is minor, but you can make various substituted piperazines, and determine their boiling points, refractive indices, things like that. [laughter] That was a big thing at that time; a UV instrument was not, in fact, anything that probably anybody had except in physics. This guy was getting a Ph.D. at the University of Florida and it may be that I started to talk to him. I remember that he had space in the lab. There was space for another person easily in that place. So it may be that this is how it started; I asked him if it was all right if I worked there, and it was all right.

And there was a glassblower. I remember the glassblower had pellagra. Pellagra is an unusual disease. You don't get pellagra easily; that's caused by a lack of niacin, I think. This poor guy had pellagra, but then he recovered from pellagra and had nothing much to do. So he was making instruments and whatever it is that I wanted him to make. It was great. I didn't have to pay for chemicals; it was really pretty good.

[END OF TAPE, SIDE 2]

STORK: So I started making quinine there, but it took longer than I thought. I actually started lecturing about quinine finally, for the first time, at the [George] Büchi symposium only two years ago at MIT, when Büchi retired. (I hope you're getting something from him because he certainly is somebody that you must have on tape.) At the Büchi symposium I did talk about my fiddling around with quinine, which was a nice sort of thing for that kind of an occasion.

The idea that I would make quinine as a thesis subject was an exaggeration. But I've learned the potentially useful but continually forgotten thing, which is that in my particular case anything which I think will take a certain length of time to do will in fact take seven times as long, if I'm lucky. Now there's an important corollary of that. There are many projects I <u>still</u> have unfinished, because there are many problems that I would start, or convince somebody to try, on the grounds that it would only take a couple of weeks. "We can perfectly well take care of it in that time." If I really were convinced that what I'm really talking about is a minimum of fourteen weeks or whatever, I would probably decide, "Well, I really don't want to spend that much time." In the case of quinine it was even worse. I thought it would take three years, and it's taken <u>more</u> than twenty-one. In this case it's been more like forty. That's a long time.

BOHNING: Do you still have that original proposed synthesis that you worked out for quinine?

STORK: I have this somewhat embarrassing document. I went to the University of Wisconsin. The story Frances Hoffman tells about this is correct, (2) that I was really planning to go to Illinois. I didn't tell anybody that I was going to Illinois. Again, it was quite a peculiar operation. I had a total lack of knowledge of the American system, based on the underlying assumption that like the European system it was a unified system. So you go wherever you care to go. It makes no difference; it's all the same. Of course, that was not true, except for the fact that various people work in various different areas. So I decided Illinois was clearly the place because I was interested in quinine; quinine has a piperidine kind of ring system and I would work on that kind of structure. Roger Adams at Illinois had done some alkaloid work, which embodied some piperidine rings. There's more to quinine synthesis than that. I would be aware of it today, but I wasn't at the time. Besides, Roger Adams was a very good chemist. At that time, he was really the tops. So I would go there. But I also knew about [Samuel L.] McElvain, who was doing a lot of work in pyridine chemistry, which was conceptually totally irrelevant to what I was interested in. It's like being interested in benzene versus monocyclic terpenes. It's not the same; that is, they are both six-membered rings, but really quite different. Aromatic substitution is not the same as making terpenes.

So the fact is that when I went to Wisconsin (or Illinois) I was prepared. I assumed that if you were going to work on a Ph.D., you were supposed to do something original. Incidentally, the field of chemistry is a mysterious field. It is mysterious in that it is a field in which the Ph.D. clearly has become a strange operation in which the one thing you learn almost nothing about, except in rare cases, is whether the person to whom you're awarding a Ph.D. is capable of original work, which this degree is supposed to reward. At that time it didn't even occur to me to question this; something original was what one had to do.

So I prepared some sort of project I gave to McElvain. I gave it to McElvain, and McElvain was pretty startled. [laughter] So I had prepared it. The only excuse you can give for that document is immaturity. It was really pretty bad. It was pretty bad. There was not even much thought there, at that point. Eventually, it became better after I started graduate school; then I started thinking. I actually refined my plan to some extent. I still have it. What was missing from it, and which became clear within the first year that I was at Wisconsin, was a feel for the problems of three dimensionality. That's a problem that I had known about for a long time. The main event between 1942 and 1950, and I don't mean just in this country but worldwide, was the sudden consciousness that most organic natural products were not flat projections. People <u>knew</u> this as intellectual knowledge, but they did not feel it. One essentially ignored it.

But my quinine involvement is really quite something. It's somewhat typical of everything that's wrong with what I do and what has motivated me. What's wrong with it is the inability to give up something to which I'm emotionally attached. If it had been any kind of

business decision, subject to criteria of reasonableness, I should have given up quinine a long time ago. Still, it's important to make clear that I have not been spending all my time since 1942 trying to synthesize quinine, but I did come back to it every so often. Last year has been totally quinine-free in thought. And it had been quinine-free maybe ten years at a time. But I would think about it again every so often, quite a bit. Now I've finally decided to call it quits.

It's not that the problem has been solved yet, not in the terms that I would consider a solution, or on the terms that modern chemistry has a right to demand, namely, control of all of the asymmetric centers of that molecule. That has not been achieved. We've come the closest to that goal of anyone, but we haven't published our work because our goal of completely controlling it has not yet been achieved. This has been a sort of leitmotif.

FINE: Between 1942 and 1950, did you ever try to build a ball and stick model of the molecule because of this question of three-dimensionality. There were ball and stick models then.

STORK: My favorite story of that—and I don't know if it is mentioned in Hoffman's article (2)—is the time that we completely failed essentially because of a lack of intelligence; yes, a lack of sufficiently focused acumen. I want to soften the blow. [laughter] It involved Carl Djerassi when he was a graduate student. Carl Djerassi and I were overlapping graduate students. I guess he was a year behind me when he started; maybe, maybe not. We would have lunch together every day at the lab. Eventually I convinced him he was wasting his time doing a Ph.D. with Al [Alfred L.] Wilds, and that he should obviously work on <u>my</u> problem. He agreed that was certainly reasonable. So he started doing that. At that time the problem I was interested in was morphine. Well, quinine was my own problem, but Djerassi's problem was going to be to synthesize morphine. This lasted two weeks, until Wilds found out about it and then we were both threatened with instantaneous expulsion. [laughter] So that stopped us.

But during that period, when he was my collaborator, *de facto* though not *de jure*, we became fascinated by a paper that was published by Indian workers (5). We became fascinated, as indeed many people became fascinated, with an early total synthesis of a terpene called santonin. Santonin had medical use because it's a vermifuge; that is, you can use it for cattle to get rid of worms. Its structure was something that was a conceivable target at that time; it looked tough, but nevertheless it was a conceivable target. It had a couple of asymmetric centers and it had two rings, so it was something that you could think about. Various people had considered this substance as a possible target of synthesis, and then, all of a sudden, there was a series of papers from this group in India, which claimed to have synthesized santonin.

What became fascinating to us (and I'm sure to a lot of other people) was that the final molecule they obtained was identical in all respects with santonin, <u>including its optical rotation</u>. That was startling because no optically active starting material and no resolution had been used. Therefore, optical activity had to have been produced in one of the steps. It's actually not

impossible, come to think of it, but the initial reaction today would be that it's a little bit like saying there's a machine that will do perpetual motion; it violates something—not everything, but it violates something. So we were intrigued by this, and it was boiled down to a particular step in the sequence. That is, at what point did the optical activity appear?" Well, it obviously appeared with the first asymmetric center. The first asymmetric center was sticking a methyl group into 2-formylcyclohexanone. Most people refer to it as 2 hydroxymethylene-cyclohexanone. So the anion of what you can think of as formylcyclohexanone was methylated. The methyl group is stuck on and that carbon becomes an asymmetric carbon. There are four different groups on it, and that molecule became optically active in the Indian work. So it was the methylation that produced the optical activity.

We decided to find out how that happened. We made these ball and stick models that you're talking about, the Fisher models. They still exist. There's nothing wrong whatsoever with the Fisher models. We built this thing to try to understand how the methylation had to have come from one direction rather than from the other. They hadn't suggested that this is what had happened. This is what we concluded and, of course, it didn't make any sense. So we made models to see whether it was possible. This was probably in 1943.

This was maybe six or seven years before [Derek H. R.] Barton became concerned about interconverting chairs. If you take Fisher's sticks and balls and you construct a model, you can't make it flat. You can't make it flat; it will come out as either a boat or a chair. Ours came out as a chair, purely accidentally. It could have been a boat, but it came out as a chair. If you take a chair, obviously there's a preferred direction of approach of the methyl group, because the two faces of the chair form we had made do not have the same appearance. What's wrong is that another chair would have been made, for which the exact opposite conclusion about ease of approach would have been reached.

These two chairs did not interconvert easily. The Fisher models did not allow that. Almost certainly, you could if you were extraordinarily gentle and really meant to interconvert them, you could have. But they would not interconvert the way these plastic things that you can get today would just begin interconverting almost by themselves. It would have to be a willful act, and we had no motivation for this willful act. We just built this thing and it had that shape. That's it.

I got Djerassi (6) to repeat the methylation experiment described in the literature and run off to a polarimeter. (He didn't have his stiff leg then.) Where was there a polarimeter? Well, there was a polarimeter in the agriculture school, which was about half a mile down the road. "We" methylated this formylcyclohexanone, and Carl went to take the rotation of the product. He ran over to the agricultural place, learned how to use a polarimeter, found out the rotation, and came back all excited. In fact, it was optically active. Fantastic! We were prepared to write up the bombshell paper. But then, I guess we were still puzzled and we repeated the experiment. We decided we'd better repeat it very carefully because it was a pretty dramatic result; nobody would believe our result. We looked at it again very carefully, this time washing the polarimeter

tube very carefully because it had been used for the analysis of glucose solutions. [laughter] This time, the second time, there was in fact, within experimental limits, no rotation.

Now, the obvious, intelligent next step we did not take. Why wasn't there any activity? Because there was this other equally possible chair, right? That would have been an important first step. This was known at the time, the theoretical basis for the two chairs and the boat. These things existed as documents, which we were not aware of. It was not our ballpark, so we didn't know anything about this. We missed it completely.

Barton and I later overlapped in the sense that he spent a year at Harvard when I was there. He developed his conformational insights at that time. I was violently opposed to it. There's no question but that I thought it was ridiculous, this conformational business, and "polar," now changed to axial, and equatorial bonds. My objection was both reasonable and stupid; his was fundamentally not rigorous but brilliant. There's a difference. The difference is simply that there are things that are not absolutely correct with a capital "C," but extremely worthwhile because they're major simplifying assumptions, which allow things to move forward. Other people focus on what the little problems are with this, "This does not explain absolutely everything, and there are exceptions to this and that." Therefore, they are bogged down with recondite concerns, rather than perceive the stylization of reality, which allows moving forward.

My objection had been with the polar-equatorial relative stability concept; you can obviously construct a molecule in which axial would be more stable than equatorial. That's obviously true, but not as important as the simplification that the great majority of cases, will be true as a first approximation so that you can start thinking about things faster than you would otherwise. Today, I think my objection makes more sense, but it remains that people would have wasted much time if Barton had gone along with me. Because of the computer, there is no special reason not to draw and minimize the energy of a structure and see what is more or less hindered. Never mind about calling it axial or equatorial. So axial, equatorial no longer makes as much sense. But it did at the time and the resulting progress advance in understanding was extremely positive. It is definitely to Barton's credit that he paid absolutely no attention to my objections. [laughter]

So at the time, there were ball and stick models; they could have served perfectly well. Barton's initial contribution was to have a machine shop make his initial model of cyclohexane that it was about that big [two feet across]. You could walk into it. You could see cholesterol from the inside. [laughter] If you put fabric on top of it, you could almost use it as a tent. But the crux was that it was easily convertible from one chair to the other. Eventually, the Barton models were used by [Louis F.] Fieser to make the Fieser models, which were the basis for various other models that are now available.

So how did I get into that? Also, what understanding did we have of three-dimensional relationships at that time? The genius at that time in organic chemistry was Sir Robert

Robinson. I go to England every so often; they still tolerate me. But one of the things they do not like is what I say about Robinson. Robinson was a genius. I knew Robinson in a casual way, not intimately. The only person who really knew Robinson intimately was [John W.] Cornforth. Cornforth's still alive, and it would actually be very worthwhile to do one of these interviews with him. It would be tough with Cornforth because he's deaf. But he can talk and you can learn to interpret what he says. His wife lip-reads, and they work together very well. To do one interview about Robinson would be very, very worthwhile. Cornforth is the only person who could do it. [Arthur John] Birch would also contribute things to it, which would be worthwhile.

Robinson was viewed as an intellectual giant and had great influence. Robinson became identified with synthesis. And this is going to be about as harsh as I can make it, but his efforts in synthesis were doomed, even making allowances for that far away time in synthesis. It was a complex psychological thing. He knew he was brilliant, but he considered three-dimensionality an enormous handicap to the exercise of his brilliance, which was just straining to burst. Some people have interpreted the supposed feud between [Antonio] Salieri and Mozart in the terms of a conflict between Salieri and God. This is a romantic view, but an interesting one. It's an interesting thought, which I happen to believe is what the problem was with Robinson. That is, Robinson essentially decided that if God had decided to make things three-dimensional, that was his problem, not Robinson's. [laughter] And Robinson was able to do actually fantastic, brilliant things—ignoring the dimensionality. He did this, but his synthesis efforts were doomed.

Now, if you think about it, it is unbelievable. How can you possibly try to synthesize steroids if you behave as though you thought that they were pancakes? There's just no way you can do it. And he never did! Robinson published sixty-nine, or some such number of papers on attempted steroid syntheses, an incredible thing. You couldn't get away with it today in a million years. Sixty-nine papers on the total synthesis of steroids, without ever synthesizing a steroid or anything looking like a steroid. What he did looked like steroids, because they were two-dimensional pictures, actually unrelated to the steroids he was trying to duplicate, and which, he was allowed to publish because he was Robinson.

He did eventually achieve an impressive steroid synthesis, but only when Cornforth decided it was enough already. Toward the end of Robinson's life, he took the various chemicals out of the lab to his place, which I think was at Shell Laboratories at that time. (Shell had given Cornforth a lab.) He managed to beat together a construction, which you could claim was a cholesterol synthesis. Not entirely obvious, really because identification methods were still primitive.

In that era there was an important effort relating to the structure of strychnine. Eventually, the correct structure of strychnine was solved by [Robert B.] Woodward, and this produced much tension between Woodward and Robinson because Robinson had devoted much of his life to the structure of strychnine problems. And there was this interloper, who moved

just one bond from here to there while leaving all the others where Robinson had put them (correctly). But of course, you see, Robinson's argument was, "Well, what the hell. There's only a one percent change, and Woodward gets all the credit." The counter argument is, "If you tried to use a key with one percent change from the key that would open a particular lock, it would very likely not work." Robinson then said, "Oh well, it's not easy to decide what the correct structure is. The obvious thing to do is to synthesize all the variants that are possible for strychnine." This would, even today, be inconceivable, especially because he had no clue what the stereochemistry was. He started with a coworker by the name of [H. T.] Openshaw and published a couple of papers trying to put together strychnine (7). There were interesting kinds of structural changes, but no conceivable possibility of any kind of strychnine. So that was the state of affairs. Robinson gave no evidence of conscious interest in three-dimensionality; it's really remarkable. The molecules that he really did synthesize were various flat things like flower pigments and things like that, which were nice, flat synthetic problems.

Robinson did brilliant structural work, intuitively and otherwise. He did one synthesis for which I'm willing to forgive a lot, which is his famous tropinone synthesis. It was 1920 or something; it was really pretty early (8). He did that, which involved mixing three chemicals, and that's fantastic. But that's it. I'd say, "Well, what did he do after inventing fire?" [laughter] But it's really pretty good. It's really not bad. But that was when he was very young. And there was really no three-dimensionality involved in it. He just looked at the two-dimensional structure and said, "Well, it should be possible to mix succinic aldehyde and acetone and hydrochloric acid with something like methylamine," and it turned out to be true. But again, there was no conscious interest in three-dimensionality.

Woodward had no great interest in consciousness three-dimensionality at first, although when he started he was being vaguely conscious of it. One of the things that has riled me over the years, as it obviously would because it has to do with quinine, was the absolutely preposterous handling of the Woodward quinine synthesis (6) by both the scientific establishment and the press such as *The New York Times* (10). What would one expect? He was only twenty-six. That's pretty good. A couple of kids supposedly made quinine and that obviously produced a big impact. The fact that Woodward never made quinine, and I'm saying this on the record, the fact that he and [William von Eggers] Doering never made quinine, was unknown to the lay population. The second fact is that if they ever had made quinine, it would have cost the national debt to make ten milligrams of it, by that operation. The third fact is that the synthesis was meant to follow the Rabe hydroquinine synthesis; except that ethyl groups of the Rabe construction was now to be a vinyl group. The Woodward contribution was an elegant construction of certain piperidine with two asymmetric centers, but the attempt at stereo control failed and they got two different compounds, one right, one wrong. It is the maximum that you can get with two asymmetric centers in a vacemic compound.

From there, the synthesis followed the Rabe construction step by step until they got to a point where they said, "Well, it's well known that this can be made into quinine because Rabe said so." Rabe went on publishing very fine chemistry for another ten years, but he never

published details that would allow anyone to repeat his supposed conversion of the two asymmetric center intermediate "quinotoxine" to target the quinine. Some people tried to repeat the word description that Rabe gave of how one could do that conversion from quinotoxine to quinine. They could not do it. So you can't make quinine that way. So quinine was not synthesized in 1944, even though it was the central story on the first page of *The New York Times* at that time (10).

So the quinine sequence had nothing to do with the control of three-dimensionality of stereochemistry. Every time an asymmetric center was encountered, two compounds were obtained. At the next bifurcation, two more compounds were obtained. It was marvelous experimental work, because before IR, before NMR, if you got two stereo isometric compounds you couldn't get anywhere unless you could crystallize them. Then, you would take your chances going on with one at a time to see which one would go on to the correct next compound. (You can't do this if you've got too many asymmetric centers.) In this case, one had to take quinine and break it apart to a point where you can identify whether the synthetic intermediate matches the degradation product or not. This, in fact, is what they did. They synthesized the piperidine, which they deconstructed quinine to, and at that point took the degradation product from quinine, built it up to compound Q, the one Rabe claimed could be taken further to quinine; which in fact, you cannot.

[END OF TAPE, SIDE 3]

STORK: So that was the state of organic synthesis in the world at that time when I tried to make some contribution to it. The quinine synthesis was in 1944. By that time I was fiddling around trying to make quinine, and as far as I know this was the first conscious effort to achieve stereo control in a synthesis. My effort was designed to make specifically the required cis-3, 4-disubstituted piperidine, rather than a mixture of the cis and the trans. The nitrogen is position one; in the three-position is the vinyl group and in the four-position there is an acetic acid residue. That substance was called meroquinene. My synthesis was designed, and eventually demonstrated, to give only this cis system. But in fact, I did not succeed in getting a vinyl group where an ethyl group is in the simple dihydroquanine, which was the Rabe intermediate. Achieving the correct stereochemistry was part of my Ph.D. thesis in 1945 (11).

I was extremely impressed by *The New York Times* reports because I had no reason to doubt the validity of the quinine synthesis. I remember I called Woodward up, because the reported synthesis was only in the newspapers, not yet in the professional journals. I wanted to know how he made it, so I called him up. I still remember it. (These are the things that stick in your mind.) At that historical moment, what were Woodward's first words on the telephone? His first words were, "Do you have a pencil?" [laughter] I still remember that. So then we started talking about the synthesis and in fact I'm still pretty impressed that I got all this information correctly on the phone. I was especially interested because I was supposed to give a

departmental seminar a couple of weeks later. This was really a hot, fresh topic, so I was able to do that.

The operational awareness of three-dimensionality in synthesis started around that time. Various things converged. Usually things get to a stage where the stage is set for something to happen and so it happens. (Quantum mechanics may have been an exception; I'm not sure. I guess relativity probably was.) So there were various people who became conscious of that problem at the time. One of them was unquestionably Bill [William S.] Johnson, who had become a young assistant professor, just before I got to Wisconsin. Although I did not work for Johnson, we interacted (and still do) to a considerable extent. He was conscious of stereochemistry. In fact, his early effort at Wisconsin was to find a way of solving the problem of making the trans-C/D system of steroids. They are trans fused rings, the so-called hydrindane system, with a so-called angular methyl group, which is placed so as to make a trans rather than a cis system. The question is, how do you achieve that? First of all you have to solve the regiochemistry problem. How do you stick the methyl in the angle? Johnson was very much concerned with that. And after you've found a way of sticking the methyl in the angle, how could you conceivably control getting it so as to give a trans rather than a cis ring junction? Consciousness of three-dimensional problems started around that time. Which is also more or less the time when we had our big fiasco with the Fisher models.

That sort of problem has been central in my own research. The major thing that I have been concerned with in my scientific career has been control. One is position control. I was extremely antagonistic to the term "regiospecificity" when Barry Trost proposed it. I was not against "stereo" specificity, but for regiospecificity, I thought, "What's wrong with site specificity? Why regio?" That's because you can make it one word while the other is two words. I think both terms have by now established themselves as very useful concepts. My own interest has been the control of regiospecificity and of stereospecificity. That concern is central to practically everything that we've done.

I actually had no idea where to go after I got my degree at Wisconsin. My background was that a job was what you needed to do in order to be able to buy some food and pay the rent. But, otherwise, you did what you wanted to do. At Florida, I did that on the side because I was allowed to. At Wisconsin, McElvain was a great man. He was both a very tough leader and very tolerant, both tolerant and intolerant. He let me do various things, up to a point, to the point where I passed the limit. I guess he became very upset when he found out that although I had claimed I was trying to synthesize quinine, on the floor above him, I was, in fact, trying to make biotin. And you could tell; you couldn't hide biotin with the sulfur in it. [laughter] He found that suspicious in the once-a-year visit that he made to the floor above his floor, where I was. It smelled of sulfur, not of ammonia, not of base. So then he found out what I was up to.

