THE BECKMAN CENTER FOR THE HISTORY OF CHEMISTRY

MAX TISHLER

Transcript of an Interview
Conducted by

Leon Gortler and John A. Heitmann

at

The Library at Wesleyan University

on

14 November 1983

Max
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TER FOR HISTORY OF CHEMISTRY ORAL HISTORY PROJECT

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Max Tishler
(Signature)

February 22, 1984
(Date)

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

MAX TISHLER

1906	Born in Boston, Massachusetts, 30 October

Education

1928	B.S., chemistry, Tufts College
1933	M.A., chemistry, Harvard University
1934	Ph.D., organic chemistry, Harvard University

Employment

	Department of Chemistry, Harvard University
1930-1934	Teaching fellow
1934-1936	Research associate
1936-1937	Instructor
	Merck & Company, Inc.
1937-1941	Research chemist
1941-1944	Section Head in charge of Process Development
1944-1953	Director of Development Research
1954-1956	Vice President and Executive Director of Science Activities
1957-1970	President, Merck, Sharp & Dohme Research Laboratories
1962-1970	Member, Board of Directors
1969-1970	Senior Vice President of Research and Development
	Department of Chemistry, Wesleyan University
1970-1974	Professor
1972	University Professor of the Sciences
1973-1974	Chairman of the chemistry department
1974	Emeritus professor

Honors

1953	Elected to National Academy of Sciences
1961	Medal of the Industrial Research Institute
1963	Rennebohm Lecture Award, School of Pharmacy, University of Wisconsin
1963	Chemical Industry Award, Society of the Chemical Industry
1964	Lecture Award, Royal Swedish Academy of Engineering Sciences
1964	Julius W. Sturmer Memorial Lecture Award, Philadelphia College of Pharmacy
1965	Elected to American Academy of Arts and Sciences
1968	Chemical Pioneer Award and Gold Medal Award, American Institute of Chemistry
1970	Joseph Priestley Medal, American Chemical Society
1972	Honorary Member, Societe Chimique de France
1974	Fellow, Academy of Pharmaceutical Sciences

ABSTRACT: This interview elucidates Max Tishler's life and career. Tishler reminisces about his family, early schooling, undergraduate education at Tufts, and graduate and postgraduate work at Harvard. He then discusses his impressions of colleagues at Harvard and the state of chemistry in the 1930s. The major portion of the interview contains Tishler's impressions of the research and development undertaken by Merck & Co. in the 1940s, 1950s, and 1960s and of his role in that activity. He also discusses individuals involved in that work and the major contributions that Merck & Co. made to combat disease. Tishler ends the interview by discussing his current activities at Wesleyan and by presenting his views about the future direction of chemistry.

INTERVIEWERS: Leon Gortler is a chemist with an interest in history. Born in 1935, he attended the University of Chicago and then received his doctoral degree from Harvard. After doing postdoctoral work at Berkeley for a year, he began teaching at Brooklyn College in 1963. Ten years later, he became professor of chemistry. He has since coauthored two textbooks about organic chemistry. His historical and scientific research focus upon physical organic chemistry. John A. Heitmann holds a bachelor's degree in chemistry from Davidson College and a master's degree in history from Clemson University. From 1974 to 1979 he worked as a chemist in the metallurgical industry. He then studied at the Johns Hopkins University under Owen Hannaway and received his doctorate in the history of science in 1983.

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INTERVIEWED BY: Leon Gortler and John A. Heitmann

PLACE: Library at Wesleyan University

DATE: November l4, l983

Gortler: We are interested not only in your scientific career, but also in your life in general: how you became interested in science and what your early background was like and so on. You have two children. Tell me about them.

Tishler: One is forty-three and the other is thirty-three. Peter, my older son, is a physician. He got his MD at Yale and his undergraduate degree at Harvard. He does research in the field of genetics. He is associated with Harvard Medical School in the teaching program. He is also in charge of the teaching program at the Veterans' Administration Hospital in Brockner, Massachusetts, which is part of the Harvard teaching system. Carl lives in Columbus, Ohio. He got a Ph.D. in psychology at the University of Maryland and does clinical psychology at the McClain Hospital and various other hospitals --particularly those that cater to young children. He has become interested in teenagers and young children particularly from the point of view of the problems of adolescent suicides. He had published quite a bit in this field. Presently he has gone into private practice. He seems to be quite busy and doing well.

Gortler: Max, I know you were born in Boston on October 30, l906; but I know very little about your family. Can you tell me something about your parents: their careers, their education, and the influence they had on you?

Tishler: Well, let me say first, my parents came from abroad: mother from Germany, father from Rumania. My grandmother was Austrian. They came quite young. My mother and father were married in Boston, about l870. There were six children in the family. For some reason which I could never really understand, my father left the family while I was quite young. We hadn't heard from him in over thirty years or so and he appeared one day. So we had a very bad background from the point of view of being able to eke out a living. All of us had to work, including my mother. We managed. One of the things that came out of the whole thing was the desire on my part to get a higher education in college. I'm the only one in the family who went to college. In fact, I and my younger sister are the only ones who graduated from high school. The others just couldn't. They had to start working at a very early age, and there wasn't any real inspiration at home of course. Why it happened, I'm not quite sure I understand why.

Gortler: Were you one of the younger children?

Tishler: I was the next to the youngest, the fifth child. There were eight in the family and I went to work very early, baby-sitting as well as answering telephones. Our physician was able to get me a job in a drug store and that impressed me a great deal. I remember medicines as well as packaged chemicals. I packed some of the drugs like epsom salts and castor oil. The man I worked for was a pharmacist from the Massachusetts College of Pharmacy. He was an inspiring person. He had a great impact on my wanting to do something beyond getting a job.

Heitmann: What was his name?

Tishler: His name was Max Goldberg.

Gortler: What was the physician's name?

Tishler: Abraham Schulman.

Gortler: Before you finish let me have the names of your mother and father.

Tishler: My mother's name was Anna Gray. My father's name was Samuel.

Gortler: He left home when you were about how old?

Tishler: I was about four or five years old.

Gortler: So you went to work for a pharmacist?

Tishler: At a very early age. I can remember delivering medicines during the world flu epidemic of 1918.

Gortler: You were about twelve years old?

Tishler: I was about twelve years old. It made quite an impression on me because people were dying. They were sick. I can still see the neighborhood and the people who were sick and dying.

Heitmann: Did this have some influence on the kind of things you did?

Tishler: Oh, I'm sure it had. It gave me a feeling that I might want to do something in the line of disease. I went to Boston English High. Incidentally, I worked all the time. And I worked at several things. For example, I sold newspapers as a youngster at a car stop where people would come to get the morning newspaper. You don't see much of that nowadays, at least I don't. But that was important in the cities of course. This followed through until I finished graduate school. I worked on the outside and was able to support myself, contribute to the support of my mother and

sisters, and pay for all of my education. I had no financial support from anybody except the universities. Tufts College, for example, gave me a fellowship for four hundred dollars a year. At Harvard I had an Austin teaching fellow which gave me one thousand dollars a year. And I worked in pharmacies while I went to high school. I worked on Commonwealth Avenue in a pharmacy. Later the owner sold the store and went to Beachmont, Massachusetts, which is right next to Revere, Massachusetts, and opened a drug store there. I worked there and used to commute from there to Tufts. Matter of fact, I recall that while I was working in this drug store, I worked nights. I was also a teaching assistant in my senior year at Tufts. There, I graded papers in the laboratory section. And I remember distinctly something that really frightened me at the time. I was grading papers and brought them with me to the drug store since I could do some of the grading while I was working. Coming home I left the papers on the street car. I was terribly frightened about this and ran after the street car. I finally managed to get to the terminal and I found the papers.

Gortler: I know that feeling well!

Tishler: Let me say this. I always did well in my courses.

Gortler: Let's go back a little bit to your high school. Did you do much reading?

Tishler: Yes. I was very much impressed with chemistry. I already had an interest in chemistry as a result of my working in a pharmacy. I read a lot of textbooks about pharmacy and chemistry. In high school I had an extremely good teacher by the name of Stone. He used to do demonstrations for the class and I can still see him there. Leo Stone was distilling mercuric oxide, or rather heating mercuric oxide and distilling off mercury. He did all the classic experiments in those days. They were elementary, but nevertheless made a great impression on me as a youngster. Then, of course, I went to Tufts. There were some very good teachers there too.

Heitmann: Can you remember any of their names?

Tishler: Oh yes, at Tufts there was David Worrall, teacher of organic chemistry. He got his degree at Harvard with Kohler. Then there was Allen, C. H. E. Allen, who we used to call alphabet Allen. Both had a great impact on me. Worrall died while I was still at Tufts. I kept in touch with Allen for many years afterwards. He was a great booster of mine. We had a very nice warm relationship until he died about five years ago. He, as I say, was a fan of mine. He encouraged me all through life. As a matter of fact everytime he heard something nice about me he'd write me. I really appreciated that.

Heitmann: How did you happen to choose Tufts?

Tishler: Well, I didn't take any college boards. I just didn't feel as though I ought to. Tufts was a school I could commute to. I didn't apply to Harvard because I thought Tufts would be a better place for me. I was thinking also of possibly going to medical school. They had a medical school to which I could go in my second year, but I gave that up pretty quickly and I got into chemistry at Tufts. So it became my school in a sense because I could commute very readily.

Heitmann: You lived at home then?

Tishler: No, I worked for the people in the pharmacy on Commonwealth Avenue. The owner's name was Jacobson. I used to live with them. This was also true when we went out to Revere, except that I shared a room with somebody my last year at Tufts. That's when I had this problem with the examination papers. I used to commute out to Revere from Beachmont and come back very late at night. I did pretty well financially in those days because I didn't have to pay any room rent.

I always did little things to make some money. Today, for example we have candy machines. In those days I conceived of a similar idea in the drug store. I would get a box of twenty-four bars of candy for sixty cents and sell them each for a nickle and make a profit. They gave me permission at Tufts to have a little commode in which I kept candy. People were honest and I made money doing this. It was very helpful.

I'll show you something that I don't ordinarily show people. I still treasure it. This is a little certificate that I used to have in the drug stores. You see the year l928.

Gortler: That's when you became a licensed pharmacist?

Tishler: That's when I became a licensed pharmacist.

Heitmann: That is the same year you graduated from Tufts? So between l928 and l930--you didn't enroll at Harvard until l930, right?

Tishler: No, the end of l929. For about a year I was in here. I took the board exam at the same time. I made a fair amount of money in the meantime so I could get things started at Harvard.

Heitmann: When did you decide that you would become an organic chemist? Was it very early on or even before you enrolled at Tufts?

Tishler: That is correct. I did a little research problem with Allen. He more or less urged me to go to graduate school. Incidentally, I am not concerned about any religious

anti-Semitism, but there was a teacher at Tufts, Shorty Baker --I can't recall his first name but we called him Shorty Baker because he was a very small person--who advised me not to go into chemistry. He said Jews have a hard job getting placed and you won't get anywhere. Allen said, "Don't believe him. (laughter) You'll break ground and you'll make things easier for people." It never occurred to me, until Shorty Baker said that, that it might be a problem. There never has been a problem as far as I'm concerned. The world's been very good to me.

Heitmann: When did you first meet Kohler and what were your first impressions of him? Do you remember the first time you met?

Tishler: Yes. I was terribly frightened. In those days students regarded professors as people on pedestals, very formal and awe-inspiring. This was my impression when I first met Kohler. I went there because Professor Allen suggested I see him. He arranged for me to see him. It was a very cold interview.

Heitmann: This was l929?

Tishler: This was in '29. That's right. A very cold interview. He was nice to me, but very austere. I knew that I had to work with him. There were two people with whom I had to work, either Kohler or Conant. Fieser wasn't there when I first came. But I went to Kohler because I took his course, Chemistry 5, which today is called Chemistry 50. Chemistry 5 was advanced organic. He was a wonderful lecturer. He very logically and clearly presented his material.

Gortler: And you took the course while you were still at Tufts?

Tishler: Oh no. At Harvard. The first year I didn't go to work for Kohler. I had to take courses just in physical chemistry and advanced organic chemistry.

Gortler: With whom did you take physical chemistry?

Tishler: At first it was Kraus. He gave us lectures until Kistiakowsky came up there.

Gortler: Did you know Conant fairly well?

Tishler: No, but later on very, very well.

Gortler: Before we get too far on into Harvard, let's go back for just a moment to Tufts. Do you remember the text books you were using at that time?

Tishler: Well, Worrall had a text book in organic chemistry.* Inorganic, McPherson and Henderson.** And physical chemistry was Getman.*** We had a book in inorganic qualitative analysis--all the schemes, separation and so forth. I can't recall the name of it. It was a very powerful book in those days.

Gortler: How about courses outside of chemistry? Were there any other influential courses?

Tishler: I took calculus. I was very fond of German. I organized a German club at Tufts, put on the first German play Tufts ever had. (laughter) Also a chemistry club. There were a lot of extra-curricular activities that I participated in. I managed to do these things even though I was a pretty busy guy.

Heitmann: Were there other chemistry students at Tufts who later achieved success in the field?

Tishler: Yes, Phil Cohen, a biochemist MD, Ph.D., at the University of Wisconsin. He's retired already. He crossed over with me. He was two years behind me but I got to know him quite well. Dick Tousey was a physicist, but he and I were very close. Dick Tousey was in my class and became a member of the National Academy. He worked at the Naval Research Laboratory, and I think he was the first one to put cameras in satellites. I still see him. I guess that covers my memories of people who have done well in science.

Gortler: Have you remained friendly with these people since that time?

Tishler: Yes. I've kept in touch with Hy Trilling from Boston. Also, Dick Tousey. By the way, I liked English. In fact, I used to write poetry while I was at Tufts. But I was discouraged from being a poet by an English professor because I wrote lousy poems. He said, "You'd better stick to science." I did. I also liked history and economics and the usual type of liberal arts courses.

Gortler: When you decided you wanted to go into chemistry did you have any perceptions of what being a chemist was like?

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*David E. Worrall, Principles of Organic Chemistry (New York: Longmans, Green & Co., 1927).

**William McPherson and William E. Henderson, An Introduction to the Study of Organic Chemistry (Columbus, Ohio: Ohio State University Press, 1904).

***Frederick H. Getman, Outlines of Theoretical Chemistry, 4th ed. (New York: John Wiley & Sons, 1927).

Tishler: Not until I went into industry. Even while I was at Harvard I never had any real conception. I wondered why they would pay me to do chemistry. There was no sense to it. It was like mathematics. All you had to do was teach.

Gortler: Maybe now is a good time to ask this question. Academia trains scientists, or chemists at least, to be academic chemists and yet ninety percent of them go into industry. What are your thoughts about this matter?

Tishler: I think industry really doesn't want people to be trained as industrial chemists. Initially, industry simply wants very good chemists--people who have good knowledge and good experimental backgrounds--rather than people who can apply their knowledge to a product or a process and enhance its economic value. When I was back in Merck I always used to say, "We'll teach them all they should know about how to be able to work in industry. But we can't teach them how to be good chemists and to really know good chemistry." The latter is something they've got to develop while in graduate school. We try to create an atmosphere which will foster this, but I think it's a mistake to try to make industrial chemists in graduate school.

Gortler: That's a good point. I never heard that kind of an attitude.