I also did not know you were supposed to put your professor's name on your papers. It shows how tolerant McElvain was. Most people would have been very upset. He flipped slightly, but not too much, when he picked up a *JACS* and saw there was this communication,

my first paper (12). That first paper also has the distinction of having only one melting point mentioned there; it's wrong. It actually had to do with furan chemistry, because I intended to transform the furan ring to the thiophene ring of biotin at the end. It could still be worthwhile. Maybe I should make biotin that way before I retire. [laughter] The idea was to build a furan system because it's much easier to handle oxygen. That is, it is much easier to do chemistry with furan than with thiophene, in particular, when you have to reduce the rings. Sulfur is a catalyst poison, so it's very hard to hydrogenate the ring. My idea was really a good idea. It turns out that biotin has all three substituents on the same side of the ring plane, all cis to each other. If only you could build the thiophene analog of biotin and then hydrogenate it, automatically the substituents would all end up cis and that would be the solution to that problem. But you it's hard to do, because sulfur is a catalyst poison. So the idea was, let's build a furan system, reduce it so the stereochemistry will be right, and then change the oxygen into sulfur. That could be done with two inversions and so, you would end up with the dull cis stereochemistry again. That was actually pretty good. It was never tested because McElvain said, "You cut this fooling around out," and he moved me next to his office. [laughter] Then I started working more seriously on trying to make the piperidine derivative, which one would presumably require for quinine.

But I had in fact no great thought at that time about how to do it better than Rabe had done, from that point on. It would be better than what Woodward eventually did, namely, to make both the cis and the trans and separate them. Nevertheless, that would leave these subsequent problems. Milan Uskokovic, several years later, at Hoffmann-La Roche, was the first one to make a major dent into these subsequent problems on the route to quinine.

BOHNING: In that first paper, at the very end of it, you said, "Work in this Communication had to be discontinued almost two years ago." What did that refer to?

STORK: Well, that was McElvain saying, "You cut that out."

BOHNING: So that was it. I was struck by that comment. That's the last statement in the paper.

STORK: That paper also is unusual in the sense that only my name was on it as author. My feeling was that I was independent so far as I knew. Nobody was paying me. I was working on my stuff. I had a job analyzing fertilizer in the state experimental station. So I was not conscious that there was a problem there.

BOHNING: That's how you first supported yourself, wasn't it, doing those fertilizer analyses?

STORK: That was kind of fun. You'd spend a certain number of hours and it was flexible. But I was interrupted by McElvain, for very good reasons.

But as I said, that melting point was a misprint; I think the two last digits are inverted. I forget what it says; does it say 113 degrees or 131 degrees or whatever for the melting point? It's the melting point of the diazide. [reading] "Melting point 166-167 degrees." Yes, I think it's 176 degrees. I forget exactly what it is, but it's one of those digits that's wrong. I was shocked. I was shaken, because my melting point's wrong, and now it's published in the literature. So I wrote to *Chemical Abstracts* and said that when they abstract this thing, they must put down the corrected melting point in the abstract. My abstract is the only abstract, so far as I know which has a note that says, "Private communication from the author" (13). [laughter] It does say that, actually; it's a private communication. *Chem. Abstracts* no longer does it. There are no more private communications to *Chem. Abstracts*.

BOHNING: Carl Djerassi has said that he learned more chemistry from you than from anyone else at Wisconsin (6).

STORK: That's probably true. That's probably true, because as I said, we had lunch together every day. Besides, even if it was for only two weeks, he was sort of my graduate student. [laughter]

BOHNING: He also said, "[Stork] worked on four different projects without his supervisor knowing it, and he conned me into working with him on the morphine approach on the side" (6). [laughter]

STORK: Oh, he said that? Well, that's pretty good. Yes, that's true. At that time he was in the hospital; when I "conned" him he was weakened. [laughter] That's true. He was in the hospital. I don't remember what was wrong with him, but it was nothing terribly serious. He was in the hospital, so I went to visit him and used the opportunity to convince him he should work for me.

There is a connection between that and this sudden interest in this Indian work that claimed to have synthesized santonin (5). The reaction we wanted to use as part of one construction of the ring of morphine was in fact one that these people claimed to have used. One major clue was this stereochemical thing. It was a paper construction, but it was an intelligent paper construction. That is, it was an interesting scheme. It involved a reaction which was unknown at the time, but which was conceivable, and which I thought was a great way to put morphine together. As it happened, we never tested it with morphine because that

project was also interrupted by the furan stuff. But it turned out that Djerassi's Ph.D. thesis with Wilds was to study this reaction as a possible way of making steroid rings (14). And it can, in fact, be done; Djerassi was the first one to bring it to practice this reaction, which supposedly had been done by this Indian worker who never went to a lab. Actually, Wilds and Djerassi found a way of making it work, but we never, in fact, applied it to make morphine.

So at that time, people like Johnson were becoming conscious of the three-dimensional problem as more than a passing thought; they were actually trying to do something about it. I was trying to do something about it. Cornforth was later, in his published stuff, but if Birch said to me that Cornforth was thinking about this really seriously then, I wouldn't be surprised.

FINE: What about [Robert C.] Elderfield?

STORK: No idea. No clue. Elderfield was a pioneer in chemistry, but his field was not synthesis; it was structure. His big contributions were damaged because he did not get the correct structure of the sapogenins. The sapogenins are steroids, which have a cholesterol side chain at the top, which is connected by oxygen atoms to some other part of the molecule. It turns out that we know today that the two oxygens are connected to the same carbon atom; it's a so-called spiroketal. Elderfield thought it was a diether, with the two oxygens on adjacent carbon atoms.

But he was a pioneer, and Elderfield did have one major contribution. Well, he made major contributions to the structure of the sapogenins. But Elderfield worked with [Walter A.] Jacobs, who was a professor at Rockefeller Institute. They did the major early work on the structure of digitoxin and digitoxigenin. (The drugs that they used on [George] Bush recently.) These compounds are what we call cardiac glycosides, because there's a steroid attached to some sugar. Elderfield did make major contributions, even though he was wrong on the structure of their side chain, to the structure of sapogenins such as diosgenin.

This diosgenin became the Mexican source of steroids for cortisone and progesterone construction. The interesting story of that is that the person who correctly got the structure for the sapogenin was Russell Marker (15). So far as I know he's still alive, although obviously ancient. Marker's reputation was so bad at the time that [Louis F.] Fieser completely endorsed the Elderfield structure, which was incorrect, simply because Marker was obviously a rogue, and therefore what a rogue does is clearly bad. There's a logical gap there, but it's a common mistake. That is, this guy is a bum, so what he says is probably not right, but in this case it was very much right.

But Elderfield did make extraordinarily important contributions. First of all, he was one of the early people to do serious structural work in this country. That's not something that has perpetuated itself, unfortunately, in the U.S. It's unfortunate that people don't do much

structural work. I mean, the major people were brought up abroad. The two major lights in this country are [Koji] Nakanishi, who's here, and who obviously was brought up in Japan. You couldn't possibly start this work here; you would never get tenure. And Ian [Alastair] Scott, at Texas A&M, who is from England. You can't start this type of work here simply because of the enormous amount of effort and work required. You really have two years to make an impact here. The system is based on marketing. I mean, it is based on marketing in part, and obviously on accomplishment as well. But it's not enough to devise a better soft drink; you've got to beat Coca-Cola. So there are two aspects to it. But Elderfield was one of the people that was doing serious structural work. He has unfortunately died.

Roger Adams also did some serious structural work. One of my first pleasures in organic chemistry was at Wisconsin when I gave a seminar on Roger Adams's structural work on some bicyclic alkaloids, at the moment I forget their names, (I think one of them was retrnecine). I concluded that the suggested structure was clearly incorrect. I felt it was a great accomplishment because at that time a graduate student did not do that kind of thing. It is not to say there was any kind of showmanship. It was just the inescapable conclusion; this thing was just obviously wrong, that's all. I still remember the palpable shock of the front row with Homer Adkins and Bill Johnson because first of all, it was unusual for a graduate student to question his elders. Second, Roger Adams was Roger Adams. Incidentally, it turned out eventually that, he was, in fact, quite wrong. So that was nice.

Elderfield's other great contribution is that simultaneously there were three major people in his research group here, who are probably the three best known alumni of that from Columbia. All three were graduate students at the same time. One was Nelson [J.] Leonard. Another was Josef Fried, Gus Fried, who eventually developed the fluorosteroids when he was at Squibb; he was director of research at Squibb. He was here the same time as Nelson Leonard; they're still very good friends. And the third one is Elkan Blout, who became director of research at Polaroid. His history is quite remarkable. He eventually became head of the biochemistry department at the Harvard Medical School. That's quite a thing, going from the director of research of a photographic company.

BOHNING: What about Louis Fieser? How did he fit into this picture?

STORK: Louis Fieser was both a major strength and a major catastrophe in American chemistry. (I assume these things can be edited.) [laughter] Fieser was a nasty man in contrast to Woodward. In contrast to Woodward, Fieser was absolutely unable to separate his emotional feeling about somebody from his intellectual, rational feeling. This is the reason he got into trouble with the sapogenin structure. If he did not like somebody, the guy was just a total loss, regardless of what he did. Woodward was able to dissociate the two. He was quite capable of viciousness, but it was a highly intellectual, structured viciousness. It was not emotional. When he was rude, he knew he was rude and was rude for a purpose. Fieser was just different.

At one time when I was at Harvard we wanted to invite [David Y.] Curtin for a colloquium there. Fieser would absolutely not allow it. He would not tolerate it; we could not invite Curtin to give a talk. What he had against Curtin is that he spent a fair amount of his time on an individual, independent postdoctoral fellowship, a National Research Council Fellowship which allowed one to do some work on his own. Today, of course, we make slaves of them as soon as we can. [laughter] Curtin annoyed Fieser because he felt he was spending too much time with [John D.] Jack Roberts, trying to learn some physical organic chemistry, rather than making some more naphthoquinones that might be good antimalarials. Fieser was that way.

Once it turned out that we had made a compound that he wanted. It was simple, but had never been made before. It was 6-hydroxycholesterol. He wanted to know whether he could have some, and I gave it to him. It turned out it was not as pure as it should be; it was crystallized, but it was not as pure as if we had crystallized it more carefully to get the melting point higher. Fieser was an outstanding experimentalist, no question about that. It was just a bitter experience for me. Fieser complained about my compound in a department meeting. I gave him this stuff as a gift, you know. I didn't say it was pure, and we hadn't published anything. It was just a research chemical that we were fiddling with. But he was capable of being extremely nasty, extremely nasty.

But, he had some good features. He was a great lecturer, clearly. Many people became fascinated with chemistry because Fieser wrote [Vladimir W.] Markownikoff's name on the board in Russian letters. He had a certain showmanship, which was in fact very suited to his teaching. He also wrote well. Mary Fieser forced him to write well, and he did that. He was nice to her. She still is alive and, personally, I find her extremely interesting. But he was very different. He liked cats, which is a positive sign, I guess; I don't like cats. But that's nothing against cats, because I don't like things that move, whatever they may be, cats, dogs, whatever. So he was obviously capable of empathy, if he wanted to. [laughter]

But fundamentally, he was a person you didn't want to cross. As an extreme case, I'm sure you've heard the story of Don [Donald J.] Cram's thesis. You must have done an oral history on Don Cram. Don Cram may be too much of a gentleman to go into this, but I still remember at Harvard, when I was an instructor, and Don Cram was a graduate student. Don Cram came in late because he had been at Merck for a few years after he got his bachelor's degree, or master's degree, or something, and then returned to doing a graduate degree five or six years later than other people. So he was older than they were, but he was a graduate student. Fieser absolutely could not tolerate the fact that Cram talked to Woodward more than Fieser thought would be reasonable, because after all, Cram was working for Fieser, and there was tension between Fieser and Woodward. Actually, Woodward did his best to exacerbate the situation by missing no opportunity to tell everybody how stupid Fieser was, including the graduate students working for Fieser. [laughter] So that contributed to the tension in a not inconsiderable extent.

Cram made a bunch of naphthoquinones. In fact, he made like forty naphthoquinones or so. In those days, you did C and H analyses. This is an art that Professor Fine is trying to reinstitute at Columbia, by getting an instrument that can do this. [laughter] The normal way of getting the analyses done then was to send them out, normally to MIT; it was a perfectly good analytical laboratory, under the direction of somebody by the name of [Stephen M.] Nagy, however you pronounce it. He ran the place, and you sent the compounds there. Your sponsor had to pay, that was the tradition. You had to pay maybe five dollars per analysis. It was quite a bit, actually. It was some number like three or five dollars, which would be like twenty-five dollars today, for the C and H. By the time the Cs and Hs had to be done on the compounds for Cram's thesis. Fieser just simply refused to pay for the analyses, even though the compounds were quite pure because Cram was a good experimentalist. He said, "I'll sponsor your thesis, that's fine with me, but..." I mean, he didn't want to pay.

The normal reaction to that would be one of despondency. Cram's response was to go to the stockroom, check out a pipe, a Bunsen burner and I don't know what, some drying tubes, what have you. Within a day, he had assembled a macro set-up. He had grams of these compounds, so he took three hundred milligrams each of these compounds, burned it in a sea of oxygen, weighed the soda lime tube, etc. He did the whole damn forty analyses over the weekend. And you say, "Well, what has that got to do with anything?" Well, that was really pretty impressive. So Cram did that and he presented his thesis. I'm not sure, in those days, that there was any public defense at all. You turned in your thesis and the committee accepted it or not. There may not even have been a final exam or anything. I think you just turned it in and it was approved or not. So Cram turned in his thesis, and eventually sent a copy of it to Fieser.

[END OF TAPE, SIDE 4]

STORK: On the acknowledgement page it said, "To Professor Fieser." Fieser called it outrageous, ripped it up and mailed it back to him. That was Fieser. And it lasted <u>years</u>. Cram was invited to give talks at Harvard in subsequent years, because of pressure by the rest of the department. Fieser would never go to them. Eventually the ice started breaking slowly when Mary Fieser, who had originally not attended them either, out of loyalty, began to go to Cram's talks. By that time Cram was at UCLA. But once in a while he would be East, and so he would give some kind of talk. I think eventually Fieser may have gone to one of them, towards the end.

But Fieser was that kind of a person—petty. On the other hand, he was a brilliant experimentalist. At Columbia there was an instructor who got himself drafted at one point, or whatever the occasion was (I now forget). A temporary replacement person was found. His name was Ed [Edward N.] Trachtenberg who eventually became a professor at Clark University in Worcester. Trachtenberg was in charge of the organic laboratory, among other things, and they were using Fieser's manual. Fieser loved cheap gadgets that you could make into useful

things, like a cleaned-up tuna fish can as a possible water bath, or steel wool to make packing for distillation columns, which is actually not such a bad idea. This was before stainless-steel steel wool, so it had its limitations. The manual recommended that you distill the compound through a distillation column "with a side arm, tightly packed with steel wool." That is the sentence that was there, in spite of Mary Fieser; that's what it said, without the comma. So, one of the sights, which was pretty impressive, was this poor guy packing the side arm tightly with steel wool, which is what it said to do. [laughter] He was trying to push the thing through, without great success.

A more serious problem in the book was with a synthesis of isatin. The whole class was doing this. There were three steps; a goes to b goes to c, and eventually you get some nice crystalline stuff. Out of a class of forty-five people, only two people got these beautiful crystals. Eventually, under careful questioning by Trachtenberg, they admitted buying the stuff downtown. [laughter] For the rest of them, it didn't work. I mean, it just did not work. So we called up Fieser and said, "This thing doesn't work. You don't get any crystals." He said, "Give me a few hours to check this." By God, three hours later he called back. He had run through the whole thing. A good experimentalist is not necessarily a good person to describe what he has actually done because he does these things kind of intuitively, right? You write down the recipe for the apple pie later. At one point Fieser had added a little nitrobenzene. The recipe said, "1 cc." The way he really did it was to add the nitrobenzene until the solution became opalescent, slightly turbid. At that point he felt it looked like a cc. So he wrote down "add one milliliter of nitrobenzene." It turned out that if you add any more than .5 cc at that point, you don't get any crystals. But he had found this out within three hours, had redone the whole thing and this time actually measured what he put in there. As I said, he was a very good experimentalist.

But he had no feeling for stereochemistry, either. In Switzerland, [Albert] Eschenmoser was probably the first one to have that as a serious concern. Some of the older people, like [Leopold] Ruzicka, became interested, but it was still just something that was looming on the horizon. He was interested, but his work was not really related to that. Eschenmoser, and of course eventually [Duilio] Arigoni, became very much concerned.

BOHNING: What about [Tadeus] Reichstein?

STORK: Reichstein was not really terribly concerned. Reichstein was concerned with intercorrelation of things and did, of course, find the structure of all these important compounds in the adrenals. It was magnificent, magnificent experimental work, which was, as you probably know, done with a great experimentalist, [J.] von Euw. Von Euw was a person who never had a degree, but was able to crystallize anything and worked with Reichstein his entire career. Reichstein himself was very good, extremely good, as an experimentalist, but he was not particularly concerned with three-dimensionality. Eschenmoser was. Eschenmoser was and, in

fact, contributed to the solution of stereochemical problems, even at a fairly early stage. Eschenmoser and I are still on friendly terms; we have antagonized each other, but we are on fundamentally fairly friendly terms. I was the first person to ever invite him to the United States, when I recognized, when he was quite young that he was really very good. I invited him to a Gordon Conference, which I was chairing at the time. That was the first time that anybody outside Switzerland paid any attention to Eschenmoser.

BOHNING: So you and Johnson were really kindred spirits at Wisconsin, then.

STORK: My interest in chemistry was much more closely related to that of Johnson. We knew that and we would talk once in a while; not as much as Johnson talked to Wilds, but we were kindred spirits, yes. Eventually after I had left with my Ph.D., Johnson is the person that I would come and visit in Madison.

My first post Ph.D. job was in Milwaukee for a year. I could not be employed by anyone because I was illegally in the United States. Not really illegally, but it was not legal for me to work because I had only a visitor's visa. When I came to the U.S. with my parents, I came as a visitor, as a tourist, and obviously I couldn't work. Now today, you couldn't get away with this. Well yes, you could be totally illegal today; you could get away with it, but you wouldn't be employed by any kind of serious corporation. That was sort of true then but, not as completely true. This particular place in Milwaukee, Lakeside Laboratories, was run by the so-called director of research, which was a euphemism in this case. He was a former Ph.D. student of McElvain. McElvain conned him into giving me a job even though I could not really, legally have a job. I actually checked with the Immigration people whether I could get away with it, and they were very, very nice. They said, "We cannot give you an answer that it's okay," which I interpreted to mean that it was okay. [laughter] It certainly didn't bother me. Eventually I got it resolved. It was not easy to straighten this thing out, because of course there were war conditions, and so various papers and documents that I needed were difficult to obtain. During the time that I was there, I would come back to Wisconsin once in a while, and I would see Johnson and talk about whatever I was doing.

At that time my main interest, other than the medical chemistry for Lakeside, was to try to synthesize estrone, which I would work on after hours, at night. The one piece of equipment they had was a high-pressure hydrogenator. So the question was, how could you use this to make estrone? It's quite crazy. I was senior research chemist at Lakeside Laboratories, a title that has to be read in the context, which I may as well explain to you. That is, I was the <u>only</u> chemist. I was the only organic chemist there. There was also an analytical chemist and a lady who set up equipment and washed the glassware. My great contribution to pharmaceutical science, which came to nothing (none of these chemicals were ever tested and it probably would have been stupid to), was essentially to plagiarize every interesting benzene-ring thing, like ephedrine or whatever, by making the thiophene analog and see what it would do, whether it

behaved differently. I guess it's not totally ridiculous in the context of the time.

I remember one paper that had fascinated me at Wisconsin; it was a paper by an Englishman by the name of either Wood or Woods. I don't remember. It was in *Lancet*. Why I got to this paper, I can't imagine. It was the first postulate of the rational design of drugs. He had discovered why sulfa drugs worked, which was something I was interested in at the time because of penicillin. He equally became aware of penicillin; the next question, was, "Now, how do these things work?" I remember reading that paper in which he demonstrated, or maybe just postulated at the time, that sulfanilamide was antagonistic to p-aminobenzoic acid, which was an essential substance. I thought it was fantastic, fascinating. So penicillin, I thought, must work that way, too. At that time, the penicillin work was kept secret, so there was an awful lot that everybody who was involved in it knew, that I didn't know anything about. So I thought I had great thoughts, and of course they were about two or three years behind the times. I wrote my great ideas up and dashed off a paper to *Science*; it became my first rejected paper. [laughter] I dashed this paper to *Science* about the mechanism of action of penicillin. I was fascinated by the fact, which I didn't understand, really—that penicillin is made up of amino acid like structures, which was a D-amino acid, not an L-amino acid. My idea was that penicillin could be a mimic of an important tripeptide, which at that time I thought was glutathione, and that penicillin, which had also a sulfur amino acid in it, was an antagonist to glutathione by virtue of the fact that one of the amino acids was the mirror image of what it normally would be. So I sent this great thought, which in fact was wrong, to *Science*, which promptly pointed out that thoughts of that type had been coming for quite some time. It was naïve.

A year later I was at Lakeside, and trying to make thiophene analogs to keep the research director off my back, and he was quite tolerant. I was trying to make estrone, and then Johnson suggested that I apply for an independent postdoctoral fellowship that had opened up at Harvard. I don't know who funded it. So I wrote up the estrone approach that I was working on. It is still great. Actually, considering the time, I think that it was absolutely great. I don't think I've actually cooked up anything better than that since then. It really was not easy. It had a least two new reactions in it. They were not known, but I presumed that they would be possible. They're both known now. They were to give complete control of the stereochemistry of all four centers of estrone. This schedule was never really attempted in the laboratory, and today it would be pointless to do, but it was really quite nice.

I sent my estrone scheme in with my postdoc application, and Woodward saw it, and Woodward talked [Paul] Bartlett, who was at that time chairman of the department, into offering me an instructorship instead. I was pretty young. At Lakeside the entire research laboratory was half this room, and the rest of it was extracting urine from pregnant mares to get some hormone preparation out of that. There was one phone in this place, against the wall; the phone rang and it was Paul Bartlett, who said, "We have your application. Would you consider an instructorship?" I said, "Sure." [laughter] So that afternoon, I wrote a nice letter of resignation from the Lakeside Laboratories. It was run by a very nice man by the name of [Evan P.]

Helfaer, who became of some importance in chemistry because he eventually set up the Helfaer Chair at Wisconsin, which [Barry] Trost eventually occupied. (Trost was the Helfaer professor at Wisconsin before he went off to Stanford.) I never was particularly concerned whether I would go to industry or academe. I never thought about it! I could do work; all I needed was a lab and equipment and I would do my stuff. Completely preposterous. It was a completely romantic, preposterous view of mine.

BOHNING: You published those two papers on the tetralones though, while you were at Lakeside (16).

STORK: Yes that's right. There was a hydrogenation machine there, so you could do those things. The tetralone was a starting material that I was going to use on my estrone synthesis, so that was the connection with that.

BOHNING: But those papers actually had some far-reaching effects. You did the acid-base work to show the potential selectivity of the catalyst.

STORK: I don't know about far-reaching.

BOHNING: Well, nobody had done that at the time.

STORK: No. Nobody had done that. They're not far-reaching, but it was an important, narrow thing. It's important because all the aromatic steroids are made starting with 6-methoxy-α-tetralone, which is made by my process. Which unfortunately, if you know anything about patenting, you know that I didn't. [laughter] So the first step is in fact the hydrogenation and yes, it was actually quite interesting. What I suggested as the reason for that, and I'm still not certain that it's not right, is this: You have two aromatic rings in β-naphthol. One ring reduces before the other. That's not surprising; it's easy to reduce one ring in naphthalene and after that it becomes a benzene. It stops after one ring. The thing that's surprising is that if you do it on a basic pH, the ring with the OH gets reduced. I'm talking about Raney nickel reduction, high-pressure hydrogenation with nickel. The hydroxyl ring gets reduced. If you do it in a neutral or slightly acidic pH, it's the other ring that gets reduced, which is the basis for the tetralone business because you want the phenolic ring to remain. The suggestion was that the reason for reducing the naphthalene in the non-substituted ring was that you produced that compound in a non-perturbed condition. You had to view that base perturbed it because now you reduced the phenolate ion rather than the phenol. But any substituted naphthalene, whether it was electron-donating or not, whether it was 2-carboxynaphthalene or 2-methylnaphthalene or 2-

hydroxynaphthalene, you would always reduce the unsubstituted ring because that resulted in the smallest loss of resonance energy. That is, it's final product was in fact stabilized by these substituents, whatever they may be, because of the interactions of the substituents. Today if you tried to validate this, you would say, "Well, that's not that completely crazy because hydrogenation and dehydrogenation are obviously related and so that it could be an equilibrium ending with the more stable of the possible tetrahydro compounds. It's not that surprising." But that was in fact an interesting thought, and in base the idea was that the O-ring was now more strongly absorbed on the catalytic centers because it was an electron donor.

We still don't understand catalytic hydrogenation, so I can get away with that kind of stuff. It's a very difficult thing to which I have made no contribution, but it was interesting. That was the origin of the easy access to methoxytetralone. But it was not any kind of intellectual conception because although one can hang onto that little bit of a suggestion, it was not developed and did not really have any impact that I know about. *Per se*, it was an important little thing I did there.

The other one that I did was patented and was actually used by people (17). The beta-tetralone was different; it was the high-pressure reduction on palladium, which actually had not been tried at that time. We actually reduced the hydroxyl ring to the dihydro stage, because in the dihydro stage the thing would become a ketone, β-tetralone in this case. The palladium was known not to be a very good catalyst to reduce ketones. So there was a chance that you could take this aromatic thing and reduce it to ketones, which in fact turned out to be right, probably for totally different reasons. But it turned out to be right, and is actually a Lakeside patent. As my contribution to show that I was actually doing something, I worked up that patent. I have never had my name on any patent, which ever made any money at all, except one, which is the Syntex patent (18). It didn't make any money for me, though, and probably didn't make much money for Syntex, either.

FINE: Did you have much to do with [Homer] Adkins? You did all this work on hydrogenation.

STORK: I had very little to do with Adkins because Adkins at that time was involved in secret, war-connected work which he was not allowed to discuss. The theses of his people were sealed; there were very special arrangements with the university to make it tolerable to get a Ph.D. under such conditions. I knew Adkins was involved in hydrogenation. I got recipes from the Adkins group on how one makes Raney nickel, which he had many recipes for. Adkins would come to seminars and make statements, so he was highly respected, but I never interacted with Adkins.

BOHNING: There's a story about how you didn't last as a T.A. at Wisconsin.

STORK: All of it is true.

BOHNING: It's all true. [laughter] Hoffman talks about that (2).

STORK: There was a preposterous guy who was running it. I was teaching a section of the Army Special Training Program, ASTP or something like that. I was supposed to teach them chemistry. I claim I invented the "flash card" system of learning nonsensical stuff, which was already known for language learning. So I didn't invent the whole system, but the idea of perverting chemistry by using this kind of disreputable technique was probably mine, and this is in part why I got fired. It was the last straw, when my section, which was stupid—they were stupid—got the highest grade on the next exam that they took. There were hundreds of people taking the exam, so it was statistically significant. All of a sudden, my group of benighted people got the highest grade on the exam. [laughter] The rational hypothesis was that I gave the answers to the questions ahead of time. This was, of course, not true. [laughter] What I had done was to make a whole stack of cards, which would say "zinc plus sulfuric acid" on one side and "H_2 plus zinc sulfate" on the other and so on, for everything that is conceivable that you could learn in that particular period. Then I went to the army barracks or the dormitories, or whatever they were. They all sat in a large circle and copied this whole stack, each one. Then I told them how to use it. You put a whole stack in one pocket. Then you don't even try to learn anything. But when you wait in line for the cafeteria, you take one card. If you know the answer you put it in the right pocket, if you don't know, you put it in the left pocket. And you keep doing this, that's all. They creamed this exam, did absolutely fantastic, and I got fired. [laughter]

But I must say, it was only the last straw. The thing that was really annoying to them was that they thought I let everyone escape through the window from the lab section. The program manager would send in someone to bar the door because he thought that since this is an army group, one should enforce army discipline. We didn't have anything to do with the army, but he thought we should definitely enforce army discipline. The bell rang at ten minutes to twelve. Some people had finished the experiment at 11:40. I could see no special reason why they should wait around on the floor for the bell, because then they had to wait an hour in line for the cafeteria. They wanted to get in early to the cafeteria, and it sounded reasonable to me. This guy in charge was not an army person either, he was just in charge of this general chemistry course. He would send an assistant to bar the door. So they had to sit on their bags for twenty or twenty-five minutes. It looked like Napoleon's retreat from Russia. [laughter] We were on the first floor lab. So one day, somebody had the bright idea that they could get out through the window. I thought it was hilarious; that's true. I thought it was hilarious. It is not true, which they thought, that a) I had engineered it, and b) that I had refused to tell them the names of the people that I knew who went out the window. The truth is I didn't refuse. I did not give them

the names, but that's only part of it. I like to think that I would have refused anyway, but the fact is there is no evidence one way or the other, because I don't remember names. Particularly, I didn't know the names of these people. I just didn't know them. But this was definitely viewed as a rebellion of the first magnitude. So by the time they'd got the best grade on the exam, that was that.

FINE: How is it that in the Wisconsin tome that was just published (19) the history of the chemistry department has almost nothing about Johnson and there's nothing about Stork.

STORK: Because the author was quite old. I forget his name, but he taught a course in the history of chemistry. I met him once. He was familiar with a much earlier era, which is what he wrote about, although not very well.

FINE: Was that Aaron Ihde?

STORK: Yes. Well, he had no feeling for it, because it's not his area. I think he said a kind word about Johnson.

FINE: Djerassi is almost totally ignored.

STORK: We did not interact with Ihde. I suppose as far as he was concerned, he was old enough at the time and we were young kids getting a Ph.D.

FINE: Just as an aside, was there anybody else at Florida, besides you as an undergraduate in chemistry?

STORK: At the same time that I was there, there was some guy who became a stock analyst for some company here. I forget his name. I saw him later, after I was here, because he wanted to know what I thought of Syntex.

FINE: Did you tell him to buy it? [laughter]

STORK: No, I think I probably told him I couldn't say; he'd probably hold it against me.

[laughter] There was some guy who became a chemical engineer. There was no one else that I remember. But I didn't interact with people very much, so there could have been some pretty good people. I doubt it. It was not a great school. There were some bright people there. One guy they can boast about is a Nobel Prize winner. Marshall Nirenberg got a master's degree there.

FINE: He's at NIH.

STORK: Is he at NIH?

FINE: Well, he was.

STORK: He got a Nobel Prize for the important work having to do with the genetic code, and maybe related to what [H. Gobind] Khorana got the Nobel Prize for. We didn't overlap; I didn't know Nirenberg. He was probably there shortly after I was there. But there were not too many people. They were mostly people who would go into agricultural things or engineering. They had a good electrical engineering department—at least it was reputed to be a good electrical engineering department.

[END OF TAPE, SIDE 5]

BOHNING: You said you had gotten a phone call from Paul Bartlett saying, "Do you want to come to Harvard as an instructor?"

STORK: I did that. [laughter] That turned out to be obviously very interesting because Woodward was blossoming at that point. In particular, he had a very rational approach to chemistry. This does not sound like a great accomplishment, but at that time, most organic chemists were a highly intuitive group; that is still true. But he was the first influential one to have had the article of faith that this somewhat amorphous intuitive feel was amicable to rational processes. It sounds trivial, but it was, in fact, a departure.

It turned out to be quite nice because McElvain, believe it or not, was one of the first people in this country to become interested in what was then called the—what was it called?—it had to with the Robinson curved arrows. Robinson did contribute a major thing here, whatever else he did or didn't do. It was this electronic theory of the English school, as it used to be called, right. The electronic theory of the English school consisted of at least the belief, the

underpinning belief, that there is some sort of rational thing underneath. Even though Robinson himself, and again this is an outrageous statement, never understood how to use his creation; he just was unable to do it. People like Woodward did. Woodward dealt with the Robinson conceptual framework much more effectively than Robinson ever did. One of the first ones to introduce this in the context of courses was McElvain, who actually was really quite fascinated by this thing. He was not really as adept at using it in a complex situation as Woodward was eventually. But he was fascinated by the underpinnings of it, which he would tell people about.

It was also an interesting time because it was the end of the war, and a large number of people of various age groups came back to Harvard, or came to Harvard, which gave it a large diversity of people. There was much more of an age spread than usual because some of them had been in the service. Harry Wasserman, for instance, was my age and I was an instructor and he was a beginning graduate student. A lot of these people were really exceedingly good people, at a time when it became obvious that organic chemistry had a future.

This included people like [Jerrold] Meinwald and [Franz] Sondheimer. [Eugene] van Tamelen was one of my own students. They had lots of very good people there. I mentioned Cram before. There were just a lot of people.

Huang Minlon was a postdoc. Do you know the Huang Minlon reduction? His name was really Minlon Huang, but everybody's called Huang in China, so he inverted it. Huang Minlon was a postdoc of Fieser's. Mary Fieser used to delight in coming sneaking behind him when he was working away in the lab, Huang Minlon, and shouting something in what she considered to be Chinese and startling the hell out of him. [laughter] There were large numbers of these talented people.

BOHNING: Elkan Blout was there. Was he doing his postdoc when you got there?

STORK: He was before my time.

BOHNING: Oh. He had left when you got there.

STORK: I knew Blout because we were very socially friendly with Woodward, so we used to get together—Blout, Woodward and us quite often. Blout still is a friend. He's still active. He's still treasurer of the National Academy.

BOHNING: Were you involved in the poker games?

STORK: No. The only time I remember a poker game is when we decided, and I can't imagine why, to take a train to a conference in Canada one time. It was on an island called Grand Manan Island. I have a photograph of this thing. The only one who still looks today like he did then is Nelson Leonard, which is really quite amazing. Nelson Leonard is perpetually good-looking, young, dark hair; it's just remarkable. And there was John Sheehan, Bob Woodward, Nelson Leonard and I, on that train to go to the wilderness of Canada from Boston; it takes forever. They decided to play poker, and decided that since there was me there, it was an easy mark. The three of them were obviously old hands at this, so it cost me a lot of money. [laughter] That's the only time I played poker for any kind of money. Sheehan and Woodward would play poker. Woodward liked poker, and these other people are pretty good. Sheehan was probably the most adept. [laughter] Woodward had no interest in sports. Poker was about the only thing; I guess you would say it combined things that he liked. It was partially rational, partially theatrical. He was pretty good.

There was nothing terribly eventful there, except that I had some extremely good students, obviously. I didn't really realize I had, because that was the first academic environment I knew. While I was at Wisconsin I really had nothing to do with the people, except for Djerassi. My assumption was that this is a normal group of people, but it turned out to be pretty exceptional.

BOHNING: One of the things I noticed is that up until this point your organic work was really classical in the sense that it was melting points, boiling points, refractive index, and carbon-hydrogen analysis. But starting with the Harvard period, in the first paper you had Elkan Blout doing your UV spectra over at Polaroid (20).

STORK: I did?

BOHNING: You put that in as an acknowledgment.

STORK: Really? That I don't know about; that's interesting.

BOHNING: It's in the paper on sex hormones, which was the first one from the Harvard period that I have. And in it you acknowledge Elkan Blout's assistance.

STORK: For UV? [laughter]

BOHNING: For doing the UV at Polaroid for you, because he was into that very heavily at the beginning.

STORK: Oh, yes.

BOHNING: Then IR spectra started showing up in your work. There was quite a difference in how you were identifying compounds.

STORK: That's normal. I would presume that 99.9 percent of people went through the same thing because that became it. At Columbia, the person who first mentioned NMR here was Louis Hammett. Louis Hammett once called me into his office and said, "I think we should do something about this new technique, NMR." The truth is I knew precisely not what he was talking about. [laughter] So very early he was sensitive to it. Woodward was sensitive to infrared. He was obviously quite interested. Woodward's interest in instrumentation came from the penicillin work during the war, where he was the first one to give a logical argument for the β-lactam structure. That was heavily based on work at Shell on the infrared spectra of a whole bunch of compounds, which were β-lactams. And Woodward's belief, which was unusual and which was really faith, was that even though one could place some faith in these tools, so far as the organic chemists were concerned, they were really statistical.

I still remember at Harvard taking an infrared spectrum, when the machine first became available from an outfit called Baird Atomic, which still exists on Brattle Street. The contraption was about that high [more than four feet] from the floor and that big around [more than three inches wide]. It was a great machine. It was the only machine I know that could be flooded and you could repair it. One of my graduate students did that. Jerry [Alan Jere] Solo who is the chairman of the pharmacy department at Buffalo, and he actually took it apart and cleaned it. The prism was that big [five inches long], but it was mounted on stilts, so you could fill that machine and not dissolve the salt prism. That machine was the first one at Harvard. It was there late because I still remember having to go to Baird to take a spectrum with [A. W.] Burgstahler, and that was in 1951. So it began to be available.

I was always taking infrared when it became available, but I took them myself. [E.] Bright Wilson, the physical chemist whose son won the Nobel Prize, came in and said, "What are you doing?" I said, "Oh, look, a carbonyl group." Pfffttt. He looked at me as if I was completely insane. [laughter] He said, "How do you know it's a carbonyl group? All you know is there's a stretching frequency at this point. It could be carbonyl. It could be a peculiar double bond. It could be any number of things." "Oh, we already discovered this." [laughter] Of course, what we mean by that is that it increased the odds that it was a carbonyl group to ninety-

six percent from an unknown number. By the time you have seen quite a few of these things, there's a high probability of their being true. Of course, Wilson was also right. But Woodward had that faith, buttressed by the fact that he had seen all these other spectra. Penicillin was a difficult situation where practically everyone, including the famous Robinson, was totally antagonistic to that four membered structure lactam [of penicillin]. Woodward's faith, based on the fact that you have to take things like infrared seriously, was in fact correct. From there on you always paid enormous attention to infrared.

So the experimental chemistry changed. It changed for everyone, although, it probably changed faster at Harvard. It's probably true that if you compare the Fieser operation to the Woodward operation, there's no question that much greater emphasis was put on paying attention by Woodward to tools such as infrared at that time than what was happening in the Fieser operation. They would have paid some attention to UV, but that would be as far as they would go.

BOHNING: Isn't that about the same time that Woodward came out with those rules for α,β-unsaturated ketone.

STORK: No that was in his real youth.

BOHNING: Was that earlier? Yes, it was 1941 when he did that.

STORK: That's right. He must have been about twenty-two at the time of this operation, something like that. These rules are interesting psychologically. They're not particularly novel; even at that time there had been lots of British stuff which was essentially the same. But it showed that he really believed it. Also, there was a simplification in what he did. I mean, these advances are to a considerable extent the ability to simplify; not so much to find out something necessarily that's particularly new, but to cut out what's important from what's not important and go with it. That's an important ability that he had.

So that was my period at Harvard. Then eventually, of course, the question was whether they would throw me out of Harvard or not. That's unlikely to be in the Hoffman article (3).

BOHNING: I have a quote here from Fieser (21). It's in a letter he wrote which states, "His departure from Harvard, although anticipated and pre-scheduled, was a source of great regret to all of us."

STORK: Well that's certainly conceivable. Pre-scheduled was not totally correct. It was a complex thing. Harvard at that time was the only institution in the country, which could afford, and still to some extent can afford, the luxury of operating on a completely financially driven scheme. At that time the Harvard endowment was constructed in such a way that every seven years a new professorship would be created. If you didn't come into that operation, Harvard could make an exception. I suppose, if [Albert F.] Einstein had been there they might have. But they really didn't feel any great pressure to do that because these were the days that if Harvard wanted Lenny Fine to go there, they would just call up Lenny Fine and say, "We would like you to come," and you would be on the train. [laughter] They could afford that scheme. In more recent years they've found out that it's not always true, but now they're recovering it because they've also found out that if you pay enough you can do it. [laughter] Everybody has their price, which is not totally unreasonable. After all, why not? If you can do your work right.

So one component was that. It's also true that there could have been a groundswell in my favor. There was, I regret to say, none whatsoever. The only one who was favorable was, in fact, Woodward. But not enough to put his career on the line, although he was genuinely sorry that I left. But the fact is that Fieser, whatever this letter says, brought up my not quite correct melting point of the hydroxycholesterol that I had given him. [laughter] If I had been Harvard, I might have very well made that same decision. I think it was not an irrational decision, given the entire sort of operation. The fact is Woodward was doing pretty well. I wasn't doing something that is terribly different from what it is that they were interested in at the time. And there were plenty of very good people, like [Elias J.] Corey, obviously a perfectly fine person (that I'm not so sure about) and a perfectly highly competent chemist.

FINE: But he came later.

STORK: Yes. But eventually they were able to add somebody, and they didn't have a crying need at that time. When they would have their seven-year itch, then they would call some guy, and he would show up. Clearly, clearly, they may not have got everybody they always wanted, but it is true that the people they got were always extremely good.

There was the usual sort of terrible time that people go through which you cannot possibly understand unless you've lived through it, of knowing a) you've got to find the future, and b) you have no clue what it will be. That is really very difficult. That is a problem with the American system; it's also its strength. It's very complicated. It is a reason we don't have people doing structure or complicated long-term projects, but it's also the reason why we don't have much dead wood. It's a complicated business, but in any event, it's the system. So then I had to try and figure out what to do.

BOHNING: When did you know that the position at Harvard wouldn't be continued? Did you

have much advance notice?

STORK: I would suspect they probably would do this thing the same way we do now—probably a year. I came here [Columbia] in the middle of a year, about half a year before I would have to go someplace. That was majorly related to Jack Roberts. I think it's true that Jack Roberts was the one who convinced them, or at least made the strongest pitch in my favor. For some reason, I didn't ask him to, but I knew Jack when he was the National Research Council Fellow at Harvard. We had reasonable respect for each other. And I think he at least made a strong suggestion to Hammett that this was something worth doing, and Hammett was interested enough to ask me to give a talk here. They were sufficiently impressed by my talk, for probably totally the wrong reasons.

FINE: Was Roberts at Caltech then?

STORK: Well that's something that one can establish. I came here in February of 1953 and I think he may have still been at MIT. He was probably still at MIT. When I came here, I think Louis Pasteur's lab in Paris was probably no better than the place here.

FINE: Nothing's changed. [laughter]

STORK: Oh, no. You'd be surprised. There were no hoods in the building here. The only hoods there were, were these little round things on people's desks that you see in some undergraduate labs. That was it. But the thing that's most extraordinary, and although this has nothing to do with history, it's extraordinary anyway, was the way the glassware was put in the desks. They had a rectangular section that was made of cast iron and had two trays that you could access by pulling this contraption out, which was that wide [about one foot]. It was not possible to pull it out level, because of the way the tongue and the frame that supported it were off the floor. So it tipped forward, exposing sideways the shelves on which the glassware was sitting. A fourth of the glassware landed on the floor with each opening of this. So they were kept open, because these things would tip over as you take them out. It was an enormous thing; no woman could possibly move this thing. They would need help to do that, with apologies to the weaker sex. [laughter] The fact is that you did it that way, and then you left it open. So the thing was cluttered with these open things, aside of which were these little so-called hoods on top.

There were no fluorescent lights. My first fluorescent light was a gift. A colleague of mine was George Frankel, who was a physical chemist in this department. He is supposed to retire about the same time as I am supposed to retire. He became dean of the graduate school

eventually and now is again in the department for a year or two. George Frankel had bought a couple fluorescent lights, which he gave me. I had one fluorescent light attached with copper wire to the steam pipe until the fire department came around and pointed out in vigorous terms that this was illegal and I could not suspend electrical fixtures to a steam pipe. [laughter] So that was the end of that.

My office had a distinguished history. It should be declared a national monument, not because of me, but because of the previous occupant. My office, 652 Chandler, was the same office which Arthur Cope occupied [Doering also was in the office before me]. You really have to see it. It's about twice the size of that desk over there.

FINE: By the elevator.

STORK: Yes. It now holds three refrigerators and it is full.

FINE: It's a closet. [laughter]

STORK: That was my office.

FINE: But you've been on the sixth floor the whole time.