Tishler: But one thing I do think though. I try to teach the students here the importance of chemistry--the usefulness of chemistry. Chemistry is not just an intellectual challenge. It's part of our society. It's our welfare. I want students to see that they can pursue very honorable and productive careers in chemistry--and not be prejudiced against it. They can then go enthusiastically into industry.

Gortler: So some time in l929 you had this talk with Kohler and it was very formal. Apparently he was generally a very formal individual.

Tishler: Yes, he was. He was never warm with people. I was his assistant for two years. The last year he began to warm up quite a bit and recommended me highly for positions and so forth. We were getting to know each other. But it was only during the last six months of my stay at Harvard that he really began to open up. Until that time it was nice. There was nothing about our relationship that gave me any problems at all. They were very good as a matter of fact. But it was a teacher-student relationship, taken in terms of those days. Today the situation is quite different.

Heitmann: Who were some of the other graduate students who worked with Kohler during your years at Harvard?

Tishler: Well, Walker, Joe Walker. Joseph T. Walker.

Gortler: You did a paper with him.*

Tishler: That's right. Take a look at my paper list. Let's see. Then there's Howard Potter. He went to teach at Alma College. He died very recently. Carl Addinall came from England. He got his doctor's degree and his bachelor's from Harvard. He died very recently. He lived to a ripe old age of about ninety. He was a good chemist and did a lot of writing. In a sense, he is the one who modernized the Merck Index. He went to work at Merck, and as a matter of fact he helped me get a position at Merck. That came about in two ways. One was when Mr. Merck spoke to J. B. Conant who recommended me for the position. And then Carl Addinall who was my instructor in Chem 5--I had kept in contact with him --recommended me to his boss, Randolph T. Major. He was also interested in the possibility of my coming to Merck.

Heitmann: Was there a lot of interaction between the various graduate students such as helping each other in learning techniques in the Kohler laboratory?

Tishler: Well, in learning techniques, yes. But problems were individual. The one thing that always bothered me though, was that in Converse there were three floors. The bottom floor was Conant's, the second was Fieser's, and the third was Kohler's. We rarely knew what was going on in the other groups unless we made it a point to find out. I happened to have known pretty much what was going on in Fieser's group because I got to know Fieser. I did some checking on organic synthesis for him. But one rarely knew what people in Kohler's group were working on. This always bothered me. And I think this tends to occur in many institutions even today.

Gortler: I think a lot of it stayed, even when I was there. People were on different floors and occasionally would talk to other guys but one didn't really know what was going on in other groups.

Tishler: That is correct.

Gortler: When you first went to Harvard you taught as an Austin fellow. Did you also teach in Chem 5?

Tishler: Yes. I was an instructor at that time, but still as an assistant to Kohler. I carried out his research and worked on his problems.

Gortler: That was later on.

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*Elmer P. Kohler, Joseph T. Walker, and Max Tishler, "Re Resolution of an Allenic Compound," Journal of the American Chemical Society, 57 (1935): 1743-5.

Tishler: That was later on, after I got my Ph.D. degree.

Gortler: You stayed on at Harvard after you got your Ph.D.

Tishler: Yes.

Gortler: Jobs weren't available? Or Kohler was looking after you? What happened?

Tishler: There just weren't any jobs at all. In those days I wanted to go into academia very, very badly. There just weren't any jobs. One didn't have a chance to do a single interview or a single opportunity to apply for a job on the basis of an opening. So academia was out.
Kohler tried to get me to interview for industry. I had one interview and that was with Du Pont. That didn't work out very well. The only other interview I had was with Merck. Randolph Major was the director of research at Merck and he came to Harvard and spent some time with me and Kohler. That was very successful. That was the only offer I had. I was so delighted to get that offer at that time. I have always been grateful for that.

Gortler: Did you know Harold Blatt?

Tishler: Yes, I knew him quite well.

Gortler: He was also a graduate student who took over the lab during that period.

Tishler: No, he was already out when I got there. He and Addinall were pretty close friends. That's when I first met them. I'm pretty sure I met Blatt during my first year in graduate school. He may have been there, but not when I was doing research. He was gone by that time, because I began to know all of Kohler's students.

Gortler: He had written a book with Conant.

Tishler: That was after I helped Conant revise his textbook.* After I went to Merck, Conant asked Mr. Merck if he might borrow me for that purpose. So I took two months off from Merck and worked with Conant.

Heitmann: This was in 1936?

Gortler: '39.

Tishler: '39, Yes. That was a great experience working with Conant.

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*James B. Conant and Max Tishler, Chemistry of Organic Compounds, 2nd ed. (New York: Macmillan Co., 1939)

Heitmann: Did Conant have a great deal of influence on the chemistry department when he became president or did he have a bigger vision and move away from the chemistry department?

Gortler: He moved away. There is no question about that. He had a lot to learn and so he tried to learn everything he could about other departments. He became a very good president. He still had an interest in chemical research. He and Kistiakowsky used to sit down and talk about problems. As a matter of fact...

Gortler: He had a project going.

Tishler: He had a project going on heats of hydrogenation.

Gortler: That's your last problem.

Tishler: That's right. I was asked to make deuterized formaldehyde. They wanted this for a study of hydrogenation at the time.

Gortler: Did you also make some large ring compounds for them.

Tishler: Yes.

Gortler: That was for hydrogenation?

Tishler: That was for hydrogenation. That was an exciting piece of research.

Gortler: Do you want to say anything more about that?

Tishler: Well, not really except that it was a large scale production. I used a lot of diazomethane. Made a lot of N-nitroso-N-methyl urethane. When people talk about the hazards of diazomethane and carcinogenesis I wonder why I'm still around! (laughter)

Gortler: Did you know how dangerous it was?

Tishler: No, I did not. As a matter of fact, I burned my hand pretty badly with the N-nitroso compound. I ran twelve liter flask reactions.

Gortler: You'd better tell me about the explosion before I forget. There's a story about the fire that's handed down and I've never heard the full story.

Tishler: Well, there used to be a time when I'd give a talk somewhere. Someone who knew me at Harvard would ask me to give a talk to his section at a school or university and he'd always introduce me. He wouldn't say a word about my chemistry but he'd introduce me as the man who had had this

fire and then mention how they saved me. It was always something to laugh about. They rarely knew who I was!

Let me tell you what actually happened. I was working for Kohler at a tiny lab right next to Bartlett's office. A door that opened into the lab was closed at the time. I picked up a liter bottle of benzene. My hands were wet and it slipped and fell on the floor. I was just about ready to sop up the benzene with rags when fire broke out. I had a flame in the hood. In those days we would clean our apparatus in hot sulfuric acid baths.

Gortler: They were still doing that twenty-four years later.

Tishler: So I was heating my sulphuric acid in the hood there and I guess that's how the fire started. The room filled with black smoke very quickly and blocked my exit. I couldn't get out that way at all. The only way was through the casement window. I hung out there.

Gortler: I don't know how you did it!

Tishler: Real emergency technique. It was a casement type of window that you could push open. Today you can't do that because of air conditioning and what have you. (laughter) I don't know how you'd get out in a real emergency today. But I hung out there above a court yard. The students in Fieser's Chemistry II lab course looked across the courtyard and asked, "Why is he hanging out the window?" (laughter) There was soot coming through the window too. Well, Fieser got up there very quickly and tried to put out the fire. He said, "Where's Max, where's Max?" I could hear him and I kept yelling but he couldn't hear me. I know I was out there for at least five minutes. Finally, some students got some ladders and rescued me.

What I think bothered me about that whole thing was the fact that I caused a fire, and we used up all the carbon dioxide extinguishers. I knew someone who filled these extinguishers and I insisted he come and get them and I would pay for them. The department wouldn't hear of it, of course. But I was really afraid that I was going to be chastised. I did appreciate what an accident meant. Well, that's the story of the fire and they have forgotten it I think. I haven't heard people talk about the fire much lately.

Gortler: Well, I was up there on the third floor and people would talk and say Max hung out that window. (laughter) But I never heard the whole story. Now it's on the record. Someplace in a New York Times article there is mention of a fifteen hundred dollar award to do any kind of research that you wanted to do.* Was that just the fellowship that you had?

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*Elizabeth M. Fowler, "Personality: Researcher Seeks Surprises," New York Times, 22 September 1963, III, p.3.

Tishler: Yes, that's right.

Heitmann: Can we move on to Merck now?

Gortler: There are a couple of other things I wanted to ask.

Tishler: There are some things about Harvard that I wanted to mention.

Heitmann: OK.

Tishler: There was another person at Tufts who had a great deal of influence in chemistry. His name was Chadwell. He got his Ph.D. at Harvard with Arthur Becket Lamb.

Gortler: Oh yes.

Tishler: He was interested in the structure of water. I understand they still haven't established the structure of water completely.
I met my wife at Tufts. I taught her in the freshman laboratory. I was a senior then.

Heitmann: Was she a chemistry major as well?

Tishler: No, no she was a psychology major.

Heitmann: From the Boston area?

Tishler: Yes, she was born and brought up in Boston.

Gortler: Did you consider any other graduate schools besides Harvard?

Tishler: No. Were there any others? (laughter)

Gortler: We were just talking about that this morning. We were saying what an amazing group of people they had in those years.

Tishler: You can tell from the picture that they have there. Kohler was a very small man. He had a delicate frame.

Heitmann: Was he a very religious man?

Tishler: No. There was nothing to indicate he was religious. He was Pennsylvania Dutch.

Heitmann: He was a bachelor?

Tishler: He was a bachelor, yes. Well, I was going to say something about the difference between chemistry in those days and the present. Maybe you were going to ask me sooner or later.

Heitmann: We'll talk about that now.

Tishler: Well, in those days, as you well know, structure determination was quite different--so different that young people today just haven't the slightest idea how this was done. Yet all the important chemical work that developed was done by methods which today are no longer useful. We have such better tools today. Spectroscopic methods: NMR, IR and mass spec just change the complexion of chemistry completely. It's amazing how we got information by deduction. By means of the logical application of thinking and deduction we were able to establish structure. Most of the time we were right. There's no question about it. We built up organic chemistry that way. It was really quite a challenge to devise methods ultimately breaking down the molecule to known fragments and then trying to put them together again. Ultimately we synthesized the compound that we separated. But you know it took a long time to get some of the complicated molecules of natural products. Morphine is a good example. It took a long time to prove the structure of morphine beyond a reasonable doubt. Today of course, we can do it very rapidly. For a while I thought that a lot of the pleasure had gone out of chemistry because that was really quite a challenge to me to determine the structure of a compound. And it was necessary to do that every time you ran a reaction. If you were studying reactions you had to isolate the products and try to establish their structure. Today, it is so easy to do this for the most complicated structures with NMR and IR and X-ray.

When I see what's being done today, I'm amazed that we've never been able to establish the structure of some complicated molecules. For example, just take the microbial metabolite that came out very recently, avermectins, which is a very complicated structure. I'm sure it would have taken decades to be absolutely sure of its structure. Yet the whole thing was done in a month's time. And the proof is so rigid that you don't have to synthesize it any more. You just know its there. Well, this whole difference I think is moving chemistry so far ahead so quickly. It's really amazing what's happened and what you can do today. The avermectins are very important antiparasitic drugs.

Gortler: When did you start moving into instrumentation at Merck? You probably got very used to it at Harvard. Did you do any spectroscopy at all?

Tishler: None whatsoever. Woodward came there. He started spectroscopy at Harvard. He did some visible and UV and began to apply spectroscopy to chemical structures.

Gortler: Right.

Tishler: I don't think Conant or Kohler even got very much into it.

Gortler: I don't think so.

Tishler: A lot of kinetics but...

Gortler: That's right. They did their kinetics by titration.

Tishler: That's right. Harvard, I think was kind of late.

Heitmann: I guess X-rays came in the '40s.

Tishler: Yes, but I don't know what Harvard chemistry was doing. Well, at Merck I think we were pretty quick to bring in all these tools and I think we had the second commercial NMR piece of equipment in the country. Du Pont had the first, I think, and we had the second. The synthesis of cortisone which was done under me when I was head of research, finally yielded a production run of over thirty percent. Now it's no longer important but in those days it was extremely important. And part of the reason was that we used IR to note what was going on in the mother liquors from which we would get material. We couldn't isolate any more material. We also learned a lot about the chemistry. It was a great application. When NMR came along it served our purposes even better. But IR was very helpful when we first got it and applied it. We had a physical chemist, Jeff Webb from Princeton. One of the things that Randolph Major had the vision to do was to set up a physical chemistry department. Its job was merely to introduce all tools of physical chemistry that could be useful.

Heitmann: When was this, Max?

Tishler: '35, '36.

Heitmann: '36 is whan Jeff Webb came?

Tishler: I think so. Matter of fact, there is a little story I'll tell you about Jeff Webb. It concerns the structure of penicillin. There were two structures that came down the pike. One was a beta-lactam; the other was the azlactone structure. The question is, which was it? It took X-ray analysis to settle that point once and for all. I guess there was also some IR work that was done by Shell on that program which also indicated the correct structure. But really, the person who gets the greatest credit is Hodgkins from the University of Cambridge. She got the Nobel prize for that. She used X-rays. Jeff Webb said that he was convinced the structure was the beta-lactam and not the azlactone. He noticed a very simple thing, the PK value of penicillin. In the beta-lactam we have a strong acid. It's not tied up like an amino acid. The azlactone is tied up, you see. This was a very simple deduction he made, and it turned out he was right. I remember arguments we used about that. Homer Adkins, for example, was one of our consultants in those days. He and a lot of other people were sure that the azlactone structure was correct. Bob Woodward, on the other hand, felt

differently. He thought that the beta-lactam structure was correct--and that was on the basis of reactions.

Gortler: That's interesting: that a physical chemist would think of it not in terms of spectroscopy but rather on a purely chemical basis. Go back to Harvard. It's my first interest. You did take Kohler's course. You took Kistiakowsky's. Who were the other people on the faculty?

Tishler: Well, of course, Louis Fieser. Also Forbes--I forget his first name now--the grand master of chemistry. Remember Forbes?

Gortler: Oh, I remember Forbes. I didn't know much about his research. I didn't realize he was a photochemist.

Tishler: Oh, yes. Let's see now, who else? Well there's Kisty, of course. I knew Kisty quite well. The person that I had the first semester before Kisty came was Sherrill of MIT. He was very famous. They had a textbook as a matter of fact, Something and Sherrill.* It was all problems. The whole course was an advanced course in physical chemistry. Then Kisty came the second semester, took over the course, and made it much better. Sherrill's course was highly mathematical. If you mastered it you probably came out better.

Gortler: Other people? Other textbooks? I guess Jones was still there?

Tishler: Jones was still there, that's right. I never took a course with Jones.

Gortler: Who was chairman at the time, do you remember?

Tishler: The chairman was a Tufts graduate. I mentioned his name a few minutes ago, Lamb, Arthur Becket Lamb. He was chairman. And he was also, as you know, editor of the Journal of the American Chemical Society.

Gortler: What about any changes in organic chemistry that were taking place at that time. Now Kohler was really fairly advanced in his thinking.

Tishler: That's right. He was an extremely good experimentalist. Very able. Worked in the laboratory himself quite a bit. And as I say, he was a very logical thinker and he made some very valuable contributions in terms of l, 4 addition. He took the Grignard reagents and showed that they can add in a Michael-type reaction to alpha, beta-unsaturated carbonyl compounds.