STORK: Yes. The office I now have is at the other end of the corridor. I shared the sixth floor with a physical chemist, who is a very famous physical chemist; he has a prize named after him from the ACS, which is the Victor K. LaMer Prize in Colloid Chemistry. He was the other occupant of that floor. Had no use whatsoever for organic chemists; he hated them. He had a thick white line painted on the floor, which was the frontier beyond which organic chemists were not to trespass. Cope was only here one year. He was involved in war work and he worked mostly in Washington when he was here, so far as I can see, and then went off to MIT. While Cope was in Washington, on one of his trips, LaMer decided he needed more space. He took out all of the equipment of Cope in a couple of the labs, tossed it out in the corridor, and put his people in. Presumably it is no longer done that way. [laughter] Then had this white line painted to boot. [laughter] So Cope told me, "I'll give you only one piece of advice. Stay away from LaMer." The next thing I know, I'm sharing the floor with LaMer. [laughter]

Well, I actually enjoyed LaMer. Although we never got along in the classical sense, nevertheless I had affection of a kind for LaMer because he was a spunky little old fellow. He cared about what he did. It was possibly silly what he did, but he cared a lot. He was really

enthusiastically teaching his students that all that people wrote on thermodynamics was wrong, because they didn't pay attention to his stuff in a proper way. But he did it with gusto and enthusiasm, and he really cared about it. Eventually, he died of a heart attack on a dancing cruise, having taken up social dancing at the age of sixty-something and was fascinated by it. [laughter] So that was the situation here.

Frances Hoffman originally came from Harvard with me, then eventually decided I didn't pay her enough and went off to Merck for seven years, before she came back as the director of laboratories here. When she became director of laboratories, they redid the floors in various sections. By modern standards, it really looked awfully crummy. But there was a major departure from what existed before, since there was in fact nothing there. That was done under the chairmanship of Ralph Halford, who was a physical chemist who was majorly involved in the eventual design of the Perkin-Elmer infrared instrument.

[END OF TAPE, SIDE 6]

STORK: Halford eventually became dean of the graduate school. The labs that were produced then were more or less feasible. Breslow's office was 552, the same damn set up I had—the refrigerator room. But that place originally had Cope in it. It was Doering's office and my office. That's pretty good! That's a pretty good succession of people. I don't know who was in Breslow's office before him; probably very good people, too.

FINE: Doering was in 552, too, before Cope?

STORK: Was it before Cope or after Cope? I think it was before, no after Cope. Then he went off to Yale.

BOHNING: Doering tells the story that he wanted to get an IR, but Hammett, who was chair then, refused to get him one (22). But Hammett agreed to get you one. Is that true?

STORK: Oh, the IR, yes. I don't have any great merit for that. There was a professor of organic chemistry here at the time, who is still alive; he's retired and lives in New Hampshire. That's Charles Dawson, Charlie Dawson. Dawson is the one who wrote me before I accepted the job here. He said, "What you should do is to make your accepting the Columbia's offer contingent on getting an infrared machine in this place." [laughter] It was his suggestion; I would never have thought of it. So I did that, and we got our first Baird infrared machine as a result of this operation; It was not a total gamble on my part, since there was an inside person

here who was suggesting it. That's when we got the first one.

As I said, later Hammett was the one who initiated that we should get interested in NMR. He convinced Benjamin Dailey, who just retired a couple years ago from the physical chemistry group, to become interested in it. Dailey was ready to have his arm twisted because he was veering in that direction anyway. Dailey did some early work. He had a very important paper with the person who did some of the early NMR development, [J. N.] Shoolery, correlating chemical shifts and structure (23); it is an important paper.

So that was introduced here, but Columbia was not at the forefront. It's a small place. Columbia has a difficulty in that it's expensive to do research, and it's clearly getting more expensive all the time. When I was a graduate student at Wisconsin, you had to make a reservation to use the Beckman manual DU instrument, two or three days ahead, so they could arrange for a member of the professorial staff—in my case it was Al Wilds—to go with you and sit there or come back every so often to see that you didn't damage the instrument as you spent two hours to do point-by-point spectra of some damn molecule. That was the sum total of the instrumentation at Wisconsin.

Eventually, towards the last two years of my stay, there was the infrared machine at Harvard, and there must have been a UV machine somewhere, but I don't remember seeing it. It was probably automated by that time. Then here there was not a damn thing, except for this infrared machine; eventually they got something. But it's difficult; it's expensive and the place is small. The place is small and therefore the cost per person, or recovered overhead or however you want to put it, is just small. So it has never been the leader in having instrumentation in the place, but it became more or less adequate. On the other hand, the Varian instrument that we got, the A60, was the third in the country. It was the third such instrument, the Varian A60, so we were getting there at that point.

BOHNING: What kind of a chairman was Hammett?

STORK: Actually, the chairman when I came was probably not Hammett but Arthur Thomas. Well, maybe Hammett had just became chairman. That's possible. Yes. Actually, Hammett was chairman before I came because I still have handwritten letters of Hammett, which I've never used as a weapon or anything because I didn't have to, which say that I would never have to teach an undergraduate course.

FINE: But you have.

STORK: Yes. I thought it was kind of silly. They also said that I would not have to teach in

the evening. I did both. I don't know. [laughter] That's irrelevant.

So he was chairman, but before that Thomas was chairman; he was obviously hopeless and disastrous from everything that I know about it. Hammett was a very fair chairman. He was difficult to approach. I don't know where I get these stereotypes, but I always thought of Hammett as a rock from Maine. But he was not from Maine. [laughter] But he was a sort of a rock, and it took me years before I could call him Louie. In fact, I did this only after repeated entreaties. Hammett was Professor Hammett and that's all there was to it. It was just that way, because he did not fool around easily. He was a little bit related to McElvain, in that sense.

Hammett was doing his best for the department in days that were fairly difficult, earlier on. He had a very important role in building the department. The one example that some people know (and I don't whether it's in here or not (2)), is how we got [Ronald] Breslow here. Without Hammett, there wouldn't have been anybody with some sense of humor and more than sense of humor, and we would never have gotten away with it. What had happened is that I knew Breslow when he was an undergraduate at Harvard. In fact, he did his first two papers with me on the structure of a compound called cedrene, the stuff that makes cedar closets smell like cedar closets (24). It actually was an important paper, because it was the first paper where there was actually an effort to correlate certain features of infrared with structure, specifically the difference between five and six membered cyclic anhydrides. It was the crucial clue to the structure of cedrene.

So I knew Breslow was an extremely bright guy. At that time he was a postdoc for Todd in England. He had been offered a position at Wisconsin, and I wrote him and said, "You really should forget about Wisconsin. You should come here." You know the way departments move. You've been around enough to know that this is not necessarily the fastest operation in the world. At that time, this place was sort of a frozen mastodon. So circumstances arose that I had to send a telegram to Breslow that we offered him this position, before discussing it with my colleagues. [laughter] Now, one should not do that, and I'm not advocating it at all. It just had to be done that way. It was a gamble that I would then be able to convince my colleagues.

So there was a department meeting. Things went slightly wrong, in that Breslow wired back a telegram to the chairman, Louie Hammett, accepting the offer. Hammett had not opened the telegram before the meeting. He'd collected together departmental stuff and he would open these letters and read them to the staff. And I didn't know anything about the telegram. Then he opened this telegram. When Hammett got a little excited you could see red climbing up the back of his neck. He was obviously getting somewhat excited as he read this telegram, which said, "Pleased to accept your offer of the instructorship." Of course, he's saying, "What does this mean?" "Oh," I said, "I'm sorry. This has no meaning. It's just a code, that he was supposed to wire back if he would accept it, if we decided to offer it to him, so we can save time." [laughter] Hammett said, "Oh, I see." Although we never talked about it, it was perfectly certain that he knew perfectly well the kind of skullduggery I'd been involved in and went along with it. So Breslow came. That was pretty good.

BOHNING: Had you had any other offers, or looked at any other places before you came here? You said that was sort of a traumatic period.

STORK: There was maybe four months before this thing came up. I am not sure, but there is nothing that I can remember, and it may very well have been nothing. It was all fairly tentative, and this one was the first one that was a real something. I happen to like cities and so the fact is New York sounded like a very good thing to me. I don't think I fooled around very much except for asking for this infrared machine. There was no game playing.

I lived in an earlier generation. I have nothing against game playing. It's rational. Baseball's a perfectly good sport, and we're moving towards the baseball operation. Well, not enough. I believe we should adopt one more thing from baseball. Let's see. We stole [William] Clark Still from Vanderbilt. Now, that's really not nice to Vanderbilt. What's the incentive for a place like Vanderbilt to develop and treat young men very well? Or, let's say Michael Kahn is at the University of Illinois, Chicago Circle. There's absolutely no question Michael Kahn is going to be out of there within a year. Now, they spent over a million dollars on Michael Kahn. He's brilliant; there's no question about it. So this should be the same as what baseball used to do; I don't know if they still do. You pay something to the club to get this guy. I think that's reasonable. Then it gives them incentive. Otherwise, what's the incentive? They get burned a couple of times, and the incentive to get someone who's better than they can afford is not great. It's a very serious problem.

FINE: We've been a training ground for a lot of other schools.

STORK: Yes. Almost by definition, this is not a bad place, so obviously they've got to go somewhere else that's outstanding; it's going to have to be at least as good as here. But you certainly could make a stellar department out of the people who are no longer here. There's no question about that. Which is, of course, probably true of a number of places.

So Hammett was sensitive to things. Hammett was succeeded by a nice gentleman named [Charles O.] Beckmann, who had not done any work at all for years; he was a physical chemist. Charlie Beckmann had done some early *ab initio* calculations of the rotations of evantiomers of certain chiral ketones. The effort to do this just simply convinced him that there must be easier things to do than continue research. He was a plausible chairman, although Hammett thought he was a total loss.

Eventually, the department passed a rule that the chairman could not succeed himself and could only serve for three years, obviously exempting the incumbent, who was Beckmann. As a

gesture, we were hoping he would volunteer that this would apply to him as well, which he did. So everybody was satisfied. But, unfortunately it produced what I think is a bad system. It produced a system of compulsory automatic rotation, every three years, which insures that a new chairman doesn't know what's going on for one year, can do something for one year, and is a lame duck for one year. It is not a good system. It is maybe a humane system, because it's also true that that job would kill most people. It's not surprising that for a long time, whoever was chairman of the department stopped doing anything afterwards. In more recent times there were more and more exceptions with this forced rotation, otherwise nobody would be doing anything. But there are obviously problems with that.

BOHNING: You were still at Harvard when you made the Syntex connection, through Djerassi.

STORK: Yes. The Syntex connection was really Djerassi convincing me to consult for Syntex when it was essentially a garage. I was very much involved with Djerassi and what was going on there. Much of it was by phone, and I would also go down there. In those days it took forever; they used propeller planes, so it took fourteen hours to go to Mexico. Not quite that, but almost.

BOHNING: Djerassi has said that when he went to Syntex in 1949, you told him he was stark raving mad (6). That's his quote. He was at Ciba, wasn't he?

STORK: He was at Ciba. Did I say that?

BOHNING: That's his quote.

STORK: That is conceivable. That certainly would be a reaction I could easily imagine that I had. I don't think I was strongly against that. I think I probably would have said he was stark raving mad. On the other hand, he wanted to talk to Max Tishler, who was at that time the industry-university connection statesman. I'll always remember what Tishler told him. The president of Merck at that time was George Merck. The president of the United States was [Dwight D.] Eisenhower. The president of Syntex was George Rosenkranz. What Tishler said was ridiculous. He said, "Syntex is just a nothing operation. When the president of the United States wants some advice, who does he call? George Rosenkranz or George Merck?" [laughter] That was supposed to be a serious point. Djerassi had the good sense, I guess, of paying no attention whatsoever and taking off for Mexico, which took a lot of guts because he didn't speak Spanish, among other things. It took guts of various kinds. At that time I was pretty much involved with Syntex, which was kind of an interesting operation. Djerassi only stayed there

about two years. Then, we both consulted for Syntex and we used to go there together, which was really a very good consulting system because we'd fight and argue without any barrier. That produced much more interesting chemistry than just the formal endeavor that sometimes passes for consulting.

BOHNING: You said you went to Mexico City several times?

STORK: Yes, I would go maybe three or four times a year.

BOHNING: What kind of operations did they have when you first started going there?

STORK: They had a pilot plant, which was not trivial. There were several Pfaudler kettles. They were not clean by today's standards, but very plausible by Mexican standards. They had research labs with no hoods, so they did some things outside on the patio in twelve-liter flasks (some were twenty-two-liter flasks), brominating stuff into the atmosphere. [laughter] Even in Mexico, I'd think you'd have a tough time getting away with that kind of stuff today. They were very primitive operations. There was an old munitions factory, called Molino de Bezares, which they had and in which they were doing things. They were mostly extracting raw material following Marker's initial discovery that a good source of something which you could sell to make progesterone was this thing called cabeza de negro, black man's head or Negro's head, which was a root from which they extracted stuff. So it was mostly doing extractions. They also made a few witch-doctor type of medicines for the Mexican or South American market.

Rosenkranz majorly changed it. Both he and Djerassi were of middle-European origin. He recognized that Djerassi was a powerful person and the person that they needed. They hit it off well. At that time Rosenkranz was working in the lab himself with an assistant. Djerassi was also, and they started doing well. The view of the outside world, like people at Merck, was "Of course they did well. They had no restraint, no restriction on publishing stuff. They had no patent problems, no patent department." Of course, these other pharmaceutical industry groups were frustrated as all hell because a certain percentage of the work Syntex published, which could have easily have been ninety percent, they had done before, but they were not allowed to publish it. So Syntex was always first in publishing it. Syntex did nothing wrong; on the contrary, it served to loosen this straightjacket that they operated in. But it did not contribute to a friendly relationship, obviously. Although Syntex was often accused of shady practices or borderline operations in the early days, there's never any actual case of that that I ever knew of. It was perfectly straight; they were making money by selling stuff that people wanted to buy, that's all.

Little by little they became known because they published all the time. That was a

Djerassi thing.

BOHNING: I think you had at least three papers during the Harvard period with Rosenkranz and Djerassi (25).

STORK: These were gestures on their part. This used to annoy me. They would do this as a friendly thing. One of them I had something to do with, another one they put my name on it, and one of them was embarrassing because nobody could repeat it. It turned out to be an important paper. There was recently a multi-million dollar patent case in which I was involved until they decided I would make a terrible witness. [laughter] It's a side chain hydroxylation of the corticoid hormone, the dihydoxy acetone side chain, so-called. Progesterone doesn't have a terminal hydroxyl. The question is how can you stick these hydroxyls on there, and so I suggested this, they put my name on the paper, and it worked! I didn't really think it would work. They put my name on the patent (18). Then this gets published, and nobody can repeat it.

I remember Bill Johnson making a public statement about it at an ACS meeting, that people shouldn't publish papers unless they give all the details, because nobody could repeat this stuff. I didn't even know at that time that my name was on the paper. It turned out that it actually is an interesting story. Everything that was said in the paper is correct. The reaction was done in tetrahydrofuran. It turns out if you do this in absolutely pure tetrahydrofuran, it doesn't work at all. It turned out it's essential that this pure tetrahydrofuran contain some peroxide. The operation was conducted in Mexico and the tetrahydrofuran contained plenty of peroxide. Probably it was not even distilled. Or maybe it was distilled, but it still contained peroxide.

Eventually somebody realized that. It was not a question of malfeasance; it was a question of not realizing the essential presence of a small impurity. The patent about putting in the oxygen at C-eleven is one I definitely did (18). There was a *Life* magazine picture, which was a great picture that I have framed at home (26). It's a picture of the research group, with Rosenkranz and Djerassi; I'm in there at the blackboard. This picture is about putting the C-eleven hydroxyl group in. That was very nice chemistry. You could still do this as a problem.

It's amazing about organic chemistry. The advance in organic chemistry has been absolutely spectacular, but it's hard to tell. The way you can tell is that no one in his right mind would have considered making a compound like erythromycin thirty years ago. I don't mean succeeded in making it; nobody would have considered the possibility of making it. Out of the question. Today people do this until you're bored to read this type of thing. I mean, there's another description of another damn macrolide antibiotic synthesis that someone made by controlling this aldol or not controlling this aldol. Who needs it?

That implies an extraordinary difference. You know, in the same sense that it's totally

boring to read the paper that somebody's making some oligodeoxynucleotides with his machine, a machine that makes things while you sleep. It's boring. But the fact that it's boring is exciting. [laughter] It's extraordinary. This is what happened in organic synthesis. But it happens in ways that are incremental. The glacier analogy is the one I like; that is the glacier obviously doesn't move. If you put a stick in a glacier and come back six months later, it obviously has moved. But you can't see it. This is the way organic chemistry has progressed: the advance is spectacular. It's really spectacular, but it's easy to see only from what you couldn't do.

The Woodward-Hoffmann rules may very well be an exception to this. That's an event, which you can date, where at one point something is recognized that was not before. But that kind of thing happens damn infrequently, and the general progress is not something you can time and say, "Oh, such and such year is the year that they controlled the aldol condensation." It's not that way. But the net result is you know how to control it now to a great extent. Whose work is it? Well, it's probably [Clayton H.] Heathcock, probably [Satoru] Masamune, probably David Evans. This one is contributing this, this one is contributing that. The whole thing is put together by someone else who himself didn't contribute very much except to put it together.

One of the phrases that grates me is, "I don't want to do <u>just</u> synthesis." <u>Just</u>. People are now taking it essentially for granted like oligonucleotide construction. It would be a reasonable thing to say. "I do not want to do <u>just</u> oligonucleotides" would be perfectly rational. But it isn't that way at all, yet. Even though there has been an extraordinary explosion. You pick up any journal thirty years ago, in the Fieser days, and it is dull, it is terrible. You pick up any lousy *Tet Let* [*Tetrahedron Letters*] today, and if there are not two articles that are exciting in there, it's surprising. There is just a lot, and it's not just the U.S. There's a major amount from Japan, once in a while from Korea. Once in a while a guy in Bangkok is publishing clever stuff. There's just simply an awful lot of very, very good chemistry. But none of it is dramatic *per se*, it is dramatic in totality.

BOHNING: How did you select your ideas? Is there a common thread to how you developed them? As I look at your list of papers, it's the total synthesis of this, the total synthesis of that.

STORK: Total synthesis and methods for total synthesis.

BOHNING: But there's such variety involved.

STORK: The thread is clearly a three-dimensional construction, and that means natural products. I don't know anything about natural products. A real natural chemist would be Koji Nakanishi. Indeed, he understands something about natural products, where they come from,

cares about their structure, wants to find out about them. I don't know. I practically never see an actual natural product. If we succeed in synthesizing something, by that time there's just enough for an NMR. So why natural products as targets? Partially, it's material motivation. You have to get some money for this stuff, so you have to pretend for the NIH, with the understanding that it's not true, your work is related to something biological. You want to get a grant to make this digitoxin they were talking about, which we did in fact succeed in making recently. But fortunately there have been enough biologically active natural products that could be snuck through the NIH door and also have an interesting shape and raise interesting structural problems. The way I get interested in a particular one is difficult to say. I'll give you one example and it's the most recent thing that we're really very much interested in; and so is half the country at this point. It's taxol, for the obvious reason that taxol is a structure that's pretty complicated; very complicated, but not impossible. Everybody's excited about it because it's the only drug that has shown major effects in some solid tumors.

[END OF TAPE, SIDE 7]

STORK: I have two very good people working on taxol now. We're about five years after everybody else who is working on taxol. [laughter] I didn't even know the thing existed two years ago when Ayako Yamashita came here. She was a professional chemist who was working at Upjohn, and got an Upjohn sabbatical. She wanted to work on something. I was desperately looking for a slave because I wanted to make oligonucleotides for some special reason which has potentially to do with cancer control, but it's a minor operation. I couldn't convince anyone to do that. People who come to work with me obviously are biased towards what they think I'm supposed to be doing, and they don't want to make oligonucleotides. So I said, "Do you want to do that?" And she said, "No. [laughter] I want to work on synthesis. Why don't you look up taxol; it's a problem a lot of people are working on. It's really quite an interesting problem."

She started working on taxol; she worked on it for a while, and then went back to Upjohn. But then I became more and more interested. But the interest is always the same. That is, there is a target, which is difficult enough that you can see some problems you don't know how to solve, but you see a kind of possible solution; and then you get into it. Simultaneously this leads to working on methods.

In that sense what we do is really very different from what I see Woodward did. I have a statement about what Woodward did in synthesis that I've got to make because I want it on tape somewhere. I said this to Arigoni, and he locked himself up in a fit of anger in a hotel room for an entire day before he would consent to emerge. Arigoni worshipped Woodward—it's a religious thing; I don't know why. My statement was that Woodward contributed nothing whatsoever to synthetic methodology, with the exception of some reagent which Aldrich peddles as Woodward's reagent. There are two of them, Woodward's reagent K, and who knows what other one, which are not much used by anyone making peptides, but are supposed to be useful to

make a peptide bond. There's no one I know of who ever uses them. Okay. Nothing else, is my claim.

Now that's an outrageous claim to anyone who's brought up with organic chemistry. It happens to be a correct claim, which I can defend any time anybody wants to hear about it. Woodward was so brilliant. It's like a great composer who does not necessarily have to invent half tonalities, or who knows what else. There are some notes out there, and if he's brilliant enough, he can do fantastic things with that. Then after that, who knows? Nakanishi may not have invented his card tricks. There's no new mathematics coming out of Nakanishi's card tricks, but they are damned impressive. That's not too bad an analogy; a better analogy would be mathematical puzzles. You probably don't create new mathematics by solving them, but there certainly are people who are brilliant enough to find solutions to these things by manipulating known things. You have to see how they could be done.

Woodward could do them, but there is almost no new reaction there. When people think it's a new reaction, what they're saying is that their knowledge of chemistry is not good enough to see where Woodward got that. But I usually would know. [laughter] The fact is that he did not create new synthetic methods. He was not interested. He was not consciously not interested, but he just didn't need it. He was able to find his way with what was available. It's a different case from George Büchi, who was violently against developing new methods, although he did introduce things that were really very novel; several were really novel and extremely exciting. He did it, but he didn't want to. He was perverted in a sense by Woodward; if you're brilliant enough, you ought to find ways out, using what exists.

We don't have that kind of a hang up. We have worked on both; the structure suggests that there's a need for finding a way of doing this, and sometimes we succeed in finding it. Some of them are showcases. There is one of the syntheses I'm reasonably proud of. To my surprise, there was recently an event that I didn't know was going to take place during a meeting in Minneapolis, where they had found some people to say more or less nice things about my scientific career. One of them was [Samuel] Danishefsky. Danishefsky came with slides, which he had made of what he thought were the most interesting things that I had done. The interesting result of that was that I was both interested and annoyed. For the obvious reason, if you're a psychologist. I was annoyed because he didn't pick Q, R and S, which I thought were great stuff. How come he didn't pick that? [laughter] On the other hand, he picked some other stuff that I thought was really not that great.

It was interesting, but the fact is that one of the ones that he did not pick, which I thought was really very good, is the lupeol synthesis (27). Lupeol is a triterpene, which has ten asymmetric centers, or something like that. It was totally constructed by methods that we had developed. They did not exist before we did it. It is something called the regiospecific formation of enolates. You want to do the reaction at this point, not at that point, on that side of the ketone, not on that side of the ketone. How do you do that? You've got to solve two

problems. One is, you have to generate this enolate rather than another enolate; it's this enolate, not that enolate. You have to find a way of doing that. And after having generated it, it has to be of such a nature that it does not equilibrate with the other one faster than you do something to it. We solved the first one by showing that lithium enolates could do that; we were the first ones to do this, although most people don't know that, with a paper with [S. D.] Darling and [Jiro] Tsuji (28) who became a major figure in Japanese chemistry. About every step is, in fact, regiospecific generation of an enolate, and a construction using it.

So we like both methods and total synthesis. The origin is the structure, and the structure needs methods. Not the method first and then the structure. Structure, problem, method, back to structure. It's kind of a sculpture. It's a challenge. Everybody gets interested; as soon as you can make a problem of something, it becomes interesting. Whether you're a chess player, or whether you try to find a way of preventing paper bags from falling apart when they're wet. If you can make it into a problem, it becomes interesting. As I said, I'm not mathematically inclined. So this shuts out thirty-five percent of what you can possibly do. Well, that's nice. Thirty-five percent. [laughter]

BOHNING: Did you and Woodward discuss mutual ideas in synthesis?

STORK: Yes. In fact, there was one time when we had to get Paul Bartlett to adjudicate which one of us was allowed to work on this synthesis problem. It turned out to be santonin, a famous sesquiterpene lactone. We both independently decided it might be a nice problem to work on. I wrote up my scheme, and he cooked up his scheme; they both used the same clever trick. [laughter] So we went to Paul Bartlett and said, "You should decide which of us is allowed to work on this." I forget what the decision was. The net result is that we both abandoned it. [laughter] So yes, we would discuss things.

I don't know why I happened to think of this now, but Harvard had a rule that instructors could not have graduate students of their own. It was the first academic rank, but different from the present assistant professorship. Of course, there was no external source of funds in those days. I got my first research money from the Research Corporation, when we became interested in the cortical hormones. We convinced them that what we were doing had something to do with it, and they gave us some money and they gave some money to Woodward also. But there were no NSF grants, and there were no NIH grants, at least for chemists, at that time. The students paid for their own chemicals and you did the best you could. Mercifully, there was no Aldrich, so you didn't have to spend all your money buying chemicals.

So I couldn't have any graduate students. My scheme was to make estrone, which is what I had started working on before at Lakeside. I had one really interesting feature, and Woodward thought it was pretty good. Woodward was pretty young; he was only five years older than I was. When I started at Harvard I was nearly twenty-five and Woodward was about twenty-nine or thirty, something like that. At that time he was driving a Packard; he should have

kept it. He was driving a Packard, one of those things with a rumble seat. [laughter] The color of this thing was absolutely indescribable. It was majorly lavender, but with patches of yellow, and non-glossy. The right fender was held together by copper wire to the rest of the body. I still remember sitting in this car in front of 25 Follen Street, which was a group house that my wife and I rented with thirteen other couples. Housing was extremely difficult to get at the time around Cambridge in 1946, when I showed up, so we shared that place, which had one kitchen and two bathrooms, with thirteen couples. They were various graduate students and what have you. We were sitting in Woodward's Packard, because he was taking me back to Follen Street after an evening seminar. He offered me this deal that he would let me share three of his graduate students if we both worked on my problem. So I said, "This is a great deal." The truth is this deal was very much more favorable for me than for him, because I didn't have any graduate students at all. So I would get a share of these guys. There was Aaron Nelson, Bob Wineman and Aksel Bothner-By, who became famous in the NMR field by designing the first 600-megahertz machine. So I had a fifty- percent ownership of those three guys and we were going forward busily.

Woodward contributed majorly to the operation. My scheme was a sort of Diels-Alder scheme. It doesn't matter what it is, just a plus b. The b part was the right hand side of the molecule and was supposed to be a precursor of the C/D rings. My part was to do the ABC construction after the C/D rings had been put together. Woodward convinced me, quite correctly, that my dienophile was not really designed as well as it could be, and that his dienophile was better, which was probably true. So we embarked on this project and things rolled merrily along.

Incidentally, and whether anybody believes it or not is not really important, so far as I'm concerned it was the first time that Woodward was made conscious that it was in fact desirable to control asymmetry in a molecule and it was possible to do that in this case. So the thing was designed to be completely stereospecific. It went on to the point where the last thing to do was to close the diacid to make the cyclopentanone D rings. The diacid was a highly crystalline solid, and that compound had previously been made in a non-specific way.

We got that compound, and it had exactly the same melting point as the previously made compound. Let's suppose it has a high melting point, maybe 240 degrees, really pretty high, and nicely, highly crystalline. We get that compound, and its melting point was exactly what it was supposed to be. So we concluded that our synthesis had been successful. I got a phone call in the morning from Woodward; he said, "Would you mind if we meet in my office this morning at ten o'clock, because the director of research of Ciba is going to be in town, and I would like to tell him about our estrone synthesis." Fine with me. So we met there with a guy whose name I forget—it starts with a P [Plattner]. Woodward was a theatrical person. I was sensitive because Woodward was Woodward, and I was—who knows. Automatically, he would get the limelight. Because this was our joint operation, I'm necessarily psychologically slightly disturbed by what goes on; nevertheless, I'm there because he knows that I have to be there. But he doesn't

mention me at all. He describes in elegant terms "the" synthesis; he doesn't say "my," he doesn't say "our." It's "the" synthesis. But the implication is that it's his synthesis. So I'm tense, and somewhat resentful. You wouldn't believe it—he goes through the entire thing, and the Swiss agree to send him a sample of the real McCoy, so he can do the only check possible at the time, a mixed melting point.

So the chemical appears from Zurich, and it melts like our synthetic diacid. Woodward, with total drama, demands that the laboratory bench be covered with white sheets, because the lab bench was not clean enough for the conclusive mixed melting point. It would have been the first stereospecific synthesis. It was a big deal. The melting point apparatus was put in the middle of the bench and he goes in to take the mixed melting point. At that point I can't stand it any more. I leave and go to Harvard Square for a cup of coffee. When I come back, there is gloom all over the place. [laughter] My feelings are mixed. I must confess, to my possible shame, that I had mixed feelings. I was not unhappy that the whole thing had screwed up because I knew that I wouldn't get any credit for it whatsoever. [laughter] In fact, the melting point was depressed some forty degrees or something like that. It turned out that the Diels-Alder reaction, for reasons, which are yet not clear, instead of going the desirable way, had gone upside down. So our methyl group, which was supposed to be up there, was in fact down there, and by extraordinary coincidence, these two acids, the right and the wrong have the same melting point. The reaction was completely stereospecific, all right, but it was upside down. [laughter] So that thing that is published in *Experientia* is incorrect, but also it was done without asking Woodward at all about it.

How did I get into that? I don't know.

BOHNING: We were asking you about Woodward and your conversations.

STORK: Yes. So chemically we had a very close relationship. Whenever Woodward was in town, we always had lunch together. And sometimes when he was not in town, we would actually go somewhere together. It was quite close, but only until the end of 1952. It was about six years, but that was before his major synthetic accomplishments. His major synthetic accomplishments were in fact reserpine and strychnine, and that was done after I had left. Reserpine not long after, although it had started before. Strychnine had been started before; this was a major, major contribution. Woodward's steroid stuff, the world considered major, but it was not. It had lousy stereochemical control. The one that he did. After the joint synthetic fiasco I mentioned earlier, we worked independently.

After that I was promoted to what was called an assistant professorship, which was like the second term of an instructorship in places that have three plus three terms, like Yale, for instance. At that point I could have graduate students, which is when people like van Tamelen and then Dick [Richard K.] Hill, who became a professor at the University of Georgia, and other people like Leon Mandell, who became the dean of science at the University of Southern

Florida. But before that I didn't have any students, except those three fifty percent graduate students.

This may have been very influential—Bothner-By may have given up organic chemistry because he was disappointed with that project; but this turned out to be to the great benefit of NMR people.

BOHNING: What about van Tamelen as a student?

STORK: Van Tamelen's a smart guy. By today's standards, somewhat dilettantish in chemistry. He had done very nice undergraduate work at Hope College in Michigan. He was a Michigan kind of person, a tulip person. His great ambition was to find out what made tulips colored until he found out somebody had already done that. It turned out it was wrong. The matter of the coloring pigments of flowers is really a complicated thing. It's essentially known, but everything that one believes about it is incorrect. All of these compounds to which the colors are ascribed are artifacts of the isolation operation. The real thing is just unbelievably complicated. But anyway, he was a tulip person, and he had done some undergraduate work at Hope College and started to work my cantharidin synthesis. He made desultory progress; there's no way that the cantharidin synthesis would have been completed, except for [Albert W.] Burgstahler (29).

Burgstahler was an experimental wizard of the time. He'd be wasted today. Burgstahler could make anything crystallize that he dealt with. I still have boxes of samples from Burgstahler, nice, beautiful, crystalline compounds. Nobody knows what a crystal is anymore. Chemistry is an intellectual thing now. Now you look at a peak in a spectrum; it's very analytical. You don't often get the thrill of making crystals, which Woodward felt more than most people. That was not put on. There was a real feeling of joy at the crystal, the crystal shape and coloring and that sort of thing; there's no question about that.

With Burgstahler, this was the time that people took three years to do their Ph.D. degree. Burgstahler was such a great experimentalist. He finished cantharidin on July 4th, 1951 at four o'clock in the morning. I know that because first, it was Independence Day, and secondly, I was supposed to catch the plane to Mexico at seven a.m. Thirdly, we finished the synthesis at four a.m. I know, because I was there to provide moral support. Burgstahler was a fervent Catholic who, every half-hour, would go up to the roof of the building to sing a Gregorian chant so that the final product would crystallize. [laughter] It was an impressive display of the effectiveness of faith, because it did crystallize, and therefore this was great. The fact that was possibly as important was that he was a brilliant experimentalist. And so, we made cantharidin. I drove to the airport, picked up my plane to Mexico, and that was pretty good. [laughter] It was incidentally, the first planned stereospecific synthesis.

Van Tamelen started this thing, but did not really make all that much progress, although he was a very, very good chemist and did brilliant work later. Van Tamelen's career, from the chemist's point of view, is a shame, because he gave up when he did, when he could have continued for another ten years. From his point of view it's only a partial shame, because he made millions of dollars in real estate. Part of the time that he was spending on his real estate operation was interfering with his chemistry. Whether he would consider it a catastrophe that he retired to take care of his holdings, I doubt. [laughter] I doubt. He had a very fine career. He was one of the best chemists in this country in what he did.

Both he and Johnson became interested in different aspects of the same fundamental operation, the polyene cyclization business. I was once asked by Djerassi and Calvin Stevens (who just retired from Wayne State) to join them at Wayne State. We were all three friends and Calvin Stevens was also at Wisconsin working for McElvain at the time Djerassi was there working for Wilds. We were all together. My point was that even if I had wanted to go to Wayne State, I happen to value their friendship, and there's absolutely no question in my mind whatsoever that if all three of us went to the same place, that would be the end of it. Forget it. [laughter] But Johnson and Van Tamelen faced that problem. They were very good friends, but eventually they would only write letters to each other through the Post Office, even though they were only two doors apart. That's what happens. Obviously it could be the same woman; in that case it was not very different, it was the same problem.

BOHNING: You mentioned this polyene cyclization, and there's the Stork-Eschenmoser hypothesis, which came around 1950 and which deals with that area as well.

STORK: Yes. There's a symposium that's taking place in New York at the end of August, that has do with this. Konrad Bloch is giving a talk, and it would be interesting to see what he says about it. This is a complicated thing, the polyene cyclization. It's a long story; I've actually written it up because I sent my version of it to Eschenmoser recently because Eschenmoser published a long, beautiful paper about the history of [Leopold] Ruzicka and the isoprene rule in *Chimia* (30). That paper is factually incorrect by my biased recollection, or my biased input. So I wrote my version of this for Eschenmoser. Actually, that was six months ago. I've seen Eschenmoser since; he said, "I will answer it." But he hasn't, and the history of it is complicated. It's very difficult to put in historical context. At the time that I became convinced that triterpenes came from the cyclization of polyenes, the stereochemistry of these compounds was not known, except with respect to the AB rings.

[END OF TAPE, SIDE 8]

STORK: The postulate was that they would turn out to be trans-anti-trans. That, I presented.

I'm amazed today that I would have the courage to do stupid things like this. I gave three colloquia at Harvard based on nothing whatsoever experimentally. I was in my late twenties, pretty young, which you had to be to do this. One of them was the one in which I proposed the steroid construction, in which Woodward shared his three students with me. But these talks were based on nothing experimental. One other one was on the structure of various morphine alkaloids, which I still remember. My poor parents. By that time I had moved to Cambridge, Massachusetts. They didn't care where they were, so they tended to follow where I went. So they were in Cambridge, Massachusetts. In fact, they had bought a two-story house. We lived in the upper story and they lived in the lower story, which was two blocks from Harvard, on purpose.

At one particular colloquium I was going to talk about the structure of certain morphine derivatives that I had figured out were just incorrect in the literature. I thought it was a good subject for a talk. So I was going to give my talk on this subject, but no work had been done by me on it whatsoever. My parents wanted to hear me give a talk once. So they sneaked in the back, and no one knew they were there. My poor parents! Fieser's in the front row, and so is Woodward. Bartlett was also there. I went through my stuff, saying it can't possibly be this, so obviously it must be this and that and so on. Fieser got up with the first question, and he's kind of snarling. He said, "I think this is outrageous." [laughter] There is Fieser, "I think this is outrageous. You have the nerve to stand up here and say this, and you haven't done <u>any</u> experimental work." He had a point, you know. [laughter] "You haven't done any experimental work at all. Lyndon Small is one of the great lights in this particular field, and you have the nerve to say that his work is not correct." (I didn't know that. He was at NIH and was the morphine alkaloid person. He was an old friend of Fieser's, and I didn't know that either.) My poor parents in the back, they really picked a good one. [laughter] That was pretty brutal. It was a place where MIT people were there, Büchi was there; all these people were there. It was pretty brutal. Eventually, when it was shown that I was right, Fieser apologized; reluctantly, but he apologized. But the point is, it was pretty dramatic. But it was, in fact, based on nothing but theory.

The polyene cyclization was the same thing, but it was early enough that at the end of my talk, Fieser didn't raise hell. At the end of my talk, Fieser came over and said, "You know, I don't believe that steroids come from polyenes. I believe they come from [what was known at the time as] the essential fatty acids." Arachidonic acid was known to be essential to the maintenance of health in rats, so it was needed for something. Prostaglandins were not known at the time; they had not been discovered. We now know that the reason they're essential is because they make prostaglandins. But it was an open thing. It was a long chain molecule and you could curl it around and get a steroid shape. Fieser believed that arachidonic acid was a precursor to steroids, which he had perfectly good right to believe.

Robinson believed carotene was closer, and was the precursor; if you attached it in a large circle and made bonds in between, which has nothing to do with reality, nevertheless it's a polyene. My suggestion was that the trans-decalin systems just happen to be the necessary result

of a concerted closure of a triene, whereas a concerted closure of a diene of the same structure would give a cis-decalin. That was a rigorously correct deduction, whether in reality the closure was concerted or not. That's another thing. But if it was concerted, it had to be that way. Therefore the possibility was intriguing that the triterpenes, which were a more obvious result of closing squalene, could come from this kind of thing. Then, if that was true, they would turn out to be trans-anti-trans.

They turned out to be trans-anti-trans eventually. Squalene had a couple of extra methyl groups in what would be the C-4 position in cholesterol. Cholesterol has hydroxyl at 3, the next position is 4 in ring A, and the triterpenes have 2-methyls, which are the same 2-methyls as squalene. So it's a lot easier to think that squalene could conceivably give rise to the triterpene, than to give rise to the sterols. Now we know sterols are made by giving these methyls up after the four rings have cyclized. Of course, there was no such thing known at the time. Nevertheless, my idea was that maybe the sterols come from a polyene, which I thought might have a plain unsubstituted vinyl group at the end. Not squalene, just a polyene. Later on, it was shown by Konrad Bloch, using radiocarbon labeling that squalene was in fact the precursor and that it's actually incorporated in cholesterol. Woodward then suggested to Bloch (I was already here at Columbia at the time) that it wouldn't be that surprising if you coiled squalene the way that I coiled the polyenes in my Harvard seminar. I always resented the fact that Woodward could perfectly well have afforded to give a footnote that perhaps only I would notice. Footnotes are really the easiest way not to make enemies. Not necessarily make friends, but not to make enemies. But that was not done and it really was not very nice.

That was the origin of that work. Eventually we did some work with that, but we messed up the chemical work. We thought we succeeded in demonstrating that you cannot do these things chemically in a laboratory, a conclusion that was false. Eschenmoser agreed, published his view that it was impossible to achieve concerted polyene cyclization in the lab. Bill Johnson takes delight in showing that quote of Eschenmoser's when he gives a talk on the subject, because Bill Johnson then proceeded to demonstrate that not only could it be done in the laboratory, but it was fabulous in the laboratory. He was a nice enough person (and undoubtedly friendship had something to do with it) that he called it, with no prodding on my own, the Stork-Eschenmoser Hypothesis. He didn't have to do that, but it's very nice that he did. But he is the one who deserves an absolutely major, major share of the glory because he showed that concerted polyene cyclization can be a very powerful tool. It was one of the really few novel synthetic construction schemes that was achieved. There's no question that neither Eschenmoser nor I, nor anyone else, would have given two cents for the possibility of making four rings at a crack with complete control. No way. So it's a jewel.

There is one thing that's really very interesting. My claim to some originality in the operation was really based on the Harvard colloquium, which was maybe in 1950; I'm not sure of the date. Now, it is demonstrable that I gave a colloquium on that subject because Harvard keeps the colloquia abstracts bound in the Harvard library. My abstract is there as well as those of other people. It's a two-page mimeographed thing, and it just says that "the implication of

this conclusion will be discussed," the conclusion being that cationic concerted cyclization of a properly constructed acyclic polyene must necessarily give a trans polycyclic system. That's in there. But that the triterpene might come from squalene specifically, was not.

Now, Eschenmoser's claim is that the first mention that triterpenes might come from the concerted cyclization of squalene in a trans arrangement was in a paper of his and Ruzicka that was published at the same time as our paper of 1955 (31). Now there are two things about this, although maybe Eschenmoser's answer, if it ever comes, would throw some new light on the subject, I don't know. It is a fact that the paper with Burgstahler that we published in 1955 is the legal basis for our claim to have something to do with the polyene cyclization hypothesis. The paper by Eschenmoser, Ruzicka, Arigoni and I forget the other [Jeger] is also 1955. But their submission date is not only later than our submission date; it's later than our publication date. It's a not trivial fact that that paper's submission date is later. It's neither here nor there, but you cannot make a great claim that they were first.

But I could never prove anything rigorously for a long time. So what? What does that mean? My coworker, Burgstahler's thesis was submitted in 1952. Maybe there's something in Burgstahler's thesis? And by God, there is; I have his thesis up there. There is a page that says, "Squalene is drawn in a chair, chair, chair ready to undergo cyclization to a triterpene." So it is actually on record, somewhere, in an official document, that that kind of thinking was certainly current in our lab a couple of years before we published it. All of this is a history, which is of interest only to the people who were involved in it. But nevertheless, it has been a sort of emotional thing.

BOHNING: You mentioned Lyndon Small. I happen to have a quote here from a letter he wrote.

STORK: I don't think I ever met Lyndon Small.

BOHNING: This was a letter written in support of one of your award nominations.

STORK: From Lyndon Small? It's a small world. [laughter]

BOHNING: It's interesting, especially in view of what you just said a little earlier, and I'm quoting, "He and I have differed in some points in interpretation of data in the field of morphine alkaloids. His contributions to the field of morphine chemistry, I feel, are eminently sound if sometimes speculative, which have my full respect (32)."

STORK: Well, this would have to be his view. Do you know there's a series called the Morphine Alkaloids? As it happens, I wrote the chapter on morphine reactions (33). But the fact is that the structures that he proposed were wrong. The structures that I deduced were right (at least most of them). He is right in the sense that they were speculative. Well, they were not that speculative. We used his data as the buttress of my suggestions. It's not that different whether I get the data myself or I take his published data. But of course, in his eyes it would be different, and I can appreciate that. It's the same thing that Robinson had against Woodward, that Woodward used Robinson's data to establish what the correct strychnine structure is, and Robinson's feeling was that Woodward was stealing his stuff. Of course, that's ridiculous; if you're on the outside, you say, "What the hell. This data belongs to everybody." I can understand Lyndon Small, though. That's certainly a perfectly plausible quote from him.

BOHNING: I've come across a number of comments about that morphine review paper, because it wasn't really a review in the true sense of the word.

STORK: No, it wasn't and I'm very pleased and very proud of that paper. That was the first review; the supplement was not very good (34). That was probably written in 1950. If one teaches anything about these mechanistic arrows, this is a very nice, elegant example. I didn't invent anything there, I was just using existing structure data.

The thing which is really worth doing is to look at Robinson, the inventor, in the discussion of a reaction transformation which is a magnificent transformation in morphine chemistry called phenyl-dihydrothebaine, which is a reaction product of thebaine, a morphine alkaloid. Treatment with phenyl Grignard, followed by water, gives the normal result of adding the elements of benzene. The structure of this substance has nothing to do with morphine; as Robinson showed, it has a large ring, and one ring is knocked open. It's just totally different. Robinson makes an effort to use his curved arrows to explain this. It's absolutely incomprehensible. One should read that; it's absolutely incomprehensible. And yet, the proper use of his curved arrows makes the transformation paths transparent. It's beautiful. He got the answer immediately by intuition; he did not have the discipline to rationalize the answer, which he felt was correct. I mean, he found the structure, after all. Robinson found the structure of this substance, and then, after the fact, tried to explain how he did it. How he did it must have been by revelation, but his revelations were to be taken seriously. Then he tried to fit them into a rational mold, but he couldn't do it. But his finding the correct structure was brilliant.