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*A. A. Noyes and Miles S. Sherrill, An Advanced Course of Instruction in Chemical Principles (New York: Macmillan Co., 1922).

Gortler: He did that during much of his career.

Tishler: That is correct.

Gortler: He took that research back to the turn of the century. You were still working on similar problems?

Tishler: That's right. I worked first on alpha-bromoketones which gave the same intermediates as with the addition to alpha, beta-unsaturated ketones. It's the same type of an intermediate. And that was kind of novel for Kohler. Worked out that reaction and worked out the relationship with alpha, beta-unsaturated ketones additions. The work, of course, I enjoyed the most was the allenes.

Gortler: How did that happen to come about?

Tishler: Well, Kohler had a student, Joe Walker, who was trying to make an allene and develop it. It's very interesting chemistry but we were never able to isolate or obtain an allene which we felt sure was an allene.

Gortler: We were talking about the allene problem. You mentioned that Joe Walker started...

Tishler: He tried unsuccessfully to make allene in a number of different ways. There was one publication that appeared in 1910 by Lapworth, a British chemist, who believed that he had synthesized an allene, although his structure proof was not conclusive.* He apparently did nothing with it from the point of view of resolution. He may have done so, but he didn't report it in his publication. Joe Walker tried to repeat his work but couldn't get this acid to crystallize. When the time came for him to write up his thesis, he hadn't yet succeeded. But he did enough work that Kohler felt he ought to go ahead and write a thesis and get his Ph.D. He got his Ph.D. Joe then went on to work in the state police laboratory to develop a lot of modern techniques of crime detection and so forth.

One day as Kohler's assistant, he asked me if I would go down to the cold room and clean out a lot of old stuff that was no longer of any use. So I went down and I discovered the Erlenmeyer flask filled with crystals left by Joe Walker. That turned out to be his allenic acid. Was it allenic acid or not? I established the structure by hydrogenation and degradation and made sure it was right. This wasn't done by the British who just assumed that they had the right structure. Then I started to try to resolve it and at first it failed with all the alkaloids I tried. I couldn't get them to form the salts. I was still not clear why. I thought it was because the allenic acid was a very weak acid. I still

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*A. Lapworth and E. Wechsler, "Experiments in Substituted Allenecaboxylic Acids," Journal of the Chemical Society, 97 (1910): 38-48.

think that's right but I talked with Frank Westheimer some time ago and he didn't think that was the answer. He didn't have a good explanation why I couldn't form the salts. I conceived the idea of changing that carboxyl group by reacting it with glycolic acid and putting on an ester with a carboxyl group on it. As a matter of fact the allenic acid wouldn't dissolve in bicarbonate but would dissolve in alkalies.

Gortler: That's interesting because I remember looking at the paper and remarking, "He already had an acid group there, why would he want to extend it and make another acid out of it?"

Tishler: Then I could extract it out with bicarbonate from organic solvents and so forth and there was no question that it was a good acid. With brucine it just fell apart. So that's how that happened.

We should have been first to publish on an optically active allene but Kohler was a perfectionist when we wrote a paper. It would take him two or three months to write a paper. He would just go over it and rewrite it--in contrast to Conant. Conant would take a thesis, underline with a red crayon, cross out sections, add a sentence here and there, and have it typed up and practically all done. Conant worked with great rapidity. Kohler just sweated with every publication, but they were masterpieces when they were done. Every word was weighed.

Gortler: Conant had some comments about the differences between Richards, for example, and Kohler in terms of seeing the bigger picture and being a perfectionist. One was able to treat a problem and the other was able to see and formulate a problem.

Tishler: Well, he's right on that. So, this is how the allene came about. I've been lucky in my life, too, you know.

Gortler: Well, I saw what was coming when you told me you went down to the cold room and there it was, it had crystallized out. I have had that happen on occasion. How did you choose Kohler over Conant at the time?

Tishler: Well, I think that the reason is that I took Chem 5 with Kohler. During the second semester of Chem 5, Kohler said, "I'll get a problem and if it works out all right, maybe you can continue it."
I then went to see Conant about working with him. He didn't know me and he wasn't very warm about saying, "Come and be in my group. I'd be delighted to have you."
Kohler already had some idea about what I could do, how I worked, and so forth. So that's the main reason why I chose Kohler.

Heitmann: Was Louis Fieser already there then?

Tishler: No. Louie Fieser came after I started research. I was there a whole year before he came.

Heitmann: So you got to know Conant later on and then he asked you to help him rewrite the book?

Tishler: Yes. I took a beautiful course with him in natural products. You know, we had two wonderful lecturers, Kohler and Conant. I got to know them through the course. I guess that Conant must have talked with Kohler about me because I don't know why he came to me and asked if I would do this. Kohler must have recommended me.

Heitmann: Did Kohler have much to do with getting you the job at Merck?

Tishler: He did when Randolph Major came to see him. He tried very hard. I know that many years later someone sent me a letter that he had written about me to Du Pont. In this letter he said that I was the best chemist he ever had. Du Pont wasn't ready to take a Jewish chemist.

Heitmann: That's right. (laughter)

Gortler: I guess Wallace Carothers was long gone before you...?

Tishler: That's right, he was gone. '27 I guess. There was talk that he wanted to come back to Harvard when he found out that Conant had been elected to the presidency. Apparently there was a period in which he was a bit disenchanted with what was taking place at Du Pont and he had considered it.
But after a while he decided he would stay where he was because he and his parents had just moved to Wilmington.

Gortler: You did have a publication with Frank Westheimer. He said you did the problem in two different halves. He finished off with Kohler and I know he's a friend of yours.

Tishler: That's right. I knew him when I was at Harvard. He was single. We used to go to my home and Betty would make lunch for both of us. We had a very good relationship. Well, actually this is work that he had done with Kohler and Conant but hadn't completed. I took it over and it turned out to be completely different than what they expected. I'm very proud of the fact that I had a publication with Frank. It was a very good problem and as I say I'm very proud. When I tell my students that I published with Frank, I have to show them the publication just to prove that I did. (laughter) I'm also very proud of having published with Don Cram when he was at Merck. He and I published a paper together, a byproduct of penicillin.

Gortler: When you rewrote the book with Conant--was most of it your writing?

Tishler: Yes.

Gortler: I ran across a review of one of your other papers. The review is extremely favorable. It mentioned that your paper was very up to date and that it included electronic theory and resonance and physical and organic chemistry.

Tishler: That's right. That was kind of ghoulish stuff in those days.

Gortler: That came from your undergraduate background?

Tishler: No, from Harvard.

Gortler: Your graduate background.

Tishler: Yes, my graduate background.

Gortler: Was there a fairly large change from earlier editions?

Tishler: Yes, there was.

Gortler: At that time, to whom else were you talking at Harvard?

Tishler: Well, Harold Fischer, whom we called Hap.

Gortler: We were talking about him this morning.

Tishler: He came to Harvard. He and I roomed together for a year and we have been friends ever since that time. I used to talk to him a great deal.

Gortler: He was an instructor.

Tishler: At Harvard?

Gortler: Yes, that's right.

Tishler: He was in charge of the Chem 2 course. He worked on alpha-bromoketones too. That's why when we first met I knew who he was and he knew who I was.

Gortler: He worked on them for Fuson.

Tishler: For Fuson. He worked on the reaction with alkali. So we had a lot to talk about. He followed my work very closely while I was at Harvard. I knew Land as a freshman. He took freshman chemistry. Of course, he didn't stay around, but he did pretty well. (laughter) There was a person who worked with him--whose name I can't recall--a student of Professor Lamb who worked with Land and helped make some of the quinine iodine sheets that became the basis of polaroids.

Heitmann: I guess Charlie Price was around in those days.

Tishler: Yes, Charlie Price was around. That's right. He was a good boy. I knew Charlie quite well; he worked with Fieser and Conant.

Heitmann: He worked with Fieser and he spent a lot of time talking with Bartlett because he was working with physical organic problems that Fieser didn't understand.

Tishler: That's right.

Heitmann: Newman?

Tishler: Newman, I knew quite well. He came to work for Fieser too. I knew him very well.

Heitmann: Was Mary Fieser already there?

Tishler: Yes. Mary Fieser is a fabulous person. When she first came there, most of us thought she wasn't much of a chemist. (laughter) But she was not a bad experimentalist. She had a way of getting men to do things for her. (laughter) For example, we were on that second floor of Converse Hall in a large open laboratory which is no longer set up the way it was. In those days it was a five-man lab and we had a sodium press there. She'd always come in and ask, "How do you do this and how do you do that?" Her questioning ended when one of us did the work for her. I learned to respect her by the time I got out of Harvard. I really thought she was quite good. And of course, she writes fabulously. There is no question about that.

Heitmann: Were there any other women graduates?

Tishler: Yes, Emma Dietz. She taught at Barnard. Recently she retired. She married a chemist at Merck, named Stecher, and she went by the name of Emma Dietz Stecher. She was a very good chemist who worked with Conant. She came to work as his private assistant, actually. She got her Ph.D. degree at Bryn Mawr. There was a relationship with Bryn Mawr and Harvard. Kohler taught at Bryn Mawr and then came to Harvard. The Bryn Mawr job was a Harvard training post.

Gortler: And Kohler was there.

Tishler: And Fieser.

Gortler: Cope was there?

Tishler: Cope was there too, that's right.

Gortler: Somebody else I ran across recently...

Tishler: Yes, Ernest Berliner who worked as a graduate student with Fieser. He received his Ph.D. degree and is now a professor emeritus.

I keep in touch with Mary to this day. We're very good friends. There's no question that she's a fabulous writer. She understands things. She reads the literature and gets to the guts of what she reads. She understands its significance. She amazes me. She's not been given the credit that she deserves.

Gortler: We were recently talking about doing an eminent chemist tape with Mary Fieser.

Tishler: She's really an extraordinary person. And she was very good for Fieser. She really was. She watched over him very carefully. When she thought he was overworking she put her foot down and tried to get him to relax. She also got him to be friendly with the students. They used to have picnics over at their house quite a bit. And if they were going to cook out of doors, she got the students to come over. (laughter)

Gortler: Did you think that any changes were taking place at Harvard? Were Young Turks coming in? Conant and Bartlett, and of course Kisty and Fieser were coming in. You knew Bartlett as a graduate student?

Tishler: Yes, I did.

Gortler: Then he came back and he was on the faculty by the time you left.

Tishler: Yes. That is correct. Well, Woodward also came in. At first, he took my lab next to Kohler's. None of us thought he was really that great when he came over from MIT. He had such a great press. Of course, we changed our minds pretty quickly. He was also sort of irritating.

Gortler: He was away for a year.

Tishler: Just for a summer. They couldn't take him for more than a summer at Illinois. (laughter)

Heitmann: He was also very young. Didn't he graduate very young?

Tishler: Yes, I've forgotten. Twenty-two or twenty or something like that but...

Gortler: He took over your lab so he didn't really come in until after you were gone.

Tishler: That's right. But I got to know him, of course, later. Terrific person. No question about it.

Gortler: Did he consult with Merck at any time?

Tishler: Yes, during the cortisone days. On second thought, he didn't really consult. We had a problem. There were one or two people who wouldn't tolerate bringing him in because they thought he'd take over. I, however, would have loved to have had him.

Gortler: I see.

Tishler: And so we didn't take advantage of him.

Gortler: So he went to one of your competitors instead.

Tishler: This broke my heart because I used to go to him and have chats with him about my chemical problems. He'd always be very free with the time that he gave me. I think I was one of the few people with whom he would sit down and chat about problems. I understood from others that he rarely would do this. He liked to talk about his problems, rather than the problems of others, but he was very tolerant with me and very helpful. Terrific person. We did bring him in on the cortisone days and the total synthesis. It was my idea to try to get him to do the total synthesis hoping that we might be able to use it. But we didn't go ahead on the total synthesis. Today of course, it's a different problem making cortisone or compounds related to it. There are much better ways. But I feel pretty sure that if we had stuck to it in those days we could have made a total cortizone synthesis competitive with the partial synthesis starting with a steroid molecule from nature.

Heitmann: This question refers to an earlier period at Harvard from 1929 to 1935 or so. Did the faculty there do a good bit of consulting during this earlier period? I know Louis Fieser would consult with Merck later on, but...

Tishler: To my knowledge they did not. I probably wouldn't have very much opportunity to know, but in retrospect from what I know I would say that they did not.

Gortler: Kohler?

Tishler: Kohler, never. I don't think Kohler would ever have done that. On the other hand he was very free with his time if you would go to him and ask him questions.

Gortler: Do you have any idea why he would never go out and talk? Apparently his classes were magnificent and the story is that he always rewrote his lectures on a regular basis yet he wouldn't talk on the outside.

Tishler: No, he would never tell me why. I tried to get that out of him, but he wasn't the kind of person you could talk to that way. The only person--or so the story goes--that could really talk to Kohler and have him pay attention was Arthur Michael.

Gortler: Oh, that's right!

Tishler: He used to see Michael quite frequently and discuss his work. I knew someone who was Michael's postdoctorate, a fellow named Carlson. Carlson told me that it was a scream to listen to Michael and Kohler talk. It was always "Michael" and "Yes, Sir."

Gortler: What was Michael's role there? I can't figure out Michael's role at Harvard.

Tishler: Well, he had some kind of post but he didn't have to teach. He had research and laboratory facilities available to him. And he had postdoctorates working there. One of them was Gustav Carlson, who had worked under Conant and had received his Ph.D. degree. The other was a fellow named John Ross. I knew these two people quite well. Ross was a British person who came to this country and went to work with Arthur Michael. As you know, Arthur Michael also taught at Tufts.

Gortler: He'd been on the faculty at Tufts?

Tishler: Yes.

Gortler: l9l2 or thereabout. About the same time Kohler came to Harvard.

Tishler: But Kohler's l, 4 addition was really a take-off on Michael. That's why they kept pretty close to each other. They were using the Grignard reaction--alkylations and so forth. You know, the one thing about Kohler's work is that so many of the things that go on now with these alkylations with different metals--the things that everybody talks about--are really kind of old stuff done under different circumstances.

Gortler: Right.

Tishler: There are two things that Kohler missed. Incidentally, one was carried out by Gilman.

Heitmann: Henry Gilman?

Tishler: Yes, Henry Gilman. Kohler was always stressing l, 4 addition with the Grignard. It was Gilman, one of Kohler's Ph.D. students, who came along later and showed the importance of copper in the Grignard. This was something that completely escaped Kohler. Gilman showed that you could get l,2 addition in many cases and that the ratio of 1,2 and 1,4 addition was influenced by the presence of copper in the

magnesium. At that time everybody used to make their own magnesium turnings. They used to buy a bar and make those ribbons out of it.

Gortler: Was Kohler getting mixed products? l, 2 and l, 4 and didn't realize it.

Tishler: Well, it could well be. Nobody's really gone over it using pure magnesium.

Gortler: I think there was some very early work that I've looked at...

Tishler: Well, I think that's right.

Gortler: And there were some problems there.

Tishler: The other one that Kohler missed...but again the evidence at the time, the tools at the time, and so forth, were such that his deductions were correct based on everything we knew at that time. But today with modern spectroscopy it is such a different type of thing. Kohler believed that 1, 4 addition of the Grignard went through the enol-OMgX structure. The proof of it was that if you hydrolyzed the intermediate Grignard structure with acids, it absorbed oxygen and formed a peroxide across a double bond at the enol.