BOHNING: I have another quote here from Louis Sarett about that paper.

STORK: It's interesting to hear this stuff. I always wondered about what other people say; this

is kind of interesting. [laughter]

BOHNING: I'm quoting here, "He did not, as he might have, merely write a chapter reviewing the data and the literature. Rather, as in the rest of his work, he made this nominal review a piece of incisive research in its own right."

STORK: That's pretty good. I couldn't agree with him more. [laughter] But that's pretty good. Sarett himself is a major and not sufficiently recognized early contributor to the business of being conscious of stereochemistry and stereochemical problems. If somebody were trying to decide which syntheses really were historical markers in the beginning of stereocontrol in synthesis, Sarett's would be one of those because his cortisone synthesis is absolutely one of the very first to deal with the problems successfully. In fact, the term stereospecific, which he defined for his own benefit, to be sure, I believe was first used in Sarett's paper. Or, maybe, he said stereoselective. It should have been stereoselective; I'm not sure which term he used. He defined this as a synthesis in which the ratio of the wanted to the unwanted isomers is at least whatever number you pick, which was the smallest number which he had in his synthesis; seven to one, I think. So he could call this synthesis stereoselective.

But the truth is, it was conscious planning. The crucial business is not whether somebody mixes a and b and it turns out to produce menthol. Menthol has three asymmetric centers, so, on eone level, that's a pretty good accomplishment. But this is neither here nor there, unless it actually contributes to the evolution of chemistry, which means that there has to be some rationale that can be transferred to something else, in a predictive way, from that thing. Sarett's synthesis meets this requirement. It was one of the first times. There may have been others. I mean, someone had synthesized camphor before that; a Finn by the name of Gustav Komppa synthesized camphor. It's awesome, it's brilliant, it's like climbing Mt. Everest. But climbing Mt. Everest does not necessarily contribute to advancement of mountain climbing equipment; it might. It may or it may not, but certainly it can be an extraordinary achievement in human terms. Komppa's synthesis of camphor was an extraordinary achievement in human terms. So was Rabe's dihydroquinine synthesis. But not in furthering chemistry. It was just amazing. What makes these syntheses amazing is that, given the inadequate means, they actually got there.

But Sarett's synthesis was a rationally designed synthesis, really very pretty and very elegant. Sarett himself was a brilliant experimentalist. He had actually, all by himself, in papers with just his name on them, modified cholic acid through forty-two steps to transform it to cortisone. Unbelievable; it's ridiculous and sounds silly. But Merck used it in a commercial process until recently; they may still be using it for all I know. Forty-two steps; they managed to make them efficient eventually, adding a lot to it, which was mostly done under [Max] Tishler. Sarett's synthesis was brilliant, and he did it all by his own hands, after having gotten his Ph.D. from [Everett S.] Wallis at Princeton, who was an early reaction mechanism kind of person. So

he was essentially totally self-taught, a really pretty impressive person. That synthesis is very, very, very beautiful. By contrast, if you ask who synthesized steroids, probably people would say Woodward. There's no comparison. Sarett's synthesis is an order of magnitude better than Woodward's. Woodward had four asymmetric centers and managed to control two and screw up two. Sarett actually controlled them all; not perfectly, but it's actually beautiful.

BOHNING: You also had several papers on the S_N2' mechanism (35).

STORK: That was good and bad. It turned out to be sort of the wrong kind of reaction to get involved with. It was intriguing at the time. It turned out to be a) enormously more complicated than anyone knows; even today, no one understands it, and b) not important. That's a combination that you cannot beat. [laughter] It hasn't been as bad as the structure of the Grignard reagent, which has cost taxpayers millions of dollars and is now understood to be irrelevant. It's irrelevant because it's a mobile equilibrium and what is it in the transition state, which is really all one cares about, and it has nothing to do with the position of the mobile equilibrium *per se*. It's interesting, but it's not that interesting.

It was not that bad, but it was not a reaction that has been of any use whatsoever. There are various reactions which one thinks of as S_N2', but they're mechanistically different. They give the same overall result, like palladium-based chemistry and various other things, but a different operation altogether. The operation which is legitimately called S_N2' is of essentially no importance, although they still debate whether it exists or doesn't exist.

It's a question of whether things come on this side or that side, and whether it does or not clearly depends on the nature of the displacing group. It's hellishly complicated. We did some work on it, and fifteen years later I went on this again, just to show that it was really much more complicated than anybody, including ourselves, knew (36). It became a known piece of work because there were not that many qualitative mechanistic things at that time, and these are qualitative mechanistic things. We ran into this because of this crazy business of some morphine reaction products; because of these compounds of Small, we decided we should really do something about it. I had a graduate student at Harvard by the name of Frank Clark, who eventually went to and still is at Ciba-Geigy as a senior research person. We worked on the structure of the so-called halocodides, the halogen derivative of codeine, and established the structures. These turned out to be S_N2' reactions. But the total structure of the molecule biases the results. So then we decided we ought to find out what would take place in a non-biased situation. So we slipped into this; we should never have messed with it. The result of our work was to add darkness to an obscure situation. [laughter] That was all.

BOHNING: I have a quote here from Sol Winstein.

STORK: Ha!

BOHNING: He says that it was a "brilliant contribution."

STORK: I wonder who conned him into writing that. [laughter]

BOHNING: What I was going to ask you about is that in one of those papers you had some footnotes about Ingold (37).

STORK: Oh, yes. That's actually amusing; it didn't have anything to do with chemistry. Woodward had developed a particular style at that time, using Latin phrases here and there to buffalo the assembled multitude. Obviously, I couldn't use Latin phrases, but the purpose seemed obvious to me. So my thing was that I would use some English words which people didn't know. The test of that was whether or not Barton had to use a dictionary to figure it out. So that paper has a footnote that the British school considered the S_N2' reaction their appanage.

BOHNING: I got out my dictionary to look it up. [laughter]

STORK: That's right. I was fairly pleased with that. But I got over that after a few more of these things.

BOHNING: Did you have any interactions with Ingold?

STORK: No. Never. I heard Ingold lecture a couple times.

I guess Winstein would have kind words to say about it because he sort of made the case that the relationship ought to come out syn. We had proof, quote-unquote, that it was syn, so he was favorably impressed. We now know the situation is more complex than that. It's sometimes syn, sometimes anti. Exactly which factors lead to that conclusion, I am not clear. But it's just not really very useful.

BOHNING: Coming to the Columbia period, I have a couple things I wanted to ask you. There's still an awful lot of chemistry, and I don't know exactly how you want to cover that.

STORK: You could say, "What is it that I consider to be the most interesting?"

[END OF TAPE, SIDE 9]

STORK: I guess if I think about what I've contributed to the field, it probably would be the business of stereo and regio control. And within that, probably the enamine alkylation (38). It turned out not to be great with respect to forming carbon-carbon bonds with alkyl halides, because the reaction rate is too slow, but it is great, and in fact you can't do it any other way, with the Michael type of operation. These are difficult things, and obviously my view and that of someone else, say that of Robinson, if he were alive, would be different. Robinson wrote the first volume of his memoirs (39) before, mercifully, the world was spared a second. The most interesting part is that he tried to destroy Ingold's reputation by claiming that Ingold stole his stuff.

But he says other things, which have some interest. Although he is at least willing to say that I "pioneered" the enamine alkylation, he implies that he actually did this before. This is baloney, because what he did before, he stole from some gentleman by the name of [J. Norman] Collie, who did the first alkylation of something with an enamine. But that was acetoacetic ester, and so the relationship is as if you said, "Well, you know you can alkylate acetoacetic ester, therefore you can obviously alkylate butyraldehyde." Well, there's a world of difference. You can't alkylate butyraldehyde. So what Collie had done is to show that if you made the amino derivative corresponding to acetoacetic ester, which actually exists in the enamine form because its vinylogous of an amide when it's conjugated (it's the enol, really, NH_2 "enol"), that thing will alkylate like the related enolate on carbon. The fact is that you can use a more pragmatic point, which is that before we published our work, no one could or knew how to alkylate something like butyraldehyde, and in fact afterwards you could. In my opinion, that was very important. The history of how we came to do that, I wrote up for *Science Citation Index* (40).

BOHNING: Oh, yes. Eugene Garfield and what he called "*Citation Classics*."

STORK: Yes. *Citations Classics*. That stuff is in there, so there's no need to discuss it here. At first, it wasn't so great with alkyl halides so we developed some thing which people have also forgotten where it came from, which is the metalloenamine alkylation. It turns out that if you want to make 2-methylcyclohexanone or 2-methylbutyraldehyde, the enamine is poor to

worthless. What we did is to make an imine and deprotonate the imine; alkylation of that, even when it comes from an aldehyde, is great. The reason being that the double bonded-N-R is much less reactive than double bonded-O, so it gives you time to form the imine anion. It doesn't self-condense.

So the alkylation of the metal salt of an enamine with alky halides of all types is something that we did, originally. I felt a great thrill at the time, because we showed that even a Grignard reagent (we used ethyl Grignard at the time) would deprotonate an R-CH_2-C double-bond NR, the imine of an aldehyde, rather than add to it. At that time everybody believed that the reaction of an imine would be the same as that of a ketone. They would just add the Grignard reagent to the C double-bond N, which indeed they do if the imine is that of an aromatic aldehyde, because they can't do anything else. This is all people had been studying because these are the ones that are easy to make. And so, when we decided that maybe our reaction would actually work, and it actually did work, it was a great thrill. Later on, I switched to lithium amide bases and also, for the first time, used dimethylhydrazones as special imines to do overall ketone alkylations.

Now, I'm sensitive about this because that is a reaction that everybody believes Corey invented. Now, Corey did nothing wrong. Corey did nothing wrong whatsoever. His first paper on this gives us credit, three years before, for the alkylation of N, N dimethylhydrazones. But Corey and his collaborators, mostly Dieter Enders in Germany, published masses of papers on this stuff. So it's now become the Corey-Enders reaction, which is the sort of thing that's frustrating. Corey's most quoted paper is not his most important one. Corey has many, many important papers. Corey is an outstanding chemist, let's not misunderstand what I'm saying. It's just simply that it is society that does this; Corey did nothing wrong in particular. Corey's most quoted paper is the tertiary-butyldimethylsilyl protecting group, the TBDMS protecting group. One paper that I love is a paper by Ian Fleming who is at Cambridge University, where the first sentence says, "Stork introduced the tertiary-butyldimethylsilyl protecting group into organic chemistry," which happens to be correct (41). This work was with Paul Hudrlik, who is now professor at Howard University in Washington. He has continued doing very beautiful work in silicon chemistry. The first use we made of the TBDMS protecting group was to protect enolates of ketones. Corey made contributions and a very important one is the fluoride removal of the silicon group. That's Corey, and that's non-trivial. We were removing it with dilute acid, but if you do it with fluoride, it's universal. So he contributed to taking the silicon off.

That sort of thing can get you annoyed after a while, because we don't really like to publish masses of papers on a particular thing. That has to do with marketing. I think marketing is important. But nevertheless, in a sense I want my cake and eat it too. I don't want to pay the price of establishing myself in a field. I know this wouldn't work. As I said before, if I want to sell a soft drink that is as good as Coca-Cola, I have to be prepared to make an effort to sell it. You can't just say, "Well, my cola is just as good." One has in the back of one's mind that science is different, because people know how to judge for themselves; but that's really not quite

true anymore.

I thought that was an important thing because it succeeded in doing monoalkylation of ketones and even sensitive things like aldehydes, with alkyl halides. This was in addition to what one could do with enamines, with the acrylonitrile, ethyacrylate, acrolein type of species, Michael type of species, among other things. So that was an important thing.

The other important contribution (and all of this has to do with the chemistry of ketones, what I'm talking about now) was this business of the regiospecific construction of enolate ions and their trapping as silyl enol ethers (42). The idea is that you would produce an enolate ion by a kinetic process designed to give that regiochemistry. You trap that structure as a trimethylsilyl enol ether, or TBMDS enol ether, establish whether it's correct or not by NMR, then you regenerate the lithium enolate from the silyl ether. That's our contribution with Paul Hudrlik. That is, the silyl ether with methyl lithium gives tetramethyl silane and a regiospecifically produced metal's enolate.

We were the first ones to show that lithium enolates could retain their structure during alkylation, in contrast with sodium or potassium enolates. This was done in the course of our work on the mechanism of the lithium-ammonia reduction of ketones, which we showed gave a lithium enolate. We showed that the thus produced enolates could be alkylated (43). This was the first time that either of two possible lithium enolates could be made at will and used in producing a new bond. That has been used a lot. We showcased that process in the lupeol synthesis (27).

Some things actually gave us a great thrill, which are not particularly important. Some were important, but not that much. For instance, the prostaglandin synthesis from glucose is a beautiful piece of work (44). It was not all that important, but in a way it sort of was one of the landmarks of establishing that you can use the chiral sugar pool to make a complex chiral compound which is not obviously embedded within the glucose structure. There were others like this. They were just simply a thrill. Like solving a mathematical puzzle. You get a thrill, but it doesn't mean that you're necessarily making an important mathematical contribution. But that one was a thrill.

In the *Aldrichimica* article (2), I put in the structures, as you might possibly have guessed. [laughter] I actually think every single one of them shows something that was not known before. I think this is true. Some are more trivial than others, that is true. The lupeol synthesis, I think I mentioned before; it is a very nice one. In this next one, there's no new chemistry. This is a Woodward type of construction in the sense that the knowledge required to build this was all available. It's a very pretty synthesis, but it's not anything new, except that it highlights the importance of blah-blah-blah, which however is something that one knows; in this case, that other things being equal, you tend to form a new bond perpendicular to the enolate plane. [Actually, it also showcased the reaction that deserves to be called the Stork-Danheiser synthesis.]

BOHNING: Which one is that?

STORK: Vetivone.

STORK: But that was known, and if anybody would deserve credit for that concept, it would probably be Corey, who was the first one to point out the importance of stereoelectronic factors in organic synthesis. I think that's Corey's greatest claim to fame, in my opinion. It's a very important one, in which he demonstrated that directionally, an enolate ion is more accessible perpendicular to the plane (axial) than equatorial. I think if one were really tracing where that comes from, it's Corey.

The yohimbine synthesis is a very nice application of the enamine construction (45). Another very nice synthesis was the erythronolide-A construction. That really is a tribute to the person who did it, Scott D. Rychnovsky (46). He is now an assistant professor at Minnesota, [now professor at U.C. Irvine] and just recently got a Presidential Young Investigator Award. That was a great class that year. Dan [Daniel E.] Kahne was another one; he got promoted and got tenure after just two and half years at Princeton. Not bad. He also got a PYI. These are great people to be associated with.

This synthesis did establish a principle, which is an important one in construction, which is that with all the advances which have been made, and which are important in controlling the aldol condensation, they have not reached the point (they might reach the point, but they have not reached the point yet), where you can sit down and in all cases predict the outcome of a sequence. You have a fair probability that it would be this, but you cannot be certain of it. One would like to have a thing that you can plan ahead of time, and you know it would give only this particular stereochemistry; this is what our construction was designed to do. Essentially it's a step backward. That is, the advances in the aldol condensation chemistry that were due to Masamune, Evans, Heathcock, are based on using metals to produce temporary rings through chelation. Because rings have more shape than floppy arrays, one can use them to predict and control stereochemistry much better than plain old acyclic chains.

But you can go one step further, which is one step backwards if you want. Namely, if it were a real ring, it would be even more predictable and certain, because in compounds, which have a lot of oxygens, chelation probably <u>should</u> involve this oxygen, but <u>might</u> involve this other oxygen. So the ambiguity has to do with the difficulty of deciding an order of precedence of which one is more likely, or not more likely. It does seem simple enough that you could do it, but as it gets more complicated, it's difficult. So this was, in a way, a throwback to covalent bonds, showing that you could use a simple, five-membered lactone system to assemble any contiguous stereochemistry that you want of a methyl and a hydroxyl, like the polypropionate

unit which is found in things like this erythronolide.

This other one is just an erythronolide sequence that we did earlier. We did not complete this to the large ring itself. This is a different construction. But it's the same sort of target as the complete erythro-molide A, which we did with Rychnovsky. This one was done with Ian Paterson (47), who is now a Lecturer [now, Reader] at the University of Cambridge in England and is doing very well. So that was an important thing.

This next thing is actually very, very good. The regiospecific enolate and alkylate formation is the first one to form an enolate of known regiochemistry, allowing to form a bond, even at the less likely position, more crowded position, because of this deterministic control. That was very important. [It was first used for regiospecific alkylation with alkyl halides.] Then we enlarged it to the Michael addition, which was impossible before because in the Michael, you start with anion and produce a new anion. If there's no proton source there, you just get anionic polymerization. With an alkyl iodide it would simply produce an iodide ion and that's the end. You don't produce a new anion. The question was how to solve this, and we solved this by introducing the α-silylated vinyl ketones, which actually do that. They will trap ordinary enolate, the reason for that being a trivial reason. You have to find something that would produce major crowding so that after the addition the new anions would be less reactive. Also, this something that makes it extremely crowded has to drop off when you work the reaction up, This happens to be true of silicon next to carbonyl. This silicon assisted aprotic Robinson annolation was actually one of the more useful silicon chemistry reactions we produced (48).

Another one, is the ring formation by the bimolecular reduction of a keto-olefin. It has led to a lot of further related work by many people. This we did by electron addition to keto alkyne with lithium and ammonia to produce initially a radical ion. Shono has shown much more recently that one can, not surprisingly, do the same thing electrochemically. Molander has shown that one can use samarium iodide as an electron source, to do the electron addition. Our reaction amounts to an acyloin condensation, but it was the first not to be between two carbonyl groups. You use a carbonyl and a different group [a carbon-carbon multiple bond], producing new bonds for various kinds of systems. That was a very important thing, which was done with S. Malhotra for his Ph.D., together with Dr. Uchibayashi, a Japanese postdoc (49).

There are many others, which I think have some importance. Our involvement with usnic acid is historically amusing, although it is a trivial point, a little footnote of history. This is a natural product, which was of interest to people because it was claimed to have antitubercular and antibiotic properties. It has a quaternary center, here, and it's optically active. When you heat it up it racemizes. Now, in the days that this work was done, Woodward and I thought, just in conversation, that this can't possibly be the structure because it does not have an enolizable center, or anything of the sort. Now if one showed this to any graduate student, he would immediately know the answer because, by now, sigmatropic rearrangements are common knowledge. This turns out to be one of the first. What happened is that this chiral cyclohexadiene isomerizes to an acyclic and achiral triene, reversibly. It's what is now called a

sigmatropic rearrangement. This was long before those rearrangements were codified. It's amusing that we both worked on this and couldn't figure it out; there seemed no way this structure could be right. Then one day I thought of what the answer was, and I called up Woodward. I was sitting in that little closet of an office in Chandler where we have two refrigerators now. I called up Woodward and said, "I know what it is." He said, "What is it?" I told him. There was a silence and he said, "It's pretty simple, after all." [laughter] But it's amusing that eventually, it turned out to be a sigmatropic rearrangement, and the genius that he was, gave a major significance [and a name] to the Woodward-Hoffman rules.

More recently, there are two things that I care about, which are not illustrated in the *Aldrichimica* article. One is our free radical cyclization work. That had a psychological impact, because although there was very intelligent work before, it was done by physical organic chemists. Organic chemists had a vague suspicion of them because the physical organic chemists were trafficking with the enemy, the physical chemists. Many physical organic chemists thought the organic chemists are intuitive clowns. Because there's absolutely no question that the bases of what one does in organic synthesis with radicals were laid by people like [Cheves] Walling and [Athelstan] Beckwith and Ingold's son, [Keith] Ingold. There is actually a nice quote. I talked with Ingold's son, and he said his father had absolutely no use for free radicals. One of the reasons Keith left England for the National Research Council of Canada, is because of what his father said. I've forgotten the exact quote now, but essentially it was, "Free radicals are just not tolerated in this laboratory. [laughter] If you want to do it, go somewhere else." [laughter] He went to Canada.

This was important work. The important thing we contributed is not so much the radical cyclization work, it is the demonstration that the shape that you produce by the free radical cyclization act can be taken further advantage of, if you're making a six-five or a five-five system. In six-five bicyclic systems, if you construct the system so that you close the five-membered ring onto a cyclohexane ring, the properties of the mechanistic situation are such that you must get a cis-fused ring, and if you get a cis-fused bicyclic ring it will have a convex shape. And if it has that shape then it's only further accessible from that convex side. Therefore, the act of radical cyclization would control the stereochemistry of what happens next if you could trap the radical resulting from cyclization (50c).

Now, that was thought to be pretty near impossible because the time scale of radical reactions can be compatible with intramolecular, more easily than but not necessarily with intermolecular, especially in the presence of a hydrogen donor. The time scale for something to happen to a radical is around ten to the fifth per mole per second, rather than ten to the minus five, which is found for some ionic reactions. We nevertheless succeeded in trapping the newly formed cyclic radical with tertiary-butyl isocyanide, to transfer a cyano group with resulting predictable stereochemistry, and that cyano group can then do functional chemistry. That was an important result that led to many other things that many people could do with this process. We made prostaglandins with it. But what molecule we made with it is not as important as the general result that once could make a particular shape; and that there were species that could in

fact trap to get something useful and of predictable stereochemistry as a corollary of that shape.

Another important recent achievement is something on which our first paper has just been accepted (50). We've done all the work; the first one I got myself to write is coming out in a month or two. I've just finished reading the proofs. It has to do with the fact that an awful lot of reactions which would take place, including radical cyclization, if only they were intramolecular, are borderline enough that they don't quite make it when they're intermolecular. The intramolecular advantage is a factor of maybe fifty, some number like that. That is, you gain fifty times the intermolecular rate; you don't gain ten thousand times, you gain fifty. But that fifty can sometimes be just the difference.