Gortler: Right, I noted that.

Tishler: The only fault with that is that Fuson, another of Kohler's doctoral advisees, showed by NMR many years later, after Kohler was dead, that it is not the correct structure. It is just an endoperoxide OOH on the carbon.

Gortler: I see.

Tishler: You can spot that pretty readily with NMR. But those tools weren't available then. The way the peroxide degraded and everything else indicated pretty much that it had to be something like what Kohler concluded.

Gortler: Yes.

Tishler: Then the other proof was that if you had a phenol group in the alpha position after the l, 4 addition took place, the hydroxyl group very, very slowly ketonized because of the hindrance effect. It no longer absorbed oxygen. If you benzolated the magnesium complex, you ended up with an O-Benzoate.

Gortler: Now, you did a piece of work on that?

Tishler: Yes, I know I did.

Gortler: (laughter) OK.

Tishler: Kohler's observations appeared to prove the l, 4 addition. I then proved that with certain alpha-bromoketones and the Grignard reagent, the same intermediate magnesium complex was formed. Where the magnesium resides is still obscure. That part is correct. Today you'd say it has a charge distribution between oxygen and carbon.

Gortler: We're at Merck. Who was your first immediate superior when you went to Merck?

Tishler: A fellow by the name of Joe Stevens, an MIT man. He was my first boss for about three years. Randolph Major was in charge of all the chemistry when I first came to Merck and then took charge of all research.

Heitmann: Where was Randolph Major educated?

Tishler: He got his doctoral degree at Chicago, no I'm sorry, at Nebraska. He then went to Princeton as an instructor. Here's an interesting story that I might mention. Initially it involves George Merck and his brother-in-law, George Perkins, the son of a famous banker. He married into the Merck family. Soon he and George Merck, Jr., began to run the company. George Merck was president; Perkins was the vice-president and financial head of the company. George Merck was a very far-reaching, far-thinking person. Consider, for example, that the first phenol process in the United States was done at Merck during World War I. At that time the nation's supply of phenol was cut off. The point is that George Merck was forward-looking and he thought that it would be nice to get into the pharmaceutical business. He wanted first to set up a research laboratory that would be manned by scientists. His hope, expressed in a talk he gave, was that industrial scientists would be on an equal footing with the best in academia. George decided that they ought to find a research director to head the laboratory. George Perkins was a Princeton man.

Gortler: George Perkins was a Princeton man.

Tishler: And George Merck was a Harvard man. For some reason or other they got to Princeton first and we mentioned this morning the person at Princeton who was a rather eminent physical chemist.

Heitmann: Taylor?

Tishler: Yes, Hugh Taylor. He recommended two people. One of them was Randolph Major and the other was Richards, the son of Theodore Richards, who at that time was an inorganic physical chemist, a combination but largely inorganic chemistry. I'm not quite sure why, since it's hard to find any record of what transpired, but they hired Randolph Major, an organic chemist. He started doing his work in organic

chemistry.
I'm not quite sure what would have happened if Richards had been hired. It could have been an entirely different company. After all, Mallinckrodt, a competitor of Merck's, never got into organics and Merck worked pretty much along the lines that Mallinckrodt did during those early days.

Heitmann: Was George Merck, Jr., educated as a chemist?

Tishler: No, he wasn't.

Heitmann: But he valued science?

Tishler: That's right.

Heitmann: He had the vision to move in that direction.

Tishler: Correct. And to the very day that he died he had that same vision. He did anything that could help science and research at Merck. He was a terrific guy. He used to go around the laboratories and talk to people. He was the president of the company when it got pretty big. He would get all excited about what people were telling him. He didn't understand it, but you could see he was getting all excited about it.

Gortler: That probably accounts for the fact that you had such a fantastic alumni.

Tishler: That's right.

Heitmann: You went to work in l937?

Tishler: l937. Right.

Heitmann: Who were some of the other scientists there?

Tishler: Well, very few of them are still around. There's a fellow named Cline, Joe Cline.

Gortler: He did the work on what?

Tishler: Vitamin B , with Bill Ruigh who was a Princeton man. I'm not sure where Cline came from. Then there was John Keresztesy, a very good isolation man. He isolated vitamin B , for example. He later left Merck and spent the rest of his life as an isolation chemist at the National Institutes of Health. He worked for R. R. Williams who was at Columbia as an adjunct professor. Then there's Gus Stein, and John Weijlard, a Swede. Weijlard had only a bachelor's degree but was an excellent experimentalist. He would make a reaction go and if there was anything in it, he could isolate it. He didn't know very much chemistry but he was an unusually good experimentalist.

Gortler: These were all people who were around when you were there?

Tishler: At the time I came to Merck. That's right. Stevens was there.

Gortler: They had a research group? When did they start there?

Tishler: Around l930. They say their research laboratories began operation in l933, the year of the dedication of the research laboratory. (I remember I mentioned to you we had a fiftieth anniversary which would make it '33.) Up to that time they had research facilities which had not been in one building but rather were spread around the factory. When I came in '37, they already had about sixty people in research. This included secretaries and helpers and so forth. They had a budget of around three hundred thousand dollars. It was pretty good for those days. And the business Merck was doing at that time was around ten million dollars.

Gortler: Was the production part of the plant nearby?

Tishler: Yes, it was part of the plant--in the same area as a matter of fact.

Gortler: Was it a single production unit at that time?

Tishler: At that time it was one production unit. That's correct.

Heitmann: What kind of freedom did someone like yourself have to make choices on what you would study?

Tishler: Let me say this. The approach to the problem was entirely in the hands of the experimentalist. The problem itself, like trying to find an anesthetic or cardiovascular drug, was assigned to you. But how you approached the problem...

Heitmann: Randolph Major would assign the problem to you?

Tishler: That's correct. And I can tell you exactly how we did it later when I took over. It's an interesting way that we developed the program. I'd like to tell you about that. Matter of fact, it's still being used at Merck & Co.

Gortler: Your first salary was?

Tishler: Two hundred and fifty dollars a month. I only paid fifty dollars per month rent. That was not a bad salary even though I had two years experience as a post-doc. They offered Joe Walker, who got through two years before me, one hundred and eighty dollars per month to go to Du Pont. Everybody thought, "Gee, this is tremendous!" (laughter) Yet he turned

it down and we all thought, "My God, how could he do such a thing." He just didn't want to go to Du Pont.

Gortler: What was your first problem at Merck?

Tishler: Riboflavin.

Gortler: That was the first?

Tishler: That was my first exciting problem.

Heitmann: What was your first impression of Merck's laboratory as compared to Harvard's in terms of physical plant and the kinds of apparatus used?

Tishler: Well, I thought it was quite good, as a matter of fact. They had everything. In those days things were very simple. They had all the equipment--stirring motors and Erlenmeyer flasks--things of that sort. In those days, you didn't require very much in the way of sophisticated equipment. I guess that pH meters were the most complicated piece of equipment we had. So, the change wasn't that drastic as far as I was concerned.

I really got excited about going to Merck. One of the reasons that I got so excited is that while I was still at Harvard a publication came out of the Merck laboratories on the structure of vitamin B . Well, up to those days, you know, the only people in the world who knew how to do that kind of thing were the Germans and the Swiss. And then to see this paper written by young squirts, just kids--Joe Cline was, about thirty, thirty-one I think....These were unknown people, not the Kuhn's and Karrer's of those days. This excited me tremendously. Someone gave a seminar on the work at Harvard. And gee this was fabulous! I mean this was a place to which I wanted to go for an industrial job. So, my reaction was very enthusiastic and I was going there because of the type of work they were doing. I recollect that prior to then, Merck was known as a producer of reagent chemicals--things like ether and acetone. I remember that because we used them in our research. All I could think when I was considering Merck was that I was going to work with reagent chemicals. But when it came to this work with B , I really got terribly excited about the prospect of doing that kind of work. One of the first things I did at Merck was to work on riboflavin, B . Randolph Major came to me and said, "We made up our minds that we're going to specialize in research in the field of vitamins. We're going to isolate every vitamin. We're going to determine their structures if it hasn't already been done and synthesize them and make them available." This was a wise choice because in those days no one was really doing that in the States. They weren't even doing it commercially abroad.

Gortler: They didn't know there was going to be a market for it.

Tishler: That's right. Now, whether Randolph Major developed the idea completely on his own or not, he nonetheless predicted that the day will come when we shall fortify flour and foodstuffs and will have one-a-day capsules to make up for deficiencies in diets.

Gortler: That was pretty farseeing.

Tishler: I don't know where he got it from, but he talked about it and it may have been completely his own idea. The point is that it was a field that Merck went into exclusively in those days. We were the first to do it and it paid off. And I think the Merck laboratories, with Karl Folkers behind it, probably has done more work on the isolation, structure, and synthesis of vitamins than any other laboratory in the country--in the world for that matter.

Heitmann: I don't know whether you would agree with me or not, but the work that was done in the '30s on vitamins provided Merck with the expertise that it employed when it did the cortisone synthesis and everything else.

Tishler: That's right. No question about it. It was a great learning experience and it initiated a tradition. And Karl Folkers--I'm sure you're going to talk about Karl Folkers.

Gortler: We were going to talk to you about Karl Folkers. But we're going to talk to him too.

Tishler: Sure, he's a terrific chemist, no question about it. I was very, very sorry when he left us.

Gortler: How soon after you began working at Merck did Folkers do so?

Tishler: I remember he worked a couple of summers for Merck before working full-time. He came in 1934, three years before I did.

Heitmann: Where did he get his graduate education?

Tishler: He went to Wisconsin. He got his degree with Homer Adkins, naturally.

Heitmann: Oh, yes.

Tishler: He then went to Illinois. He did his post-doc there for a year. He then went to Yale and did another post-doc.

Heitmann: Getting back to Merck in the '30s. How did Louis Fieser ever get tied up with Merck?

Tishler: Oh, that was in the cortisone stage.

Gortler: You were doing work on vitamin K first?

Tishler: Oh, that's right, you're right. I forgot about that.

Gortler: Wait a minute, riboflavin was essentially your first big success.

Tishler: That's right. Randolph Major wanted me to develop a method for making riboflavin that would be different from that used by the Swiss and Germans. Patents were issuing in Germany on the synthesis of riboflavin by Kuhn and also by Karrer. Major knew that, and as a matter of fact, he went to both people. Kuhn was tied in with I. G. Farben whereas Karrer was tied into Hoffman-LaRoche. Randolph went to both companies and asked if they would license in America. They said, "No," even though they didn't go into manufacturing. They knew there was something to it and they just weren't going to license it. So Randolph Major said, "It's got to be free from Karrer's work and it's got to be free from Kuhn's work." This is what I tackled.

It was a matter of devising a synthesis that would be practical and at the same time free from any possible patents that might issue. By that time I knew pretty much what they were doing because the publications were already in existence and patents began to appear both abroad and in this country. Improvements appeared also. The synthesis of riboflavin was carried out by both Kuhn and Karrer independently, each making an ortho-phenylenediamine with the ribose nucleus tied in and condensing it with alloxan. The diamine was made from the corresponding azo compound. In other words the ortho-amino azo compound was reduced catalytically and then was reacted with alloxan. Well, I devised a method that I started with an ortho-amino azo compounded in barbituric acid in a sort of enamine type of reaction. And this worked out beautifully. This meant that I didn't have to make alloxan which you make with barbituric acid; and I didn't have to reduce the azo grouping to make the ortho-phenylenediamine. It was an improvement therefore over the method that was devised by Kuhn and Karrer. I had to devise a method to make a ribose. In those days to make a ribose you had to extract it from yeast nucleic acids. There was good reason, however, to make D-ribose from glucose. The first step required its degradation to D-arabonic acid. This is an interesting reaction that I always meant to go back and study. You take glucose dissolved in aqueous alkali and shake it with oxygen. You knock off a carbon atom and you end up with the arabonic acid. I've always wanted to go back to that but I never did. It is an old literature preparation. The yields are awfully good.

Gortler: That's not one of those standard degradations of the sugar.

Tishler: No. It's not a standard degradation.

Gortler: It's like a Ruff-Fenton degradation.

Tishler: That's right, reminiscent of an iron peroxide type of degradation. This, however, is just air and alkali. The products separate as calcium arabonate. All you do is measure the amount of oxygen. You run it like hydrogenation equipment except you use oxygen, you see. You measure the amount of oxygen--I forget how much that was--and then you add calcium hydroxide or calcium. Yes, you add calcium to it and the calcium arabonate crystallizes out. Beautiful. As a matter of fact, when we first started out the material situation was unfavorable. We had to make our own ortho-xylene. They weren't separating it yet from petroleum. We started to make it from xylene and toluene. Well, fortunately we didn't have to do that very long. That's a hell of a nasty thing you know. Soon the petroleum people came through with ortho-xylene from petroleum fractionation. So this turned out to be a very good thing to start on and I was very proud of that the first year I was in industry.

Gortler: That eventually became a commercial process?

Tishler: Oh, yes. They built a plant on it.

Heitmann: I was going to ask you, Max--sometimes I picture you being in the research laboratory--did you extend yourself and your expertise out from the laboratory and take the product you were working on on the bench all the way to the plant?

Tishler: You hit it right on the head. Yes, I used to work awfully hard. I used to come back at night and go to the pilot plant and help the operators and supervisors. They were very tolerant of me and I got my points across. I believe that if a person wants to do something you let him do it, even though you sacrifice some basic research by taking the time to do this kind of thing. Even in the production side inside the plant I played a very important role in design of the equipment. I don't mean design of the actual equipment. I knew damn well what I wanted on a reactor, for example, how you filter and all the problems that you run into.

Heitmann: So you really did things that would be considered chemical engineering?

Tishler: That is correct. We worked with chemical engineers. But you know in those days, and I still think it's largely true, chemical engineers had very little understanding or feel for organic reactions. They are probably better today because now you have computers and what have you. In those days, however they could talk about flows and agitation among other things, but didn't know how to handle a compound. Still, I think that I taught them a lot and got my points across. Researchers actually played a very vital role in the

design of every plant that we built. We used to go over the flow sheets with the engineers. They would bring them over to our place and we'd sit down and go over them. We told them if we objected to this or we didn't like that or we had to do something else. At times we had a few difficulties trying to convince anybody but we won out in the long run. (laughter)

Gortler: That is an interesting approach to design and planning.

Tishler: One of the greatest thrills I had in riboflavin was when the plant was producing the first kilogram of stuff. I was there! (laughter) It was a great thrill. That plant cost five million dollars. That was a lot of money in those days.

Gortler: It took a lot of courage to have one of your processes put on the line like that. (laughter) Anyway, we're talking about the time the vitamin K problem came along.