One such case is that you have a radical somewhere, and an acetylene somewhere. The rate of addition of the radical to the acetylene is too low to do anything useful involving trapping. It just won't make it. Let's say its butyne, a simple, non-special alkyne. On the other hand, one knows that cyclization into a triple bond can take place. So that's one of those cases, where if only you could make the intermolecular reaction behave as if it were intramolecular, then it probably would work.

Obviously, what you want to do is to have a temporary connection, which falls off after the reaction. So you connect a and b, they now react in an intramolecular mode, and the connector then falls off. It is as if you never had it. So ideally, the connector has to fall off in the process that you use to work up the product. This turned out to involve silicon again. So you attach the two reactants to a silicon atom. We've done this with photochemistry, with Diels-Alder reactions, and with C-glycoside formation, which is the subject of the paper that we have in press (51). It concerns the formation of c-glycosides of known stereochemistry at the anomeric centers, which now bears a carbon rather than an oxygen. There are all sorts of methods of making anomeric c-glycosides, but this one is totally predictable stereochemically. If this reaction gives a product, it has this structure, that's all. That is very interesting. But insofar as methodology is concerned, the temporary silicon connection is probably the most important thing we've done in some time. That's something that's important.

It also allows you to reverse normal regiochemistry. If you have a Diels-Alder reaction, which normally goes this regiochemistry and you now tether the two pieces it now can only get together this way, because the tethering constrains it to do that. So we can add ethyl methacrylate to a diene. Normally the carboxyl ends up next to this substituent, but you can make it produce the reverse regiochemistry, just by attaching and then, dropping off, a silicon tether.

BOHNING: One of the things I'm struck by, and I'd like you to comment on whether I'm right or wrong, is that it seems to me that Woodward's synthetic targets were picked in a much different fashion than the way that you picked yours. You had a methodology, which you then used to explore your targets, whereas Woodward seemed to have to go one up each time in

complexity. Did he pick the target before he worried about the methodology? Let me ask the question that way.

STORK: One important element in Woodward's targets, given Woodward's personality, not surprisingly, was drama. That is, Woodward would not be likely to synthesize a triterpene, because although it might be complex, it's not *New York Times* material. So one of the criteria, spoken or otherwise, was *New York Times* suitability. This was spectacularly successful. That is, the connection between Harvard and *The New York Times* was, and often still is, an impressive one.

[END OF TAPE, SIDE 10]

STORK: Nobody has synthesized tetracycline, as of this day. A Pfizer group with Woodward synthesized a compound that has the tetracycline four rings. But one of the major pains in the neck of the structure of tetracycline, a tertiary methyl carbinol in ring C, is not present in the simpler compound they synthesized. It's a perfectly interesting compound, but that sensitive feature is not there. It's not a natural product, although it has been claimed that you can grow some cultures in which this simpler tetracycline analog will appear; that's possible. It's not obvious. In any case, that synthesis made an editorial in *The New York Times*. Not just a mention, it was an editorial, on the editorial page about "one of the great triumphs of the human mind." Another case in which they were even more absurdly enthusiastic, and which did not involve Woodward, was when the Chinese synthesized insulin, which *The New York Times* claimed was also "one of the most monumental feats in the history of chemistry." This is just absolute hogwash; it's just ridiculous. It is equivalent to saying that a man spending five days on a flagpole without food is a real triumph of the progress of culture, or something. It's ridiculous!

So one of the criteria is that it had to be glamorous. That's not unreasonable. There's nothing wrong with that, particularly if other people haven't done it. So long as you find enough of these targets, why not? It's perfectly reasonable. In retrospect, if one analyzes what was motivating Woodward, unbeknownst to him, it could be this or something else.

I was asked to write, and did write, a small two-page obituary of Woodward.

BOHNING: That's the one that was in *Science* (52)?

STORK: Right. In that I quote something that is actually true; you have to understand the person's character to some extent. It <u>was</u> about his wearing red suspenders. His answer at the

time, which was when he was still struggling as an assistant professor, to the question was, "That's what the public expects of their heroes." So that was a picture that he had; that was perfectly clear. His other statement came when someone, half jokingly, said that something he did was slightly crooked. He took great offense to that. Not to the word "crooked;" that was okay. It was the word "slightly" that was intolerable. His response was, "If I'm going to be a crook, I want to be the biggest crook there ever was." [laughter] So there was that aspect which was certainly very important and obviously motivated him to do great things; it's not necessarily wrong. So I don't know what motivated it, except that one thing was that he anticipated glamour.

My selection of targets is not clear-cut. My involvement in taxol is clearly a slip. (I shouldn't really be doing this, but I can do it, it's okay. It's interesting.) So there's an element of that. Of course, this has been encouraged by NIH. You could not today get any money to make lupeol. You could "steal" money to make lupeol; you could get a grant from NIH to make C-glycoside and use it for lupeol. You can get away with it for a while, but not for all that long. So NIH also had a hand in the process, if you want. They support work, and I'm trying to synthesize some biologically active thing, more a thing that just has an interesting structure. NSF will support work, but NSF has practically no money. I mean, it has a large amount of money, but the money that's available from NSF, as I'm sure you know, is on the average enough to support two or three graduate students. Period. So, majorly it comes from NIH, and if it comes from NIH, so long as there are structures that have some sort of a shape, you'll do well.

So I'm not sure how Woodward selected targets. Well, part of the structural thing, he was involved in earlier; his Ph.D. thesis was involved in a minor way with steroids. What he factually accomplished was to brominate estradiol. Not one of the largest accomplishments in the world, but, on the other hand, it was early. He also did a very pretty thing, which was the so-called abnormal Reimer-Tiemann reaction. It's not useful, but it is a very cute way of sticking a methyl group between two rings. Pretty good. So he had some emotional involvement with steroids. There was strychnine, which had been one of his great structure solving successes, so that was understandable that he would try to synthesize it. And there's something that he did work on with Wasserman, relative to penicillin. This never got to anything, but that would have been a reasonable target. Eventually, he got back into this through the connection with Ciba with cephalosporin.

So B_{12}. There are things that I consider classic. The *Mona Lisa*, for example. To my taste it is difficult to dissect ninety percent of its history from the *Mona Lisa*. I'm not sure if you succeed in doing it, it would basically be as great a painting as everybody thinks it is. I am not sure that I would want anything to do with a woman who looked anything like Mona Lisa. There's just a lot of cultural overlay there. B_{12} is for chemists that sort of thing as well. A lot is to be learned from what Eschenmoser did with B_{12} or what he was forced into doing because of B_{12}. Not a hell of a lot from what Woodward did with B_{12}. Now, Woodward claimed that's how he got into what is known as the Woodward-Hoffman rules. That could be true; I have no

way of saying that's true or not. Of course, that could be an argument for drinking straight bourbon because you might not get a great idea otherwise. I don't know how compelling that is. But with Woodward, it could have happened to him with any other target; it just happened with that one. I don't know.

But if you look back at a piece of work and you say, what is it that you know now? There are several aspects, one, which could legitimately be what is it that you now know that was not known before? That's a tough one. For example, making polyethylene is not synthetically complicated stuff, it's not mechanistically complicated. It's not the multi-step, Mount Everest kind of stuff. But nobody could deny that it's enormously important. So something could be not terribly glamorous, but extremely important, or vice versa. I think that B_{12} was vice versa. It's enormously complicated.

There's a worse example. A recent example would be [Yoshito] Kishi's construction of palytoxin, which *The New York Times*, with its usual perspicacity called the Mount Everest of organic chemistry, or maybe it was Kishi who called it that, I don't know. It's nonsense. It's a common nonsense in current organic synthesis. The reason why the public, and by public I mean chemically-aware public, thinks that synthesis does not have much future is an argument that goes something like this. It is clear that you can now make things like B_{12}, so you can make whatever you want to make. This impression is reinforced because the Kishi palytoxin thing has I don't know how many asymmetric centers in it. If you tell me that it's one hundred, it's quite possible. It's some really phenomenal number; maybe fifty. It's some huge number. And people can put that together, asymmetry and all. Fantastic. B_{12} does not have that many asymmetric centers, maybe four or five, but generally it takes forever to write it and most people can't do it, so it must be very complicated. Besides, it took forever and masses of people, so it must be complicated. But the fact is that the state of the art is nothing like what people believe, and that's easily demonstrated. That state of the art has reached perfection in only one area. It <u>is</u> perfection in the field of oligodeoxynucleotide synthesis. That is absolute perfection. You can make a molecule with forty asymmetric centers in three hours, all while you sleep, by linking together ten pieces; each one has four asymmetric centers. You produce a molecule automatically in a predictable number of hours with a predictable purity. It's incredible. So that is perfection.

Contrast this with something like taxol, which is a perfectly good example. People have been working on its synthesis now for several years, and serious work has been going on this target. When it will be done, it will be something like thirty-five steps. Assuming somebody works with reasonable seriousness you should be able to do one reaction a day, so it should take thirty-five days, so about seven weeks, if you work on Saturday and Sunday. But we know, you know and I know, that it's likely to take something like years. The difference is the state of the art because these are not stupid people who concoct these constructions.

Furthermore, there's another thing that gives a hint that there's something funny there. By now, there must be at least forty groups worldwide, probably more, working on taxol. In the

greater New York area there are at least six. They're all different. They're all different syntheses, which sounds nuts but you don't get a huge waste of money because everybody's trying to do the same damn thing. This would be a problem if you were doing mechanistic work or structural work. If people work on a structure they must all end up with the same structure if they are right. If people work on a mechanism, mechanistic work, they must end up with the same mechanism, if they are right. But in synthesis, they can all end up with something different; it's like writing a novel or something like that. But that also suggests that the state of the art is not that advanced when all these people, who are very competent, all try to do the best they can and they all come out with different answers! [laughter] So that is the state of the art. It's nowhere near the sort of perfection which you know is possible, as with (and admittedly much simpler because it's repetitive) oligonucleotides. But even with polypeptides, we can't quite do that. That is less repetitive than the nucleotide business. Even if polypeptide synthesis is not that automatic, it's getting close.

Another problem is the following. People say, "Oh, there are sixty asymmetric centers in palytoxin," which is a red tide poison for fish. But these people are all cheating. How do they synthesize a sixty asymmetric center compound? They link together, let's say, ten pieces with six asymmetric centers each. Anybody who makes a polysaccharide or a polynucleotide or insulin, for that matter, does that. Insulin has a hundred asymmetric centers, and somebody has made it that way. "Oh, that doesn't count!" But that's exactly the way they make these one hundred asymmetric centers. They don't solve any hundred asymmetric center problems. If that could be done, they would be right. Chemical synthesis would have reached perfection. But they only solve a six asymmetric center problem over and over and over again, and then link them all together like sausages. That's a very different thing. That's not the same thing at all. So the state of the art is not nearly what people perceive. Essentially the public, and by the public I mean the educated press and the chemists who are not doing synthesis, don't really understand what's involved in this kind of synthesis, because it's not easily comprehensible, and so much showmanship is involved anyway.

Part of the Woodward mystique was due to the fact that he could give a lecture that was absolutely fantastic. He would just start at one end of the blackboard, and the structures were good enough to be photographed and used directly. You didn't need Chemdraw; just use his structures. And they were drawn in color, too. But he would do things like drawing the first seven steps upside down. Nobody knew they were upside down. You'd see it there, and you were killing yourself trying to find out what the hell was going on, and then magically he changed the drawing by turning it around—ah! This is great; as a theatrical experience, it was fantastic. Educationally it was not that great, because people had no clue what the hell he did and could never reproduce it in a million years. But it was impressive.

In that sort of thing, the magic is that the audience is simply told that A goes to B, which goes to C, etc. The lecturer spent seven years trying to make this molecule; he gives a fifty minute lecture. The picture that is conveyed is that he knows what he's doing, A goes to B goes to C. Obviously nobody wants to take two hours to tell you about each step. Who cares? It's a

little bit like somebody who climbed Everest; do you really want to know everything? So, the picture the audience gets is of a much more rational and controlled process than it really is.

A lot of people are doing very good synthesis in this country and in Japan in particular. It's less today in England because they are in such bad financial shape; it's not their fault. The truth is the British are still doing extremely well, considering the circumstances. The Japanese are doing great, unfortunately. I should not say unfortunately, but, well, they're doing great. And we are doing quite well. There's a lot of very good synthetic work. There are people like Danishefsky, [Paul A.] Wender, [Larry] Overman, [Clayton] Heathcock, but not that many others. It's not that many. [Incidentally, all four were postdocs at Columbia.]

There are lots of very competent people who do great things. Some of it is moving the field forward; there's no question about that. The total number of people who do intelligent and important things is higher than it's ever been. There aren't that many people who could put together a strychnine synthesis. Strychnine has only once been synthesized by Woodward; nobody else has done it, [since this was taped, it has been accomplished several times] which is really impressive. To my taste Woodward's strychnine and reserpine syntheses are an order of magnitude more important than B_{12}. That is not necessarily what the population believes.

I'm sure that was more than you cared to hear. [laughter]

BOHNING: No, absolutely not. I just wanted to ask you a few more things about Columbia. You've been here for some time. Did you ever have offers to move elsewhere?

STORK: Well, I think we mentioned Pauling. Incidentally, Pauling visited me in that little closet that was my office. That was impressive. That little closet also had Pauling in it. Some of the molecules in there are exhaled by Pauling and are stuck on the wall. [laughter] Yes, Pauling came in to talk me into going to Caltech. He actually came, personally. This story is one I couldn't resist telling. I told that story and I think it's in there (2).

BOHNING: Yes. It is.

STORK: About how he came to lunch.

BOHNING: You said you liked the large city.

STORK: Yes. I went through all sorts of rigmarole with the Caltech thing. I told Hammett I

had this offer. It was not a question of playing games at all; today people would think I was crazy. I told Hammett that I would just think about it, and that I would certainly let him know when I decided one way or the other. He'd be the first to know; it was not a question of playing games. I went through making various lists; plus this and minus this.

There's actually a very useful way to tell what a person's subconscious feels. You get them to make lists, or maybe you flip a coin. I've used this with friends of mine, trying to decide should I take this job or that job: you can just flip a coin. You can tell from their reaction what their gut feelings are, which they're not necessarily aware of. If it comes out in favor of doing this or that thing, they say, "Well, I don't know about that." [laughter] So any time my lists came out in favor of going to Caltech, I adjusted the parameters, so after a while I decided I just didn't want to go out there. [laughter]

I could be happy anywhere; the truth is I was quite happy in Madison even though, when it was minus twenty degrees Fahrenheit, you get the acute experience of having your scalp shiver—a strange thing—if you don't wear the proper clothing. [laughter] But you get used to it. I must say, if you have to be stuck inland, Madison is one of the nicest places. Have you been there?

BOHNING?: No, I've never been to Madison.

STORK: It is a nice city. It has a nice lake called Lake Mendota. There's a cafeteria where you take your tray on the terrace overlooking the lake with boats. Pretty good. Nice woods. I liked it there fine. Most chemists spend so much of their time in the lab environment that they care about the quality of the students, and their lab, and plausible colleagues, and bothersome colleagues (only minimally). They could be almost anywhere.

I have to prove this. I've convinced myself that I like an urban environment much more, but I'm not sure that this has really been tested. It's been the environment I've been in, whether I was in Paris, or even Nice. Nice is an urban environment; it's over a million people. Where else was I? Madison was not a large city, but then I was in the lab. Boston and Cambridge were an urban environment. This is an urban environment. I have a feeling I would go nuts, if I was not in a large city. But that's probably not true, because I would be in the lab, and I would be quite happy. [laughter] My kids would probably like it better not in a large city, so it's not so obvious.

What it may represent is a considerable amount of inertia. If you are at ease with this particular chair, you don't necessarily give it up for this modern looking contraption.

BOHNING: Frances Hoffman also credits you with building up the organic group here at

Columbia from obscurity in 1952 (2).

STORK: That's her word, which she gathered I guess from other people. Well, obscurity is not fair, because the fact is that the major person associated with organic chemistry here was a gentleman by the name of Marston Taylor Bogert, M. T. Bogert, Col. Bogert. I guess he was a colonel in the chemical warfare service or something like that. No, maybe it was not colonel, but it must have been something of that type. It's very difficult to look at things and decide if they were important or not, because now they no longer are. If I look at Emil Fischer's work, I say that's kind of a silly way to make glucose. But if I put it in context, it's awesome, it's awe-inspiring, it's extraordinary. Bogert was one of the pioneers in terpene-related synthesis at that time. You say, well, that's pretty trivial, but at that time he was a pioneer. Bogert was before Fieser. I really don't know what the dates are, but he might have been contemporary with Roger Adams and people like that.

BOHNING: Oh, yes. Probably even a little earlier than that, I would say.

STORK: Probably even earlier than that. But if earlier than that, there would really not be all that much stimulation. So it's pretty impressive. Bogert was here long before my time. I don't know when he was here. There was a time when Columbia was really not obscure. Elderfield, whose name was mentioned before, was, in fact, a major figure in American chemistry. That's correct. Curtin was mentioned before in another context and is a person who has not published very much. He is at Illinois, as you probably know. He has not published very much, but what he does is extremely intelligent and sophisticated. He studies reactions in solid crystals, and such; he is really a pretty sophisticated person.

So, by the time I came here, there were great people. Physical was always pretty good. [Harold C.] Urey was here at one time, and so was [George] Kimble. So there were really outstanding people. LaMer was well-known. And at the same time here there was Doering, Elderfield and Curtin, all of whom were outstanding people. At that time Curtin was one of the very definitely recognizable names. Any one of them could not stand the other two. So they all simultaneously decided, "I've had enough of this. I'm leaving." As it happened they all left, because they all came to that conclusion. And so the place emptied. Doering went to Yale. Elderfield went to Michigan. I remember he became interested in growing various kinds of roses in Michigan. It was either Michigan or Michigan State; it was one of those places [Michigan]. So he went from here to there. And Curtin went to Illinois, and that was that.

The only person who was left here, believe it or not, was a former student of mine, one of my first students, Harry Conroy. In many ways it's a sad story, that of Harry Conroy. He was one of the early geniuses of structural chemistry. I mean early in his lifetime, not early in the history of chemistry. He actually did something that was certainly easily as good as anything Woodward ever did in structural chemistry, which was to deduce, just from reported chemical

transformations, the structure of picrotoxin. He later added NMR data. He was an early practitioner of NMR in complex structure analysis. The picrotoxin paper of Conroy is a classic. There's only one name on that paper; Conroy did the entire work in an independent year as a postdoctoral fellow at Harvard. It was just absolutely a brilliant piece of work. He came here as an instructor.

The entire department consisted of Conroy in organic chemistry, one instructor and another person by the name of Layton McCoy, who eventually went to the University of Missouri. Layton McCoy was a good organic chemist, but also non-tenured. So there were two non-tenured people representing the entire organic or non-physical area because there was probably no inorganic chemistry at the time. There was food chemistry, which was the closest thing here to biochemistry. There was a gentleman named [Charles Glen] King, who claimed to have had a major part in discovering vitamin C. That's not totally inconceivable; that could be true. He did some feeding of rats, or something like that. But that's all. So the fact that there was friction and that it was an impossible situation is certainly clear. There was nobody to act as a spokesman for the organic group.

Conroy decided he had enough of that and left in midterm. He essentially told people to go to hell. He was a young man and he was all alone here. He expected major approval from Woodward and Doering, who by that time had left here and was at Yale. Woodward and Doering were very good friends and their verbal attitude towards the world was essentially the men on a horse picture. If you don't like it, tell them to go to hell. So Conroy, having actually performed according to this message, expected, minimally, to be patted on the back. What they told him was what I had told Conroy before, "You are crazy." The minimum that I had tried to explain to Conroy was, "When you quit a job you should have another job lined up; then you can be as outrageous as you want. But it's bad to do it in reverse order." [laughter] Poor Conroy. It took him a half a year to get a job after he got out of here. And it was only because Max Tishler at Merck was extremely impressed with Conroy, whom he had met at Harvard. Tishler created a position at Merck to let Conroy do whatever he wanted for a year. Remarkable. Then Conroy went from there to Yale.

That only left Layton McCoy at that time. Otherwise, I would probably be selling soap somewhere. But the fact is that Roberts was pushing my coming here. I think this happened because they offered a position to Jack Roberts in this department. He was not willing to come, but he suggested that they needed to get me here, which was nice. And it also was nice because they actually needed someone. Oh, there was Charlie Dawson. Dawson had become interested in biochemically related things, such as purifying the proteins that are involved in poison ivy transmission. So even though he taught elementary organic, he was not really involved in research in organic chemistry, except in a very peripheral way.

[END OF TAPE, SIDE 11]

STORK: He was making various phenols to see where they complex with proteins to make antibodies that were related to poison ivy.

The department was not obscure when I arrived; then it just exploded. As I described the laboratories to you, this was not a place that was even conceivable at that time for an organic chemist. Even now, after we spent an outrageous amount of money, it's barely plausible, in present modern times. Any time that we bring somebody in here it costs a million dollars to set up a place that is operational, which is not unlike what it costs anywhere else, but it does cost that here. So it was rejuvenated.

Now, you can say that I built the department; one of the major things I did was to bring Breslow in. After that we both decided that we should add Tom [Thomas J.] Katz. Tom Katz has not published all that much, especially in recent times; he's having some trouble adjusting (and so have I, so has Nakanishi, and so has Breslow) to the difficult, let's put it that way, to the difficult science support climate at the moment. It's difficult. But Katz is an extremely valuable member of the department. He's very smart and he is a very good lecturer. He is perennially young and interactive with the people whatever age they may be. We brought him from Harvard, where he actually got his Ph.D. with Woodward. He did not postdoc, but came here directly.

[Nicholas J.] Turro came through the Jack Roberts connection. I was involved in bringing him here, but only as a conduit, not as an initiator. It was Jack Roberts who was visiting at Chicago and said it would not cost us much to bring him from Chicago to New York; it was well known that we were cheap. So we could afford to bring him over here, which we did. I was sold on Turro. I have no idea what he is talking about in his photochemistry. The truth is I don't know that much about it, except in general terms. How or where it fits in the development of photochemistry I would have no way to tell. But the main reason why I was suggesting bringing Turro here was that he told a joke that was so bad, so outrageous, and so long that I decided he must have enormous self-confidence, he clearly has enormous drive, and is clearly intelligent, so obviously he would be perfectly okay. But it's an exaggeration to say that I was involved in building the department. The initial thing was really convincing Breslow to come here. That's essentially it.