Tishler: Yes, that's right. Well, Fieser was in on the problem initially and I came in kind of late. When I saw Fieser's publications I thought I had better go and see him. He did a remarkable thing. He greeted me with an open hand and was glad to see me. I called him beforehand and he said, "I'll have something ready for you when you come." He said, "Bring along some of your alfalfa extracts." I did. He took the alfalfa extracts. The isolation was from alfalfa. He took it down to dryness and picked it up in alcohol and Claisen's alkali. Do you know what Claisen's alkali is? It's strong caustic in absolute alcohol. This forms two layers with petroleum ether. So he had the alfalfa residue dissolved in petroleum ether which he shook vigorously with a reducing agent and then extracted with Claisen's alkali. First he'd shake it up with the reducing agent, sodium hydrosulfite, before using Claisen's alkali. The reduced mixture, which contained dihydro-vitamin K extracted into the Claisen's alkali, also had some sodium hydrosulfite in it. He did this just to keep the reaction reduced all the time. And then he took the Claisen's extract, acidified it with acetic acid, and extracted it back into petroleum ether. On chilling to 10 C, the petroleum ether layer deposited the hydroquinone form of vitamin K. He separated this in centrifuge tubes. Vitamin K was readily obtained by oxidation with silver oxide. He did that all in two hours time. I was so impressed.

Heitmann: This is the afternoon session. I'd like to get us back to the discussion that we had this morning. I noticed that in the late '30s and early '40s, you and Fieser collaborated with a man by the name of W. L. Sampson. Who was he?

Tishler: Well, he was a pharmacologist who did our testing.

Heitmann: At Merck?

Tishler: At Merck, that's right. He was a very good pharmacologist and he had developed a method of assaying for vitamin K activities in chickens. We measured the anti-hemorrhagic activity of a number of different compounds related structurally to vitamin K.

Heitmann: So by the early '40s you already had a team concept of research?

Tishler: Yes. That's a very distinct advantage that I think industry has from the point of view of taking a concept all the way through to reality. You need a team approach.

Heitmann: And that was there when you got to Merck?

Tishler: Well, in the beginning. I had a lot to do with making it more effective.

Gortler: A couple of your other early colleagues on some of these problems were Norman Wendler...

Tishler: Yes.

Gortler: Kurt Ladenburg and Karl Pfister. What happened to these people?

Tishler: Wendler is still at Merck. He came to me as an assistant with a bachelor's degree. He went back and got his Ph.D. at the University of Michigan and then came back to Merck. He is a very good chemist, very soft spoken; and he published a great deal. He has not tried to do too much speaking around the country so he's not very well known as a chemist but he's published a great deal. Awfully good work.

Gortler: He worked on a lot of the problems.

Tishler: Yes, that's right. Very able person.

Gortler: He went back?

Tishler: He left Merck to take his Ph.D. at Michigan. Then Kurt Ladenburg came to us. I have forgotten whether it was Princeton...

Gortler: Princeton.

Tishler: That's right. Very good chemist. He left Merck to join one of these large chemical processing companies that put up factories around the world. He retired. I hear from him at Christmas, but I'm not sure that I know what he's doing now.

Gortler: He left Merck after just a few years.

Tishler: That's right. He didn't stay too long. Incidentally, he's the great grandson of Ladenburg.

Heitmann: I was going to ask you about that. I thought that was too much to ask, but he was really?

Tishler: Yes. Then Karl Pfister, Huntress' student at MIT.

Gortler: Whose student?

Tishler: Huntress? Maybe he was before your time, but he was at MIT. Karl was a very good organic chemist. He published with me quite a bit. Later he became vice-president under me in research. Very capable chemist. He is responsible for Aldomet and several other compounds which turned out to be important drugs. Aldomet is a drug for hypertension which you can talk about some time later.

Heitmann: That came out in the sixties I guess?

Tishler: That's right. It is alpha-methyl-dopa. He conceived the idea of making amino acids with an alkyl group, particularly a methyl group in the alpha position on the same carbon atom that holds the amino group. It turned out that alpha-methyl-dopa is an extremely important anti-hypertensive agent--probably the most widely used today, even though it's been out for fifteen or twenty years now. He retired from Merck at a relatively young age. He owns property in New Hampshire. He left to become a farmer.

Heitmann: How did Max Tishler's responsibilities with Merck change between l940 and l945. Once the war started, did it change your responsibilities?

Tishler: In l945 I was in charge of developmental research and all of the projects that involved process development. I was also responsible for putting these developments into operation. I had engineers under me at that time to design the plants and to get the data to design the plants. I had a fairly large group.

Gortler: You rose up the ladder fairly quickly. How did things change for you when you came in essentially as a bench chemist? At what point did you start to take on greater responsibility?

Tishler: Joe Stevens, my boss when I first came to Merck, had some personal problems and left the company. I took his place, probably by default, because there wasn't anybody else around that could qualify. We were quite small and Randolph Major asked if I would take the job. I was in quite a dilemma at the time. Should I or should I not? If I did it meant getting away more and more from the lab even though I was very close to it. I did a lot of thinking. What probably motivated me the most was that I felt I could do more in the

long run by doing this. That's why I accepted the job.

Heitmann: Did it mean an increase in salary?

Tishler: Yes, it did. But salary never really meant much to me, and I say that very sincerely. We've always gotten along. We enjoyed the job. That was most important.

Heitmann: During the war did you do a lot of travelling back and forth from Washington?

Tishler: Not much. I did travel quite a bit, however, to a plant that we built in Virginia. We built a riboflavin plant and all sorts of other things. During the war we produced sulfa drugs and then, of course, penicillin. We launched a big drive that took a tremendous amount of effort. Even things like DDT...

Gortler: I didn't realize that you were in the DDT business.

Tishler: Yes, we were the first American company that got into DDT. Even though a company located in the U. S. A. and partly owned by the Swiss could have made it, we were asked to produce large quantities quickly--and we did so. We didn't even have appropriate equipment to make it. You know, DDT is a rather low melting solid. I can't recall the exact temperature, but I would say that it melts at about forty or fifty degrees. We didn't have any place to solidify it, so we used lead dishes placed on the floor. We just poured the liquid into the lead dishes. I'll never forget it. We'd then use an ice chopper and break the solid into pieces. (laughter) So that's how we made it. It was, after all, a time of emergency. We made a lot of it for the army. We didn't make DDT for too long, however. We got out of that business shortly after the war ended.

Penicillin was probably our greatest effort at the time. We got into it quickly and developed a practical way to produce it. It was a very successful venture. Merck penicillin was the first used in the United States on a patient. That occurred at Yale where this woman had had a general septicemia. We sent material and saved her life of course. It was very dramatic at the time. We even collaborated with other pharmaceutical companies in the early days. It was encouraged by the government at that time; you can't do it today. Pfizer, Merck, and Squibb; we worked together on the process, each one sharing its know-how with the other. We also did a lot of the chemistry.

Gortler: Had you had any experience at all at Merck growing molds and things of that sort?

Tishler: This was completely new to Merck. Actually it was new to the pharmaceutical industry with the possible exception of Pfizer because Pfizer had been in the citric acid business for many years and had made citric acid by fermentation. But

Merck had absolutely no experience in fermentation. We had to learn the hard way, but we learned pretty fast.

Heitmann: Did you begin to make some organizational changes in the lab, since you had such a much bigger group? Did you start thinking in terms of how to make your scientists work better together and did you start making changes along those lines?

Tishler: Well, I had people divided into groups and very early in the game I pulled people like Karl Pfister into management. In those days we used to call them group leaders. I never liked the term so we made them directors. Using the right term is a very important factor in morale.

Heitmann: That's true.

Tishler: I'll never forget how this very point used to annoy me before I got into the management part of research. In the old days you could never have a letterhead with your name on it. One of the first things I did was to let everyone have stationery with his name or her name on it. It was a tremendous thing. It only cost a couple of thousand dollars, but morale was boosted. (laughter) Then I said, "Look, titles are what you make them. Make some title changes."

When a person writes to the outside particularly, the impact on the reader is very important. It isn't so much the person who writes the letter as the person on the outside. "Oh, he's the director of endocrinology." He may have one person working for him, but he's "director of endocrinology." It makes a lot of difference.

Those are the little things I put in because I remembered that this used to rankle me a bit. In the old days, someone would say you can't have stationery, you don't have this title yet; but when you are grade so and so, then you can have your own stationery. It's all nonsense.

Heitmann: When did you begin hiring chemists yourself at Merck?

Tishler: Well, every year Karl Folkers, who supervised research, and I, who supervised development, used to make trips around the country looking for people. I used to go to Cornell and Columbia, Harvard, Michigan, Illinois, Minnesota, and Wisconsin. Karl used to visit some of these places as well as others. We covered a great group of universities and we exchanged information. If I saw someone I thought would be good for Karl's group I'd give him the name of that person and tell that person to write to Karl.

Gortler: When did the company divide up into development and research?

Tishler: Major did that. That was a good move.

Gortler: Karl Folkers started about three years before you did. You told me about that.

Tishler: Yes. That's right. At first Randolph Major ran the research, but then his responsibilities got heavy so he appointed Karl Folkers--an extremely good choice. Karl went to Princeton and covered some of the same ground I did, but he also covered a number of schools I didn't cover, Maryland for example. Both of us worked together pretty much on personnel matters. If he saw someone he thought I'd be interested in, he'd tell me about it. And I would do the same for him. It was a good relationship.

Heitmann: You complimented each other in some ways?

Tishler: That's correct.

Gortler: And you were going to tell us about the fact that it wasn't called development; it was called developmental research.

Tishler: That's right. I called it developmental research and gave the department the name. I wanted the term research as part of it.

Gortler: So people wouldn't feel like they were engineers or second class citizens or something like that?

Tishler: That's right. And they could publish as well. As a matter of fact my group published quite a bit. They gave papers at meetings and so forth.

Heitmann: They were encouraged to do that.

Tishler: Absolutely. I worked out a procedure whereby so long as we filed a patent application, we didn't have to wait until the patent issued. We could publish. We may have lost some things but I think that we gained more than we lost. We published some things too early. In spite of it all we've done well. The same with Karl Folkers' group. They published a great deal of their research. In fact, we got it down to the point that if we had something that was hot, we felt we had to publish. The patent people had three weeks to file an application. This put them on the spot. They had to hurry to get it out.

Gortler: So you really felt competitive with the academic world in terms of getting research done?

Tishler: That's right.

Heitmann: That's probably why they had such a collection of top flight scientists.

Tishler: There are companies today that encourage publication but they wait until a patent is issued. That can be two or three years later.

Heitmann: When did Sarett come to Merck?

Tishler: I guess in '4l. Maybe a little before World War II started. Sarett worked for Wallis at Princeton. Good strong man, Everett Wallis.

Heitmann: I noticed that Per Frolich arrived immediately after World War II. Did he take Major's job?

Tishler: Well, he was being prepared to take Major's job. He came from Esso. He taught at MIT and I think that he also got his Ph.D. at MIT. It didn't work out as well as they anticipated. That was the time when someone talked George Merck into bringing in an industrialist chemist. Frolich had a good reputation. I learned a lot from Frolich. That's one thing I used to tell my people. I've learned from every man for whom I've worked. I've always felt that if this man was put in a position of leadership there must be a reason. And I must discover that reason and see if I can benefit from it. Instead of griping and being critical of the person, I would learn from him.

Frolich had one positive characteristic. You know, I used to work hard and demand the same from my people. He taught me how to be human; to get a lot out of people by being warm with them--like the picture I showed you back in my office, babies and stuff like that. How to really get to know people who work for you and how to motivate them by being good to them and expecting to get the same in return. Work hard, don't be less demanding, but do it in a way that is not offensive. I learned that from him.

Heitmann: Was George Merck, Jr., still around?

Tishler: Oh, yes. He was still around. He was around until about the early fifties.

Heitmann: And still exercising that vision of research.

Tishler: Yes.

Gortler: How long did Frolich stay?

Tishler: About five years. Maybe a little longer. It was under him that I got my first promotion--to the top part of research.

Heitmann: You became the president of...

Tishler: No, I became the vice-president of research under him. Then I took his place.

Heitmann: It was Merck Sharp and Dohme.

Tishler: Merck Sharp and Dohme came later. This was Merck. I was made vice-president in charge of research at Merck. Three years later I became vice-president in charge of research at Merck Sharp and Dohme.

Heitmann: It went from Merck to Merck Sharp and Dohme. What happened with Sharp and Dohme?

Tishler: I'm not sure I can recall correctly the history of Sharp and Dohme now. I did know it once, but I'm trying to tell it accurately. Sharp and Dohme was a company, a separate company that resulted from a merger of two companies in the pharmaceutical industry. They made some drugs from inorganics, made serums, tinctures and suppositories, and sold them in drug stores. They started a research group about l945 or l950. They hired some chemists and pharmacologists and began to get into things.

Merck was a chemical company, although also interested in medicinal agents. Merck's policy was to make these things available so that pharmaceutical companies would buy them and sell them in the form of prescription drugs. We didn't sell vitamins, for example, to the consumer or to the physician. We sold them to companies like Parke-Davis and Upjohn. They formulated the vitamins into tablet or capsule form and then sold them to the physician and the consumer. Some even went over the counter. We consider ourselves manufacturing chemists rather than pharmaceutical vendors or whatever you call it. This was fine but when we tried to sell cortisone, streptomycin, and penicillin in bulk, we were competing with these companies. Upjohn, for example, also made steroids. They had a vested interest because they were selling extracts of the adrenal gland. And here we were putting out cortisone which is a greatly improved substitute for what they were selling. So they felt that they had to get into it, you see, to preserve their business and to expand. The same with penicillin. You sell the penicillin in the form of something sterile for injection purposes. The pharmaceutical companies like Lilly and others said, "Why shouldn't we make our own penicillin? We're in this business. This is our bread and butter. We'll make it. We'll go all the way through it." Of course, Merck was being left out. We did all the research, but we couldn't dispose of the stuff.

George Merck, and Mr. Kerrigan, who was vice-president under him, said, "Well look, the only way we're going to survive and take advantage of our research organization is to set up a team of pharmacists." We didn't have any pharmacists in our organization. That's important. It's very important in pharmaceuticals to know how to formulate a chemical to make it in suitable dosage form. We didn't have a sales organization. When you have competition you have to send people around to make sure that the physician is going to prescribe your product. So they decided they had to do something and it so happened that Sharp and Dohme was one of

the organizations. They talked with me a good deal. There was a good reason for it. There was a person who was head of Sharp and Dohme at that time who had worked for Merck previously.

Heitmann: Who was that?

Tishler: Mr. Jack Zinsser, a cousin or a brother, I think, of Hans Zinsser who was a famous bacteriologist at Harvard. Well anyway, Jack Zinsser and Mr. Merck got together and decided to merge. Actually, that was a merger made in heaven because we just fitted perfectly with each other. The merger gave us a pharmaceutical organization and a sales organization. Sharp and Dohme did some good research too. So we gained a lot. This is where the Merck Sharp and Dohme comes in. The Sharp and Dohme people felt that they wanted to keep their name before the doctor. So, we had Merck Sharp and Dohme Division of Merck & Co., Inc.

Heitmann: Let's see. I suppose that Don Cram worked with you on the penicillin project.

Tishler: That's right. He worked with Kurt Ladenburg directly but he didn't consider Kurt to be a very bright chemist. Don was a very bright person obviously.

Gortler: He didn't mention Ladenburg when he talked to me. He said, "You know Max Tishler was my boss." (laughter)

Tishler: I know that, yes. He completely ignored Kurt. He used to come to me all the time. I couldn't stop this and fortunately Ladenburg didn't mind.

Gortler: You were apparently very influential in getting him to go back to graduate school.

Tishler: Oh, absolutely. I saw potential greatness in him. And I recognized that this man was going to get places. I encouraged a lot of people to go back, by the way.

Gortler: I know there were a couple of other people. I can't remember who. Someone else had gone back to Harvard.

Tishler: Yes. Norman Wendler went, with my encouragement, to work with Bob Woodward as a post-doc after receiving his Ph.D. degree at Michigan. And there were a lot of others whom we sent back to school. We had a policy of encouraging people to go back for advanced degrees.

Heitmann: That still exists there?

Tishler: Yes.

Heitmann: And then you rehired these people after they got their degrees?

Tishler: That's right. Sometimes they didn't want to come back. I can understand that. For example, John Babcock at Upjohn worked for me. Very good man. He left us in order to get the Ph.D. degree at Harvard. He felt that when he came back he wouldn't have the opportunities that he would have in a completely new place. I could understand that.

Gortler: One more word about Cram. You told him to go to Harvard and work with Fieser.

Tishler: That's right. He didn't like Fieser.

Gortler: He said afterwards he understood why you did it. Later on he appreciated having done this, but he wasn't happy at the time.

Tishler: No, he wasn't happy.

Gortler: You knew that?

Tishler: Sure, I knew that.

Gortler: Was there a reason why you said he should work for Fieser?

Tishler: Well, because I felt that Fieser would push him along. I tried to tell Cram, "Hold yourself in check, then you'll come out of this on top. Just don't worry about it." But he was an impatient young person with a lot of ability. He wanted to get there fast. And Fieser wasn't always right. His grasp of theoretical chemistry wasn't as good as Don's. You could see that. He was a great experimentalist, however. I'm glad that you spoke to Don because he and I kid each other about it now.

Heitmann: I would like to ask a very general question. Could you reconstruct a week of what Max Tishler did during a typical week at Merck's, say circa l949 or during the cortisone work.

Tishler: Well...

Heitmann: Did you have various responsibilities to discharge?

Tishler: I had teams working on the development of the cortisone. I mentioned before that there was a tremendous improvement in yield and substantial change in the reactions --sometimes the chemistry as well as the conditions. The whole synthesis (which consisted of about forty reactions when we first started) was brought down to less than thirty, about twenty-six actually. I used to tell my teams "You worry about the last five steps," "You worry about the next five steps," all the way through. Well, once a week I'd meet with each team and bring the whole group together to discuss the

highlights and to see what was going on. The different teams could ask questions and make suggestions. This took up a fair amount of time. We had other programs too, of course. The work with penicillin wasn't completed. We had streptomycin. We had other antibiotics as well. We had already developed an anti-hypertensive agent, mecamylamine, on which we also spent a lot of effort. I'd also go round the pilot plant to see how things were going there.

I went into production areas. For example, we had a big problem with osmium tetraoxide, used in our first cortisone production process for introducing a hydroxyl group in position-17 of the steroid nucleus. After seeing the large-scale operation with osmium tetraoxide, I concluded that we had to get rid of it, replacing it with a better process. The osmium tetraoxide process was pretty messy to begin with, damn expensive, and also dangerous to use. We had the recovery yields up around about ninty-eight percent but that's still not good enough when you use an expensive reagent and even use it over and over again. So we had to develop other methods. This was all a part of the responsibility of development. Lou Sarett was satisfied when he made his stuff in .0035 percent yield from desoxycholic acid. (laughter) That was all right. It accomplished the purpose. But we had to make it in big kettles, in big stills, with much greater overall yields.

Heitmann: So, Sarett was working in research under Folkers?

Tishler: That's right.

Heitmann: Then the process would come to you.

Tishler: That's correct. And so this was what I was doing much of the time. On the other hand about l95l, '52, I think it was l953, I was promoted to director of all research and development. But in '49, I was still in development and very active in trying to get things to the manufacturing level. Everybody did a splendid job. Dividing it the way we did was extremely important. For example, the person who was worried about the last set with the osmium was the leader of development. He thought he had to do something about getting rid of osmium. We spent a lot of time and finally did get rid of it. We used permanganate. We had to work out the conditions, but it worked just fine. It's hard for me to give you a lot more detail.

Heitmann: That's fine.

Gortler: When you went up the ladder in '53 to become president of Merck Sharp and Dohme Research, did someone else take over your position in development?

Tishler: Yes, a fellow by the name of Bob Denkewalter, University of Chicago Ph.D.

Gortler: A student of Schlesinger's?

Tishler: Sletzinger was one of the chemists in the group. Very good chemist. Are you talking about Mike Sletzinger?

Gortler: No, I was talking about who Denkewalter worked for. Herman Schlesinger.

Tishler: He worked for Schlesinger, that's right.

Gortler: And you had a Sletzinger in your group?

Tishler: Yes, I had the two men confused. I thought that's what you were referring to, S-L-E-T-Z.

Gortler: You've got several papers here by him.

Tishler: I would say that Sletzinger was an extremely capable chemist. Incidentally, we sent him back to school to get his Ph.D. at Columbia. He was a junior chemist in the late thirties and he worked for me.

Gortler: Right, I read a couple of papers of his. I was fairly impressed with the things that he did.

Tishler: He's done terrific stuff. Even after I left he did terrific stuff.

Gortler: Anyway, Denkewalter took over.

Tishler: He took over some of the responsibilities I had and Pfister took over some of the other responsibilities. Denkewalter took over all of development and Pfister reported to him.

Gortler: And they reported to you? Did the people in research also report to you?

Tishler: That's right. Folkers reported to me. Sarett worked for Folkers and when Folkers left I put Sarett in charge. We had good people.

Heitmann: Yes. A fellow by the name of Mozingo was there?

Tishler: Ralph Mozingo, that's right. Ralph Mozingo was Homer Adkins' student. He was a specialist in hydrogenation --particularly high pressure hydrogenation. He discovered the desulphurization reaction: replacing the sulphur via hydrogenation while using the Raney nickel catalyst as a reagent.

Ralph really did a tremendous job for Merck and for organic chemistry. In the penicillin structure work penicillamine was one of the first things they isolated by degradation. I'll never forget the day that Mozingo ran the desulphurization reaction on penicillamine and got D-valine.

That was a terrific triumph. He had taken a precious compound like penicillin, worked on the structure, and finally got a known substance out of it. You can imagine the morale boost that was. Such a simple thing as D-valine.
Ralph left Merck in the early fifties. He was a great chemist and we were sorry that he left.

Heitmann: Sure.

Tishler: Then we knew exactly. Then we synthesized D-penicillamine quickly, you see. That was his work; desulphurization using Raney nickel.

Heitmann: In the fifties, I guess, one of the great changes took place in industrial research. My information about works laboratories in the fifties comes from something you wrote in a little book called By Their Fruits.* You wrote about modern scientific laboratories and how they differed from those of the thirties. You also wrote about links with university and government. What are your thoughts about how the government's presence at Merck differed after World War II? What I am thinking of here is...I noticed that Merck had a very large cancer project in the fifties sponsored by the NIH.

Tishler: We never took any money from them. Never. That's one thing that Merck prides itself on. We never had a contract for more than a dollar. We never took a contract, as a lot of industries have, on regular grants. We had to take a cancer contract, they insisted pretty much that we do that. We thought if we turned it down, we'd be embarassed. So we did take it on, but as a one dollar proposition. We did the same during the war for penicillin and a for a few other things. The government wanted to get whole groups working together. We always prided ourselves on it.

Gortler: You commented that a project like the penicillin project couldn't be done again because of the cooperation it entailed between companies.

Tishler: Yes, that's correct. As a matter of fact when Kefauver was prosecuting, or rather persecuting, the pharmaceutical industry, he tried to raise the point that the development of penicillin had involved a lot of collusion during the war years and that the industry profited because of it. Yet, Vannevar Bush, who was Tsar during the war years, and was one of the people who sanctioned our working together, just clobbered Kefauver. He said that this was just nonsense. He said that these people did a remarkably good job at a dollar a year, and they didn't profit by it. He pointed out that the companies made a very reasonable profit. No question about that. But what was your question?

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*Merck Sharp and Dohme Research Laboratories, By Their Fruits (Rahway, New Jersey: Merck & Co., 1962).

Heitmann: Under the circumstances wouldn't the companies do it again?

Tishler: During the war years we were urged to do this kind of thing. But during the war years Congress passed legislation which allowed this to take place with about no possibility of....You couldn't do that today under ordinary circumstances because even if you tried to cooperate with another pharmaceutical company you would be subject to antitrust investigations. So that's why we could collaborate during the war on this kind of thing but can't do it under normal circumstances.

Gortler: OK. So, with a crisis situation you could probably do it.

Heitmann: Bush, I was going to ask you about Bush. I understand that Bush was chairman of the board. How did he get that honor and...

Tishler: He was a great friend of George Merck who was in charge of biological warfare during the war years. Camp Dietrich was his place. I'm not sure who was directly under him, but the point is that he was involved in it. He was given the job to mobilize biological warfare. So this is how we got to know Vannevar Bush. He was invited to join the board. He had been there only a few weeks and they made him chairman. He was a very good chairman and he was one of the few people on the board that I knew who would come around to the laboratories and talk to the chemists and biologists. He was a remarkably bright and stimulating person. It was a great experience for me.

Gortler: When we were talking a bit earlier you wanted to tell us how decisions were made about what the company would work on.

Tishler: Well, I've always said that the way we selected problems was based on the people at the bench. They were the experts. We hired people who had backgrounds in certain fields, particularly in biology and medicine. We'd know, for example, that we wanted experts in parasitology because it could lead to some important products. So we hired some good people in parasitology. They would know the literature and the problems.

The one thing about the health field is that where there's disease, there's a problem. It isn't very difficult to select the problem. Chemists like to be in on this sort of thing because they know that whatever they are going to do is going to have some utility. It isn't like making a polymer that one may or may not be able to sell. If the drug is more effective than the existing one, you know there is going to be a need for it.

So what we do once a year, about September or October, is

to have people begin thinking about what they want to work on next year; that is, what they think they should be doing on the basis of where things are now. They then write a very brief report. They state what's been accomplished during the year and then what they propose to do the next year. Now if they want to drop it, this is the place. Say, "This is leading nowhere. I want to drop this project." They might then propose something in its place or they might propose continuing their work, perhaps modifying it a bit or maybe not at all. And they would also tell of their personnel needs--either to keep the number the same or to add more people. The whole enterprise started therefore with the people at the bench making suggestions.

We usually collated these suggestions, went through them, and found that there'd be about fifty to seventy-five of these projects. Different senior people would then work on these projects with their people. They would send their people literature to find out certain things and expand their reports. We'd then put this enlarged collection together. We used to call it the "green book." It contained every project we were working on, where the projects stood, what we proposed to do with them, where we thought they were going, and the personnel we were going to need in order to undertake them.

We'd then have a meeting on this at Absecom near Atlantic City in New Jersey. There's a big golf club there. We'd spend a whole week there. We'd take the top people in research and when appropriate also bring in some people from the bench in Rahway. These people would discuss the work they've done, why they think they should continue, what they think they should change, why they think they need twenty people, or whatever else they wished to discuss. We'd start at 8:30, go all day, and, if necessary, continue into the night. We took Wednesday afternoon off, but finished our work in one week nonetheless. That was the important thing. We got together for one week and we stayed close to it. After that, we had our financial people rough out a budget estimate. We'd discuss this and get back to the top people in research. I would say that we accepted ninety-five percent of the proposals.

After we got all of this together we'd present our proposal to management. We did it in two ways. On the one hand we'd present it to the top people of each of the individual divisions, for example, the pharmaceutical division in the United States. They'd argue with us and tell us what they thought. But again, I'd say ninety-five to ninety-eight percent was fine. They'd question only two or three or four percent of our proposals. We'd follow that procedure in the international division, in the chemical division, indeed, in all the divisions of the company. Each would have a chance to go over the program that we presented to them. After that was done, we made any changes that we thought should be made. Then, and on the other hand, we would present our modified program to top management. We'd spend a day with them and it was done. They'd tell us about two weeks later it's all approved, or you've got to cut back ten thousand or ten

million, or whatever the situation may be. But again, I would say that we got ninety-eight percent of what we asked for. There never was any drastic change--not as long as I was there. It was a godsend from that point of view. Once that was done we were set for the year.

We could make changes within the program or decide not to change. If we wanted to change the project, then we consulted with our operating committee in research, because we were changing direction. We would sit down and listen to the people involved. They would come and say that we think this is a blind alley, or we don't think this is the way to go about it any more. They might say that we ought to change either the project or completely change direction. We'd all go over it and make a decision. We usually got the signal to go ahead. In two weeks we gave them an answer.

Heitmann: Was this a mode of operation that you had started?

Tishler: That's right. They still run it that way.

Heitmann: There was a quote (laughter) in that New York Times article where you said, "I'm not a good administrator."* Obviously, that's false. Are you overly modest?

Tishler: No. I'm not a good administrator and I'll tell you why. I involve myself too much in everything. On the other hand I've always had a personal approach to problems. People knew I was interested in what they were doing. They even tried to get me to go to the Harvard Business School to take...

Heitmann: Yes?

Tishler: I refused to do it. Someone came to my boss Henry Gadsden, president of the company, and said, "Tishler is not going to do it, what are you going to do about it." He said, "Well, I can't argue with him, look what he's done for us. If he doesn't want to go that's up to him." Some people can put in systems and operate so they don't have to get so much involved. That isn't my way. With me it used to be a twenty-four hour job. From that point of view I was not a good administrator. This is what I mean.
On the other hand, I think that my relationships with people were a hell of a lot better because of that. They knew I was interested. For example, I'd read their reports and if I saw something interesting I'd make a comment and send it to them. This was great. Or, I'd ask a question. They knew very well I was coaching them, you see. This was important.

Heitmann: You weren't so far removed from the laboratory.

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*See page 13 of this transcript.

Tishler: That is the point.

Heitmann: You weren't just a figurehead. You were actively participating.

Tishler: They appreciated it. Oh, I would delegate.

Heitmann: You did delegate.

Tishler: Oh, I did delegate some of it, sure. But I had to know what was going on. I mean I'd walk down to the laboratory and ask a person, "How is it going today?" or "What happened with that reaction?" or something like that.

Gortler: How did you feel as you got further and further from research.

Tishler: It was kind of frustrating. I used to have what I call a Friday letter. We'd call it an "F" letter. Anybody could write a couple of sentences about what happened during the week. It didn't have to be proved so that he could swear by it. I used to read every bit of those things. Each "F" letter was no more than two pages in length, yet if there was something that interested me I'd call up the person who wrote it and find out more about it. I might then call a group meeting and get the author to make a presentation. This kept people on their toes. They knew, by God, that there's someone that cares about what they're doing.

Heitmann: So you would say that that is the greatest asset a manager could have?

Tishler: I think so. Today modern management has moved away from that. I think that this is one advantage that the Japanese have over us. They take greater interest in their people. The boss is in there all the time, encouraging people, showing that he cares about what they do. He shows that he's trying to help them.

Heitmann: I think that with most people the primary driving force behind the quality of their work isn't money. It's personal involvement with their bosses.

Tishler: There's no question in my mind about that.

Heitmann: Did you retire from Merck in '70 or '69? How did it happen?