Oh, there is Clark Still. Clark Still got his Ph.D. at Emory with one of my early Columbia graduate students, David Goldsmith. So he got his Ph.D. with one of my graduate students and then became a postdoc in my group. I made what he would describe as an outrageous mistake. (He is a very kind person, so he might not say this.) The outrageous mistake was to exile him to Vanderbilt, which I think is what made his career. It forced him to work on his own. His ideas and his skill were so much better than anything they could get, that it immediately became obvious that he was doing great stuff, and we brought him back here. So that was pretty good.

Then there is the Paul Wender case. He got his Ph.D. with Fred Ziegler, who was one of my graduate students here, and then was in my research group. In fact, he got his job at Harvard

as an accident. Woodward called me up to ask about person X, whom I will not mention, who was in my group at the time, because they thought that maybe they should consider him seriously for a junior appointment at Harvard. X is actually very good and has made a nice career, and he's doing fine. But I really didn't think there was a chance that he could make it, and what I said is, "Well, that's perfectly possible, but you have to look at Paul Wender." He said, "I've never heard of Paul Wender, but okay." So they did, and they did offer him a job. As they say, the rest is history. He's done very well, and obviously became a very fine person. I remember that Paul Wender had an offer at the same time from Indiana. We spent a lot of time discussing it. "Do you want to go to the safety of Indiana, where it's unimaginable that you would not get tenure, or do you want to go to Harvard, where it's essentially unthinkable that they would give you tenure. But the experience may be worth it." So eventually he had the courage and guts to go to Harvard and said, "Okay, let's do that and I'll do the best I can." That worked out pretty well.

Now, we have slipped here. I didn't realize this until recently. One of the bad by-products of having a sort of family department is that we did not realize that we are growing old. All of a sudden Turro, who I permanently think is thirty-two, turns out to be fifty. And Breslow is having a party at an ACS meeting to celebrate his sixtieth birthday. Now, he doesn't look sixty, even if you know that he's sixty; he looks and he behaves as though he was forty-five. But the fact is that he is sixty and Turro is fifty, and we've let that happen.

Probably it was not our fault. Until we got this outrageously expensive modest addition to our space, the structural situation at Columbia was just that we had no place to put anybody. It was the combination of possibly poor planning and financial difficulties, the fact that New York costs twice as much to do anything as anywhere else, whatever it is. That together with the fact that we didn't realize in a conscious way that we're getting older and that something should be done about it, turned out to be a serious problem.

So we wasted a lot of time. We wasted more time because we decided to build a new building and did three years of work with architects to produce this building, which was supposed to be on top of the gymnasium. Three-dimensional models of the building were constructed and discussions were held about whether there should be a sofa against this wall or against that wall and were they in the student room or was it the entire sofa group, which I liked. [laughter] After that a member of the administration finally said, "Incidentally, how much is this going to cost?" There were two architects, and one shuttled back and forth from London, where he was, across the Atlantic, at the university's expense. He was a very good architect. His three-dimensional model looked nice. At that point, the whole thing was killed, because the answer was thirty-two million dollars. The university said, "Well, we were thinking more like eighteen million dollars." I don't know if you've ever been involved in construction, but once you have some plan, you can remove anything you want from it and it will not decrease the cost. It just simply doesn't do it. So you have to start from scratch. So that cost us another three years. Three years doesn't sound like much, but it's a lot.

Then we made another appointment to the department. There's a young man who's very

good. In fact, he is probably going to be heard by the operation much beyond anything that is reasonable. That is Bob Kennedy, Robert Kennedy. He's a very intelligent guy and he has good ideas. When there's a colloquium here, he always asks not just a question to show off, but it's an intelligent, to the point question. He knows what he's doing, and he's not going to make it. Why not? Because a by-product of the operation is that there is a certain personality to the department, and we are responsible for this.

The Columbia personality has been unkindly described as a group of people whose natural tendencies would be to grab the microphone while someone else is still using it. That's an unkind statement, which is not any kinder because I made it, originally. [laughter] But it has some truth to it. This may be the description of anyone who is going to make it in this world of chemistry; it's not that different. But it is damaging. This is one difference with the European system. Overall it may well be beneficial to society, but it's a difference that is tough on people, which militates against doing things which are long term, and starting them too soon. It's difficult. He does not have the glamour, if you want, or the marketing, that will make it likely that my colleagues would accept him. They wouldn't even involve me because by that time I will be officially retired. He probably won't be promoted, which means we will lose another six years. Quite aside from human problems and what have you, if he doesn't stay, you've lost him, and it's also money; you've lost both financially and in momentum.

You don't always do that if you have a system like Harvard, which is built on a rotation of people through the department. That's okay, but that's not what we've been doing. Then you'd have to have more than one at the same time. You'd have to have several. We finally added young people in other areas. We have some very good inorganic people, one of whom we just lost to Harvard. That's [Charles M.] Leiber, who was impossible to keep because they really offered him everything he could want. In fact, they included things that he never thought of. But he's really very good.

But the only one we have left is outstanding. Gerard Parkin is outstanding. We're promoting him to tenure now. There is also a young physical chemist; he's outstanding. I don't know what his future will be. We imported a beginning, middle-aged physical chemist from the University of California, Irvine. He is [James J.] Valentini. Everybody tells me he is an outstanding experimental physical chemist, which is probably true. He certainly seems to be an outstanding person. So we're making progress in getting this ship back into shape.

But we do have a problem, which is a serious one in organic chemistry. Well, take the field of synthesis and the people that we have left here. Nakanishi does not really do synthesis as a contribution to synthesis. He may actually synthesize something; that's different. The good news about the department is it still has a remarkable range, from touching biological things with Nakanishi, to touching physical chemistry with Turro in photochemistry. In fact, he could just as well be a physical chemist, but he is an organic chemist. Nakanishi does organic structure and biological things like the mechanism of vision and things like that. Breslow does mechanistic biochemistry and mechanistic things, but also a little synthesis. Katz is not all that much any more and was interested in a pretty narrow area of organometallic chemistry.

Synthesis is where we put him, when we added him to the staff. It was like when they added Cram at UCLA. Winstein thought he was adding a natural product chemist, because that's what he was interested in. But to survive at UCLA you had to do mechanistic stuff because Winstein was overpowering. So in order to show he could do it as well as the next person, he became, I guess probably to the world's advantage, a physical organic chemist.

Breslow does not really do synthesis, except in a minor way. Still has now switched over to very outstanding stuff, there's no question about that, which deals with modeling, which he was majorly involved in putting out. There's no question that this place owes a lot to Clark Still. This place has strength and self-confidence as exhibited by the fact that both Breslow and Still turned down full professorships at Harvard. That's pretty good, after all, because whatever Harvard's quality, it can't be that bad. [laughter] So it's not so bad. But it's the renewal part that is bothersome. Still is not that old. I don't know how old he is, probably more or less Wender's age, I would guess, something like that.

So that is the problem, but how to solve it is not so easy. I mentioned that we would love to bring Wender here. We would love to bring even half of Danishefsky here. There is this peculiar deal that he has with Sloan-Kettering, and his postdocs could stay there doing biochemistry. That's not ideal; it would really be better to bring Wender here. Or it would be great to bring Overman here; we tried in fact to bring Overman here. He was willing to come, but his wife likes California, which many people do, and so she didn't want to move here; she has a nice job there. Paul Wender also; his wife has a job that she likes, unfortunately in the administration; she is an assistant dean at Stanford. What's in our favor is that Stanford is in a kind of a minor destabilized situation because of the trouble with their poor president. And it's possible that Barry Trost, who's an outstanding chemist, may be driving Wender nuts; that's conceivable. [laughter] I mean, no reflection on either one, but two highly motivated people could do that. So there could be some perfectly good possibility of doing it, but the problem is always one of space.

So we do have problems. These are tough financial times. The university has already spent an outrageous amount of money constructing whatever they did construct. The department eventually borrowed money from the university, in the flippant belief that the university would not collect it back. But the university in fact is recovering one-tenth of that loan every year from the fund that it gives the department. It was really a loan. We said, "Sure, we'll pay it back," and they said, "Oh, yes you'll pay it back, because we'll take it out." We thought we would get the money and then we wouldn't have to give back it to them. [laughter] This is not the time that it is all that easy to do things, so there is a concern about the future.

There is a very good thing about Columbia, a major good thing without which we could not survive. They own a lot of real estate around the place, and it is possible for both professorial additions and graduate students and postdocs to be housed at about half the going rate because Columbia makes up the difference. The counterpart of this is that Columbia does not make as much on its investments as it ought to because its money is tied up in this non-productive real estate, which if it didn't have, it wouldn't have anybody. So it's complicated.

It's complicated, but there is New York. New York is great. What makes New York great it's not that you do all these things. I would have no doubt whatsoever if somebody tells me that they do more, that they go to more ballet, more concerts and more theatrical productions in Ames, Iowa than they do here. I would not be surprised at all. It's probably true, because in Ames, Iowa, the ballet company goes through, you go. [laughter] Here, you just never go. You never go because it's there all the time. It's like you don't go to see the Eiffel Tower if you live in Paris. It's there, and you can always go there. I never saw the glass flowers in Cambridge, Massachusetts. They were next to the chemistry building. I should go and see the glass flowers. So you could go to this, you could do that. You know you could. You could just drive down and go. Once in a while we actually do, but not as often as you might think. For a certain type of people, and I think it could be true of Paul Wender, that sort of thing is important though not used. It's also expensive, so the counterpart of it is that it's tough for people. For young people, starting a family here would be tough; tough or maybe even ridiculous. I'm not sure which. They can live outside the city, but even that is expensive.

BOHNING: Harry Gray was here for a while, wasn't he? But he left quite early, or he was quite young at the time.

STORK: We sort of established Harry Gray. He came here directly from a postdoc abroad in Denmark.

BOHNING: That was with [Carl] Ballhausen, wasn't it?

STORK: Yes. He left here to go to Caltech and has remained a friend of the department. He is the one who sent us Lieber, who's now left us to go to Harvard, but at least he came here. He's also the one that's contributed to stealing Jackie [Jacqueline K.] Barton. So I guess it works both ways. So he was here and is obviously an outstanding inorganic chemist.

Another outstanding person who was a shame to lose, but there was nothing we could do about it, was [Richard N.] Zare. Zare is an outstanding physical chemist, really outstanding, at Stanford, and is doing very well. He was not unfriendly to the place. He left on good terms. Let's say it was just an offer he couldn't refuse. They built him up an entire research laboratory in a new building. We can't do that, so there is a limitation as to what kind of person you can get here. This argument that we can succeed in doing something worthwhile with the organic part of the operation, and now with the inorganic, if we ever succeed, and possibly biochemistry, by taking people that are quite young. They get used to being in New York; they learn that it's possible to do it. But by the time you get somebody who has young children and is established somewhere in the Midwest, and he sees how much he has to pay for a house here—that's hopeless. So the only place you can get people that will not be shocked out of their minds

would probably be the Boston area or the California/Berkeley/Stanford area. That's it! Everywhere else, they'll say, "This is ridiculous. You can't do this." So that makes it difficult. Probably that is the strongest argument for hiring young people; but then if you do, you have to be either very lucky, as we were, or a combination of that and special circumstances. Or you'd have to add several at a time, which we cannot really very well do. So we have a problem. We have a problem.

BOHNING: What about attracting graduate students?

STORK: I've mentioned two of the most recent graduate students I've had. Well, I had three at the same time. Two of them are becoming well-known, and the third one is an assistant professor at the University of Arizona. The other two are Rychnovsky, who has not yet been promoted to tenure, but obviously would be, certainly within four or five years. The other one is Dan Kahne, who's getting to be known all over the place. We offered Dan Kahne to move here, but we were not willing to do what our mind told us was the wrong thing to do, namely to give him tenure immediately. He would have been an idiot, as I told him, to accept it. We were right in doing what we did, and he was right in staying there, especially since that forced Princeton to give him tenure. So he's doing all right. These people are as good as anyone in the country. As I said, they both are Presidential Young Investigators.

Why they show up here, that's something else again. But we've had extremely good people, either as postdocs or graduate students. Overman was a postdoc of Ronald Breslow. Wender and Danishefsky were postdocs in my group and so was Heathcock. Other graduate students were people like John McMurry at Cornell or Bruce Ganem, also at Cornell, and [Jeffrey] Winkler at Pennsylvania. These people were graduate students here, and there are many others who were really very, very good. Paul Grieco is the one who finished lupeol. Burgstahler hasn't done as much as he should have. He's been a professor at the University of Kansas. There are no complaints about them. The only complaint conceivable is that once in a while one has the feeling they could work harder, but that is a feeling we probably would all have, no matter what they did. So I'm not sure that that's reasonable.

BOHNING: That's an interesting comment, because I've heard that from some other people.

STORK: Yes. You always look back to the good old days. The fact is in the good old days you had no choice, because unless you crystallized a compound, distilled it, and purified it, you didn't get anything. That took time. The operation demanded your presence. Like when you feed rats; you've got to show up, otherwise they will die. So you show up in the middle of the night if you have to. Today the thing is much more intellectual. You have to think more than you used to; there's no question about it. You do have this mass spectrometer data, you do have this NMR data. You have to make something of it. You spend much less time trying to get this

material to crystallize or something like that. There's much less that's involved in developing technical skill. Anyone can pretend to be a nurse, as they all do, and inject some stuff through a rubber septum and then take a spectrum. There's major disaster if it crystallizes, because then maybe your sponsor will demand that you crystallize it again and take a melting point. Do we have such a machine? [laughter] It's different; it's something else. So it's a different game, which requires more thought; there's more information to digest, and more stuff to learn.

It's always true; it more or less almost takes care of itself. The very best people work the hardest. Dan Kahne and Scott Rychnovsky could have sailed through with no problem at all working minimally, but they worked hard. Kahne was in here Saturday and Sunday, all the time; so was Rychnovsky. These people worked so hard. Why? Because they're very good. Part of being very good is being very excited about it and so those people work very hard. The ones that don't work so hard are the ones that rationally should work much harder because they're not that good, but they probably would never become that good. [laughter] Still it's frustrating. Once in a while I come in here. Say, it's ten o'clock in the morning. Nobody. Where are they? One the other hand, another time I've come in here on Sunday, and they're working. So it's just simply that they have a different kind of operation.

BOHNING: Did you ever have any interaction with Kurt Mislow when he was at NYU?

STORK: Socially only. That is, I know Kurt; I've seen him recently at Princeton. He is a very, very likable person. He's obviously a very smart person. I don't understand why he's fascinated by that complex problem of chirality. I know he's doing it extremely intelligently because he's that kind of a person. I don't emotionally relate to it. The apple business is interesting. He's interested in the mathematics of cutting an apple. You know what they say, that if you cut an apple in a certain way, which was worked out long ago, the so-called *coupe du roi*, which was initially done in the French king's household by someone, you get two particular pieces, if you do the cut right. I've massacred so many apples because of Mislow. [laughter] But the fact is, you get two pieces which are obviously both the same absolute configuration and you put them together and it produces an achiral apple. The question is, how can you mix plus with plus and get dl? It's obviously intellectually a very interesting problem, and that one I relate to, to some extent, because I can understand it and I've seen these pieces of apple. [laughter] But otherwise, no.

[END OF TAPE, SIDE 12]

STORK: These people are important. Even though what Kahne does is nothing like what Mislow relates to professionally, Mislow is able to see that Kahne is an outstanding guy. You can judge; obviously I'm biased towards things which I can understand, like intensity. How much does the guy seems to care? Which is very related, so that I say, "I know he's a very good

physical chemist." What I really mean is, "He seems to be intensely interested in this stuff, and if he has some focused drive then I guess he can probably do good things." Now, whether I would be able to recognize someone who is totally withdrawn and will be the next Einstein, is highly debatable.

And that's a problem, because obviously the American higher education system is to some extent focused on the easily recognizable focused drive and enthusiasm, which is important. It's certainly important in "making it." Whether in the process we eliminate people who would become very important, I don't know. Whether it matters, I don't know. One can argue that if they end up in industry, so what? That's a perfectly good place; there's nothing wrong with that. Whether they're diverted to become second rate lawyers, that's more serious, if it should be happening; maybe it doesn't happen.

I know at least one who became a patent lawyer, through no fault of his own, and would have been one of our outstanding chemists. What happened to Conroy was his own fault. What happened to Conroy I mentioned before.

Whatever this little book (53) on Woodward says, Woodward originally had no use for x-rays. The reason for that was that in the early days of x-ray structure, Woodward knew the structure of penicillin and strychnine before Dorothy Crowfoot determined it. So it was easy for him to become convinced that there was a good chance that these people could not figure out what it was with their x-rays, unless they already knew what it was, which he held onto. Now, the physics of x-rays is such that this makes no sense whatsoever, but that was not involved. You see, they were suspicious.

But then, one of the first times that the situation was clearly reversed, involves a structure that Harry Conroy became interested in. It was different with tetracycline. Woodward figured out the structure of tetracycline before x-rays. So that all added up. Conroy was very much interested in an alkaloid called gelsemine. Gelsemine has a certain structure, and Conroy, fresh from the great achievement of the structure of picrotoxin, dealt with gelsemine. He made one mistake. One connection was wrong, which was painfully made clear by the x-ray structure. The x-ray was correct, and that shook Conroy very much. Structure solving was what he loved. Somebody was stealing his girlfriend. He just gave up organic chemistry altogether and decided to become a quantum mechanician. Now, that shows how smart he was. How many organic chemists can switch to doing quantum mechanics? He locked himself up at Yale for two years, just showed up to teach his course. He taught himself quantum mechanics, inventing methods. I've talked to [John A.] Pople about it, because I couldn't believe it. It's one thing to love quantum mechanics, but it's another thing to actually make any kind of contribution. Pople said, "No question about it." He said there was this type of differential equation or integral equation that wasn't solved until Conroy became the first one to show that you could do this by using Monte Carlo methods. (These are words for me; I don't know what they mean.) He was the first one to produce ab initio the energy surface for a three-electron system, when before that it had only been done for two electrons.

My feeling is that what Conroy did is fabulous, but there is no way that you can have extended the method to any real molecules. It was an incredible achievement to do this [before computers] with three electrons. It's really fantastic. Eventually, Yale tossed him out because they said they had hired a person that they thought would be a synthetic chemist, and there they had a half-baked, so far as they could tell, or half-believable, certainly not believable, quantum mechanician on their hands. They could not give him tenure.

And at that point, Bothner-By, whose name came up before, was at what was at that time the Mellon Institute. He knew Conroy when he overlapped with him at Harvard. He offered Conroy a permanent position on the Mellon Institute staff as a quantum mechanics person. It took tremendous courage. Conroy slowly came to the realization that his approval did have limitations, and that he could only go so far. If Conroy had become interested, let's say, in x-rays, he would have probably have made great advances in x-rays, with the combination of what he knew. But he was damaged psychologically by x-rays and could not forgive them.

He went to MIT for a postdoc for a sabbatical year, trying to get interested in problems having to do with biology or something like that, but he did not get interested in that. He went back to some complications, because Mellon had merged with Carnegie. They decided that Conroy had to teach, because it was now a university. Conroy pointed out, quite correctly in my opinion, that he was hired to be at the Mellon Institute, and he'd be damned if he wanted to teach. He didn't feel like teaching. Eventually they bought him out, as far as I can see. I once called Carnegie-Mellon up (and I don't know if it would be true now) to try to find out where he is, and they denied he was ever there. [laughter] I mean, they wiped him out in the Russian tradition, the way they used to do with various people they didn't like. The rumor is that he is a photographer in Pittsburgh, and that's possible. His father was a press photographer, and he had some cameras. It's possible that he became a photographer in Pittsburgh. That's a shame. So that was the story of Conroy.

BOHNING: Well, I've run out of questions at this point, although I know there's more that we could discuss. Is there anything else that you would like to add that we haven't covered?

STORK: Not really.

BOHNING: I appreciate your taking the time to spend the day with me.

STORK: I appreciate your taking the time. I enjoyed it. I guess there's nothing one likes better than talking about oneself. [laughter]

One of my favorite pets is a reaction that is well known, the Arndt-Eistert reaction, which has nothing to do with either Arndt or Eistert. That's the only one I know that you can

say that about. It always fascinated me. You can't say that about the Diels-Alder reaction. [Otto] Diels and [Kurt] Alder really did that. [laughter] Okay. There's a reaction that is called the Birch reduction. Charles Wooster discovered it, but nobody paid any attention to it because it was a DuPont patent (54).

There is also a large ring acyloin cyclization.

BOHNING: Oh, yes.

STORK: Virgil Hansley discovered it (54).

BOHNING: Really.

STORK: It was really quite interesting. I don't know Hansley or Wooster. I've never met them. All I know is that these patents antedated what made these academic types famous. That's one.

There's another person whose name I think is John W. Copenhaver. I'm not absolutely sure. That person was at General Anilined Film and he did reactions, which essentially were what are today called Mukaiyama aldol reactions (55). That is a reaction of a cationic species with an enol derivative. This guy, whose name I probably have wrong, this so-called Copenhaver (could turn out to be Cooper for all I know) did that like four years before, with enol ethers, instead of enol thioethers. It's not terribly different. It's the same kind of thing. That process is used industrially in parts of some processes to build up vitamin A, by Otto Isler, Hoffmann-LaRoche, based on what I call the Copenhaver, or whatever his name is, chemistry. Actually, if I'm going to push this, I've got to find his name. [laughter] Maybe I'll find his name and send it to you, and you can see if this person exists.

These are two names that I can remember. After a while in industry you learn (or maybe it doesn't take very long) that your future and your impact depends on internal publications and patents and not so much on making it, unless you intend to leave, with the outside world. That's a difficult thing. I'm sure there are many other cases of that sort. But these two are good examples, especially Ainsley. That always impressed me because these are really pretty important reactions from this guy nobody has ever heard of. [laughter]

Anyway, I have the feeling, because I have seen some list of the people that you've interviewed for your program, that it was biased completely the other way; and that is that you mostly interviewed industrial people that made polymers.

BOHNING: Yes, we did have a polymer project that was funded by the NSF, and for several years we focused only on polymer chemists. That project also produced a traveling exhibit, Polymers and People, and a small booklet (56).

[END OF TAPE, SIDE 13]

[END OF INTERVIEW]

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INDEX