Tishler: I wasn't sixty-five. I was sixty-two when I started thinking about it. Well, it happened because one day I got a telephone call from a person I respect very much who asked me to meet him in New York and have dinner with him. I did. He asked me if I would like to go to Israel and head the Weizmann Institute? I said, "Why should I want to do that when I've

got an organization in the United States equally as distinguished as the Weizmann Institute and I don't have to worry about funding?" He said yes, but don't forget that when you are sixty-five, out you go.
Mrs. Tishler and I decided against the Weizmann Institute because it meant being out of the country for at last six months of the year. Mrs. Tishler felt that she didn't want to do that--and, of course, our children are here.

Heitmann: Merck has a retirement policy?

Tishler: Oh, sure. I hadn't realized that here I was sixty-two. It bothered me, so I spoke to a friend of mine, Nils Wessell, who used to be president of Tufts. He retired as president, not because of age, but because he had served for nine years and thought that a person should not be president of a university more than ten years. So he headed the Sloan Foundation. I had dinner with him one night. I was beginning to think I ought to be planning ahead. He said, "What would you like to do?"
I said, "I don't know. I certainly don't want to go into industry any more. I can't, but maybe academia."
He didn't say a word to me. Later however, I started getting letters and telephone calls (laughter) asking if I would I be interested in discussing the matter with him.
Nine different schools expressed an interest in me. (laughter) I finally narrowed it down to two, Rice and Wesleyan. As I said when coming over here, the weather made a big difference to us. I'm so happy that we joined Wesleyan. It has been a wonderful place for my wife Betty and me.

Heitmann: They were just starting here...

Tishler: They were starting the graduate program, that's right. It had functioned for only a year or two.

Heitmann: Actually, you had to retire after a short while from here as well.

Tishler: I retired and became emeritus, but I didn't have to leave the establishment. I have a letter saying that as long as I am able, laboratories and facilities are available to me. That's why I'm here so long.

Heitmann: You don't actually take a salary.

Tishler: I took a salary initially--more or less to prove to myself that they wanted me. I never used it. I didn't need to use it. I put it into research.

Heitmann: Did you send some of your students to Merck?

Tishler: I've sent undergraduates to Merck. I haven't been able to send any of our Ph.D. graduates to Merck, however.

Heitmann: Just to round out the Merck business. What do you think are your most important contributions, the most fascinating contributions?

Tishler: Well, in general, I got a great deal of pleasure thinking about our contributions to medicine. I think that we saved the lives of a lot of people.

Heitmann: OK. We were talking about what you thought your major contributions were.

Tishler: Yes. I think that we contributed to the control of disease and made life more pleasant for a lot of people. This has given me the greatest pleasure. We had a fiftieth anniversary, as I said, of direct research and as I look over what we have done during the period of time that I was there, it has really been a fabulous era as far as work is concerned. I brought along a list of products that Merck has come out with in the last fifty years. All those with check marks are products that originated while I was an important part of research. You can see we were very productive and developed, besides the drugs mentioned previously, such important ones as the thiazides, vitamin B , the antiparasitic drug thiabendazole, and vaccines. This has really been a golden era as far as medicinal chemistry is concerned. I'm not saying that we're the only ones. A lot of companies have had a similarly spectacular era, but I personally feel as though we made an extremely important contribution. It has also set up a tradition as to what the pharmaceutical industry means and can do. It has justified the industry in spite of criticism. It is a very important tool for the country and for the world.

Personally, if I look over what I've done, I can't choose which development gave me the greatest thrill: cortisone development, streptomycin development, or penicillin development. It's like saying which of your twelve children you like best. It's hard to do that. Every one has had an impact on me. Consider, for example, the commercially unimportant drug that I helped to develop, namely, actinomycin, an organism that Waksman discovered. This substance turned out to be an important compound useful for treating a very rare form of tumor, called Wilms tumor. This afflicts children. The number of cases that occur each year are not very great, but for the individual child and his family actinomycin is damn important. And I can remember making it available. The late Sidney Farber who was a great pathologist, set up the Dana Farber Institute in Boston. We supplied material to him. One time he called me and said "Max, I'd like to have you come up and see some of the patients that have been getting actinomycin." He introduced me to about a half dozen children who had been treated with actinomycin five years earlier. It was really a wonderful sight to see those kids. They looked so robust and they were considered to be permanently cured.

We also developed penicillamine into another small drug.

Penicillamine was found to control Wilson's disease, which is the inability of the body to excrete copper. During the course of this disease, copper settles in the brain tissue and in the liver, and in the case of the brain tissue, causes a degeneration or a lack of development of the brain. If it is not treated quickly enough, the child becomes a moron. Well, I lectured on that when I first came to Wesleyan. Afterwards, one of the students came up to me and said "You know, I have a cousin that was treated with penicillamine. He had this disease. He just graduated at Connecticut University." He even introduced me to the cousin.

These things give you a terrific amount of self-satisfaction. It makes everything worthwhile when you see things like that. I can talk about Diuril. I can talk about cortisone. I can talk about a lot of other things. We used to get letters from patients and their families and circulate them among people on the job so that they knew what was happening. They appreciated it. This is enough to give anybody a terrific psychic reward.

Gortler: I keep thinking back to your delivering medicines in l9l8. Somehow you are getting your reward. You have done something to help those people. I asked you about this story earlier. It's symbolic of Max Tishler's toughness with his workers. How you came into the lab? Do you remember that? The situation where the compound was dropped and...

Tishler: Dropped it on the floor, that's right.

Heitmann: What was it?

Tishler: A very precious compound--the synthesis of hydrocortisone. It was dropped on the floor and we sopped it up and finally isolated material out of it. And I did make the crack that I hope this isn't your blood. (laughter)

Gortler: You were pretty active in the ACS during some of these years.

Tishler: That's right, yes.

Heitmann: That can be fairly time-consuming and not always rewarding.

Tishler: Don't forget my greatest activity in the ACS was after I joined Wesleyan in l972.

Gortler: Right.

Tishler: I came in that period of time when there was a lot of unhappiness at the so-called grass roots. That's when the "grass roots" was with Alan Nixon who followed me as president of the ACS.

Heitmann: Oh, I didn't realize that.

Tishler: Yes.

Heitmann: That's the Nixon I was talking about this morning, not the other Nixon. (laughter) Now I know who you're talking about.

Tishler: Anyway, at that time this situation threatened to break open the American Chemical Society. I felt that I had to do something to quiet it down. Nixon became president-elect when I became president. I thought it best to put him on the job to see what he proposed. He was more talk than action. But I do think that I made industry more aware of the fact that it can't just fire professional people, particularly chemists, unless as a last resort. Industry had to treat its people as professionals.

Heitmann: So you were really pushing for ACS professional standards or...

Tishler: That is correct.

Heitmann: A professional relations group that they have now.

Tishler: But not to the extreme that some of them are talking about today. In those days, for example, we published names of companies that didn't treat their people well when they let them go, like not giving them sufficient notice or severance pay or whatever. I thought that companies didn't want to have their names associated with that. I think it made them very conscious. That was a tool we could use. Creating a strike situation was something else, an impossible thing in my opinion. But I think we managed to hold the organization together. That was a crucial period. I wish it hadn't been because there were other things I could have done more effectively. But that was the emergency situation we had to face.

Gortler: So you opted to run for president during that period because of this.

Tishler: That is correct. I saw this coming.

Gortler: Actually, about twenty years earlier you'd been chairman of the Organic Division.

Tishler: That is correct. Then I got involved in Merck.

Heitmann: I see.

Tishler: Then I also worked on Organic Syntheses. I played a role in that.

Heitmann: You had been checking Organic Syntheses as a graduate student. You were editor of Organic Syntheses.

Tishler: Yes, I was. That's right.

Heitmann: You were also chairman of the American Section of the Society of Chemical Industry. I don't know what society that is.

Tishler: Well, not a very large organization, but it goes back to Great Britain. That's where the mother organization is. The Society of Chemical Industry is a large organization in Great Britain. They put out a weekly magazine or journal in which even scientific papers are included. I was elected chairman of the American Section. In general, people from industry join it. I didn't expect to become chairman, but I did. I served for two years, one as vice-chairman and then one as chairman. During the third year I was honorary chairman. They make you serve the third year in that capacity. It didn't take an awful lot of effort on my part. We had two meetings a year. That was it. We gave out awards, like the Perkin Medal and the Chemical Industry Medals.

Heitmann: You've won many awards. I guess Leon could mention some of them. Of all the awards that you won, was there one in particular...

Tishler: Priestley is the one that I remember the best. The one that I treasure the most. There's no question about it.

Heitmann: Being a member of the National Academy.

Tishler: Yes, I treasure that too.

Heitmann: I sort of tagged the Priestley when I saw that.

Tishler: I treasure that too. You know, life has been very good to me, as I said before. Been wonderful. A lot of it is timing. I came into the world at a time when effort really paid off. And I was lucky too.

Heitmann: You teach these two courses, the one you call, Discovery and Development of Drugs. I take it that goes through a series of cases, or what kind of course is that?

Tishler: Well, yes. I try to make it a chemistry course. There's a lot of chemistry involved in it. It's really medicinal chemistry in the broad sense of the word. But I start off by saying how research is done, where its being done, and the steps it goes through. The first lecture gives background. Then I take up drugs of antiquity, drugs that have been used over the centuries: atropine, belladonna, opium, and morphine and how this led chemists to isolate the active principles. One of the things I am trying to do here--and I think I've succeeded in doing it--is to give students a feel for the usefulness of chemistry. It is not just an intellectual challenge. Today with all they have to

learn about theory and all kinds of things, they say, "What good is this?"

Heitmann: This course, by the way, is taken by chem majors?

Tishler: Chem majors and non-chem majors. So long as they've had a course in biology, organic chemistry, and inorganic chemistry they can take it.
Students tell me that they begin to understand that chemistry does have a place in our welfare. Until then they just don't understand what it's all about. Prior to then, they see it as something that they have to learn if they want to go to medical school or graduate school.
After we go through drugs of antiquity I try to show how working with drugs led chemists to isolate things in order to find out what they are chemically and then to modify these things and try to improve on nature. This is how drug development was started. Later on, they began to make discoveries by screening, sulfa drugs for example, and this led to a whole bunch of new drugs not only to control infectious diseases but also diabetes. I then show how chemists made all of these various things and then how uses were found for them. Then I consider the rational or biochemical approach to drug development. We see that by knowing the relationship between abnormal biochemistry and disease we can treat the abnormal biochemistry, and therefore control the disease. Hypertension is a good example. I just go through the whole thing and finally get to the point where I talk about structure and drug relationship.
On the final exam, I'll give them a compound and say what do you think this is good for. It may be something out of my imagination or I may give them a structure and say now if you were told that this is a drug that has a certain type of activity, how would you modify it in order to get a better drug. They would have to think of compounds that may have better activity than the original compound or that are less toxic. We also get into cell membranes and how their configurations are important in drug metabolism.
I'm not trying to make my students medicinal chemists. I'm trying to give them an appreciation of what medicinal chemistry is all about. My course forms a good basis for them if they go into that kind of work. We give some industrial courses too, for example, Chemistry of the Chemical Industry.

Gortler: That's what I was going to ask about. It's a fascinating name.

Tishler: I'm not interested in teaching engineering to students, but I am interested in teaching the chemistry that's involved in the chemical industry. I start with petroleum and go on from there. I treat the compounds you get out of petroleum, how you get them, what's catalysis, and homogenous versus heterogeneous catalysis. I'll even give them complicated synthesis, ascorbic acid for example. One of the things I do is give them an exam in which I say, "Given that

we want to make some compounds in large production, give me the best method. Use any source you want. Talk to anybody in the world about it. Tell me how would you go about doing this economically and the best possible procedure you can devise." Now that doesn't mean just a synthesis, rather it means that they're being graded on how good their synthesis looks to me. I'm not interested in the fifty step synthesis. It's got to be something that looks pretty decent. This is the way it is in industry. Nobody says you can't go to the library. Nobody says you can't have a consultant. It's all right if you want to call someone in industry or someone like Bob Woodward and find out how he'd go about doing it. That's your business. I want the best method. This has been very successful, too.

The last couple of years I've been slowing down a bit, so I brought some people from the outside to help me, for example, the director of chemical research of a pharmaceutical company, Boehringer Ingelheim, located in Ridgefield, Connecticut, about thirty miles from here. He and I share the course in medicinal chemistry. And it's good because he's right on top of it. You see, I'm getting a little old for this kind of thing. I do the same thing on the industrial side with a man who was research director of Uniroyal. Then I have a man from Upjohn plastics division give a course on industrial polymers.

Heitmann: It's a comprehensive course.

Tishler: I orchestrate it.

Gortler: When you worked twenty-four hours a day outside of chemistry what did you do?

Tishler: Well, I always had a garden. I planted big dahlias and different types of flowers. When I didn't have much to do, I thought of building a greenhouse. I started collecting plants, growing them, even hibernating them. I get a big kick out of it. My wife does, too. She helps me.

Heitmann: We've seen some examples of Dr. Tishler's plants. They're not only beautiful; they're enormous.

Tishler: You know, I get calls. For example, this last Saturday, the Malcolm X house had to put on a play. They wanted plants to set on stage. They came and got about a dozen big plants. This happens quite frequently. When our museums have a special exhibit they'll call and say, "Do you have a plant we can borrow?" They send a car down to pick it up. Three years ago we had a graduation exercise and it rained. If it rains you can't have the exercise outside, so we go into the gym, although it's really not a gym. It's a hockey arena. Well, to make the hockey arena presentable they asked me if I would bring twenty or so plants to put on a platform. I got a big bang out of that and not only that, I like plants. I like to get my hands dirty.

Heitmann: Somewhere I read that at least once a year while you were at Merck you would disappear for a period of time. You would go to the Catskills or somewhere.

Tishler: The Catskills. That's right.

Heitmann: Without a telephone.

Tishler: No telephone. That's right. If they had to contact me they'd call people at the far end of the lake about a half a mile away from my house. They'd come up by boat and tell me to call so and so.

Heitmann: A convenient way to get away from the pressures.

Gortler: Just a way to make sure that you spent some time with your family.

Tishler: That's right.

Gortler: Where do you think organic chemistry is going today? Science in general?

Tishler: Well, I wish I were twenty-five years younger. I think there's great excitement ahead. As I mentioned before, structure work has progressed tremendously. There is nothing too complicated when you can understand how it's made and from what it's made. Making these things is the big problem. It's getting more and more complicated. I think our understanding of what life is or of what is abnormal, of what disease is, what aging is, that's all becoming very clear. There is no question that in the next twenty or twenty-five years the knowledge we are going to gain on life itself, what it is, and how to control it, is going to be fabulous and tremendous.

Now what does this mean? Well chemistry has an important role to play because there is so much to be done. Even this business of the environment. Sorry to say, but as you know, we are told that we're poisoning the environment. But all it means is that we'll be creating new problems for chemistry. There's no question about it, we can't go back to where we were fifty years ago. Nobody's going to sell us on the idea that we're all going to live like people in Maine. We just have too many people for that to occur. Furthermore, nobody's going to stop the expansion of populations. God forbid that we have a nuclear holocaust of one form or another. That is a different story, but I can't believe that's going to happen.

The point I'm making is that we've got to find better ways to do things in order to keep up with the problems that society has created. I think, for example, what's happened in recombinant DNA has shown the way. I think that chemistry lost out a bit. I think chemistry should have been in the forefront; instead microbiology got into the forefront. They use chemical tools to get all of this information and to make these things. After all, getting something made by microbes is a synthesis. We've always known that there are certain

things like B , for example, that microbes can make much better than man can make--so it isn't a new tool. It's just that we have a new concept about how to apply that tool. I think that we should have gotten into it before this. Since we haven't, I think chemistry has got to turn to it and we're beginning to see more people turning to it. At Harvard for example, you have Jeremy Knowles and the young boy who joined the faculty there as a Harvard junior fellow. I'll think of his name. He was a Harvard fellow and now is an assistant professor.

Heitmann: Was he a student with Benser?

Tishler: Not quite. Benser or Benzer. He was here at Wesleyan last week. He gave a seminar and it was fabulous.

Heitmann: Westheimer thought that he was probably one of the finest young people on the faculty at Harvard.

Tishler: Yes, I agree with him. Frank was the one who steered me to him. His first name isn't Ted, is it? I have it on my desk. Oh, wait a minute, I have it here. Benner, Steven A. Benner. And I think these boys are going to contribute very materially. Chemists are beginning to realize that there is a place for chemists, honest to goodness chemists, on this thing. Incidentally, I organize this seminar program each semester of each year. This is something I feel is going to march ahead and that's going, in my mind, to open up things we never dreamed of before.

Heitmann: Has Merck gotten into recombinant DNA?

Tishler: Yes, they have, although not as much as I think they should have. They may be right. There are a lot of people who have gotten into it. They're trying to use it in places where they think it's important, but I really think that even when it comes to genetic diseases it's going to be a matter of time. I really feel that they ought to make a heavier investment.

Heitmann: Do you have any advice for a young person who would want to go into science?

Tishler: Yes. Tell him or her that future problems and opportunities are much greater than they have ever been because we can begin to see something down the road which we have never seen before. The sciences, particularly chemistry, have changed dramatically in the last ten or fifteen years. I mean you don't have to go back much further than that. It's a grand opportinity for the young. He or she is going to find the world ahead very exciting and he or she is going to contribute to it.

Heitmann: That's interesting. Some people would say that we've come to the end of science. We know it all.

Tishler: No, no. I've heard people say we're scraping the bottom of the barrel, but I think that's crazy. Even this business about restricting chemicals on account of the environment means that we've got to do something more.

Heitmann: And you can find that in every period there are always negative people.

Tishler: That's right.

Gortler: I was going to say one or two things more. One was to ask about Waksman. You worked with him and I didn't get to look him up. Tell me about him.

Tishler: When Randolph Major brought Waksman in he got to know him very soon. Waksman was interested in fermentation. He had a method of making fumaric acid by fermentation. Major thought there'd be an interest in getting into that.

Gortler: This was about when?

Tishler: Oh, I'd say the very early thirties, when Waksman was professor of microbiology and bacteriology at Rutgers. He was an extremely imaginative, able, wonderful scientist and a very dedicated and prolific writer. And he knew a great deal about soil and bacteria. He was probably the best living scientist of the soil. No one has approached his expertise since then. He was a giant in the field. He had a knack of finding things. I think that he discovered more antibiotics than any other person, with the possible exception of one person in Japan, Homeo Umezawa. Waksman was a wonderful learned person. He was very learned in the Talmud, for example. He came initially from Russia and he never forgot his roots. There's not much else I can say about him, except that he was a very great man.

Heitmann: And so, he essentially worked in a bacteriology group.

Tishler: That is right. We collaborated on streptomycin and even before then he was looking for antibiotics. Rene Dubos was a student of his.

Heitmann: Oh, OK.

Tishler: Dubos discovered antibiotics in the soil. He found tyrothricin. Waksman followed up on that when he saw what was possible. At that time, people were also working with penicillin and it became known that penicillin combatted infection in animals. When Waksman saw what was possible, he too searched for antibiotics in the soil. In time he could say that what he did best was to find antibiotics in the soil. He found a number of different things. He collaborated with us at Merck.

Gortler: He stayed at Rutgers and he didn't come over to Merck?

Tishler: Yes, but then we were only ten or fifteen miles apart. He screened organisms and when he found something that looked active in vitro, he'd send it back to us. We'd grow it and try to extract and isolate the component responsible for it. We did this several times before I worked on actinomycin with him. Waksman found streptothricin. It turned out to be toxic, however. Streptomycin followed. It turned out to be a very useful control of tuberculosis. Merck had a contract with Waksman. We supplied him with funds and materials. He agreed that we would get exclusive rights to whatever he found. When streptomycin came along and proved effective against tuberculosis, George Merck said, "You know this is too important to be controlled by one company." He passed the patent back to Rutgers. That's how the Waksman Foundation was started. Royalties were given to him, or rather to his institute. Today that's a big operation. They get government support too, of course. Royalties from all of the other antibiotics he discovered went to the Foundation. The story is true about Mr. George Merck giving it back to Rutgers. That was part of George Merck's greatness. He used to say that if we discovered a cure for cancer he'd not patent it. How can you keep it away from people? How can you charge a lot of money? What's the excuse? You can't do that.

Heitmann: Once George Merck stepped down, he didn't continue to guide the company, did he?

Tishler: No. It's amazing though how a tradition continues once a top person sets a policy. I can see that even today John Horan, who's currently president of Merck, has some of the very same concepts that George Merck had. Incidentally, John Horan used to work in research. He worked for me at the time as a lawyer. He is a very wonderful person.

Gortler: Max, what else did you want to talk about?

Tishler: Well, I thought that you might want to talk about the seminars that I organize each year.

Heitmann: Sure. If you have a copy of this we could put it in the file.

Gortler: I was looking at this set of seminars too. Is this an extra copy that you've got?

Tishler: Yes, you can take it.

Heitmann: It will help us to edit.

Gortler: We better make the point that you had a hand in producing probably seventy-five percent of those products that you showed us before.

Tishler: You mentioned the publication list.

Heitmann: Yes. I want to take that along.

Tishler: I would like to go through the list with you briefly pointing out the important publications.

Heitmann: Sure.

Tishler: Suppose you pass this one. You and I will look at this.

Heitmann: I have one checked with single marks or double marks.

Tishler: I consider those with double marks to be more important. The first paper that I ever published means a lot to me for sentimental reasons.* I felt, my God, look at me, little me, having a publication. Then, of course, the allene, I consider that a first rate and important publication.** The tetrahydrofuran publication was, at the time, considered quite important largely because of Westheimer.*** Next comes the sulfaquinoxaline publication which is on the next page, page 3.**** I put a single check next to riboflavin, but really ought to have put a double check there.***** On second thought I do have a double check next to it. I did a lot of work on the synthesis of amino acids, that's why I checked this thing.******

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*Elmer P. Kohler and Max Tishler, "The Reaction between Organic Magnesium Halides and Alpha-Bromoketones," Journal of the American Chemical Society, 54 (1932): 1594-1600.

**See page 8 of this transcript.

***Elmer P. Kohler, Frank H. Westheimer, and Max Tishler, "Hydroxy Furans. I. Beta Hydroxy Triphenylfuran, "Journal of the American Chemical Society, 58 (1936): 264-7.

****John Weijlard, Max Tishler, and A. E. Erickson, "Sulfaquinoxaline and Some Related Compounds," Journal of the American Chemical Society, 66 (1944): 1957-9.

*****Max Tishler, J. W. Wellman, and Kurt Ladenburg, "The Preparation of Riboflavin. III. The Synthesis of Alloxazines and Isoalloxazines," Journal of the American Chemical Society, 67 (1945): 2165-8.

******Max Tishler, Karl Pfister, R. D. Babson, Kurt Ladenburg, and A. J. Fleming, "The Reaction between o-Aminoazo Compounds and Barbituric Acid. A New Synthesis of Riboflavin," Journal of the American Chemical Society, 69 (1947): 1487-92.

Heitmann: What, in fact, prompted the company to get into amino acids? It saw that there was going to be...?

Tishler: Well, at one time, the thinking was that there would be a place for individual amino acids. When people are debilitated, you can feed them human serum albumin, largely for the protein. You can feed them amino acids as well. The idea was to make and use a synthetic mixture of amino acids that is easy to produce and control.

Heitmann: Did that ever pay off?

Tishler: It never paid off.

Gortler: You mentioned at one point to me over the phone that you had found a non-alkaloid resolving agent.

Tishler: Yes. I wrote about that matter in one of the papers.* I didn't check it off. During the war years we couldn't find any brucine or quinine. They were scarce. The Japanese had taken over the East Indies and as a consequence we had to look for different resolving agents. Pantothenic acid production was threatened. We found tartaric acid, as the dibenzoyltartaric anhydride, to be a superb resolving agent. Since that time there have been a number of publications on its use as a resolving agent. Here's something on vitamin A I consider quite important.** I've got it double checked. Near the top of page 6 we have another important topic, the hydrocortisone synthesis.***

Heitmann: You weren't in competition with Sarett on the cortisone? You were working two different parts of it?

Tishler: That's right. Matter of fact, we went to him at the time and said "We have this idea how would you feel if we carry it out?"
He said, "God bless you, go right ahead."

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*John Weijlard and Max Tishler, "2-Amino-Dibenzo(F,H)quinoxaline-3-Carboxylic Acid, 2-Amino-Dibenzo(F,H)quinoxaline and 2-Sulfanilamido-Dibenzo(F,H)quinoxaline," Journal of the American Chemical Society, 67 (1945): 1231-2.

**N. L. Wendler, H. L. Slates, and Max Tishler, "Synthesis of Vitamin A," Journal of the American Chemical Society, 71 (1949): 3267.

***N.L. Wendler, R. P. Graber, R. E. Jones, and Max Tishler, "Synthesis of 11-Hydroxylated Cortical Steroids. 17( )-Hydroxycorticosterone, "Journal of the American Chemical Society, 72 (1950): 5793-4.

This hydroxylation on page 8 uses permanganate instead of osmium.* I previously mentioned putting hydroxyl groups in seventeen positions of steroids. It took us off a real serious bind in cortisone. On page l0 we have the synthesis of a pyrazole derivative of a cortisone analog--the most potent anti-inflammatory agent known to man.** It's active in microgram quantities. That's why I was interested. It's pretty important. The rest of these things are non-scientific talks that I gave.

More recently, I think I mentioned, I've gone into alpha aminophosphonic acids. Since I've been at Wesleyan, I published about fourteen or fifteen scientific publications. The two important ones are on page l3.***

Heitmann: This one is extremely recent.**** In fact, it's just in press.

Tishler: They said it would be appearing before the end of the year. Now, there's one other publication, sulfaquinoxaline.***** Here it is, page 6. I didn't even check it.

Heitmann: I'll check it.

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*Roger Tull, R. E. Jones, S. A. Robinson, and Max Tishler, "Hydroxylation of -20-Cyanopregnenes by Potassium Permanganate," Journal of the American Chemical Society, 77 (1955): 196-8.

**Ralph Hirschmann, N. G. Steinberg, Paul Buchschacher, J. H. Fried, G.J. Kent, Max Tishler, and S. L. Steelman, "Synthesis and Structure of Steroidal 4-Pregneno(3, 2-c)pyrazoles. A Novel Class of Potent Anti-Inflammatory Steroids," Journal of the American Chemical Society, 85 (1963): 120-2.

***Albert Szent-Gyorgyi, Rack H. Chung, Michael J. Boyajian, Max Tishler, Byron H. Arison, Erwin F. Schoenewaldt, and James J. Wittick, "Agaridoxin, A Mushroom Metabolite, Isolation, Structure and Synthesis," Journal of Organic Chemistry, 41 (1976): 1603-6.
Also, Ann A. Jakubowski, Frank S. Guziec, Jr., and Max Tishler, "Total Synthesis of Cerulenin and Tetrahydrocerulenin," Tetrahedron Letters (1977): 2399-402.

****Shu Feng Chen, Shiv D. Kumar, and Max Tishler, "The Synthesis of D,L-Phosphotryptophan," Tetrahedron Letters (in press), (1983).

*****Karl Pfister, A. P. Sullivan, Jr., John Weijlard, and Max Tishler, "Sulfaquinoxaline. II. A New Synthesis of 2-Aminoquinoxaline," Journal of the American Chemical Society, 73 (1951): 4955-7.

Tishler: They mentioned two things when they gave me the inventors' award at the inventors' hall of fame. One was sulfaquinoxaline and the other was riboflavin. Sulfaquinoxaline is on page 3.* This latter drug effectively controlled coccidiosis, a parasitic disease that affects poultry. Sulfaquinoxaline turned out to be a prophylaxis as well as a cure. We were able to convince the regulatory agencies that we could put this in poultry feed and prevent the disease. Every bit of feedstuff had some of this in it. This was really the basis of modern poultry husbandry. Before poultry farmers used sulfaquinoxaline, a whole flock of chickens, say up to five thousand of them, confined in a pen, would suffer an outbreak of coccidiosis and perish. So, the development of sulfaquinoxaline was of great importance. Today, its use is not as widespread as previously. Newer drugs that are used the same way; that is, that are mixed into the feedstuff, are used more often. All of this has made poultry one of the cheaper forms of protein.

Heitmann: Did the Merck people work with poultry scientists at Rutgers?

Tishler: No, they worked on it at Texas at one of the agricultural schools. I've forgotten the name of the man with whom they worked.

Heitmann: College Station Texas?

Tishler: I think that's where it was.

Heitmann: Texas A & M.

Tishler: I think so but that was many years ago. This article gives you an idea of the path we followed to develop riboflavin. Incidentally, being inducted into the inventors' hall of fame really tickled me. It didn't tickle my grandson however, because he only knows of the hall of fame for baseball players. (laughter)

Heitmann: It makes sense. I didn't ask you about the Tishler Award. How did that come about? The company wanted to reward you in some way?

Tishler: The board of directors conceived of the idea of having these awards for people who had done outstanding work for the company. Sarett has one. I have one. There have probably been about a dozen given out. In those days the company gave twenty-five thousand dollars to a university of the recipient's choice, thereby setting up an award of some kind. I chose Harvard and Tufts. Today it's been raised to fifty thousand dollars. Harvard has done pretty well with its investments.

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*See page 68 of this transcript.

Gortler: Yes. I used to marvel at that and, of course, I didn't know who Max Tishler was at the time. (laughter) I said, my God, I wonder who this is bringing in all of these marvelous lecturers?

Tishler: They were very good. I think that Merck did a nice thing. It pays off in the long run.

Gortler: Anything else?

Tishler: Let me take a look; I made some notes. Oh, here's a list of products that I've made. Also every year I take on fifteen new freshman. I'm their advisor for two years.

Heitmann: That's the sign that's on the front of the office door.

Tishler: You didn't see that?

Heitmann: The freshman advisor sign--a colorful poster.

Tishler: This is a great source of enjoyment for me because I really work with these kids. I've built up quite a group of graduates that keep in touch with me.

Gortler: That's a real reward.

Tishler: Yes, it is. Every so often they'll come and visit me. Both Mrs. Tishler and I get a big kick out of that. It makes us very happy. I would say our life has been marvelous, truly a wonderful ending to what I call a very exciting career. I don't know how things could have been nicer.

Gortler: Max, this has been a real pleasure. Very exciting.

Tishler: I enjoyed doing it. Let's hope we get something out of it.

Heitmann: I think we've learned a tremendous amount about you, the chemical industry, and industrial research in the twentieth century.

Tishler: I'm glad to help you. So I will hear from you some time again when you have put this together?

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