CHEMICAL HERITAGE FOUNDATION

WILLIAM S. KNOWLES

Transcript of an Interview
Conducted by

Michael A. Grayson

at

St. Louis, Missouri

on

30 January 2008

(With Subsequent Corrections and Additions)

CHEMICAL HERITAGE FOUNDATION
Oral History Program
FINAL RELEASE FORM

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William S. Knowles

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

WILLIAM S. KNOWLES

1917	Born in Taunton, Massachusetts on 1 June

Education

1939	A.B., Harvard University, Chemistry
1942	Ph.D., Columbia University, Steroids

Professional Experience

	Monsanto, Dayton
1942-1944	Chemical Research and Development
	Monsanto, St. Louis
1944-1951	Organic Division
	Harvard University
1951-1952	Academic Leave, Total Synthesis of Steroids, R.B. Woodward
	Monsanto, St. Louis
1952-1966	Group Leader, Scientist, Research Advisor
1966-1970	Senior Scientist
1970	Distinguished Science Fellow
1982-1986	Agricultural Chemicals Division

Honors

1974	IR 100 Award, Asymmetric Hydrogenation Process
1978	St. Louis American Chemical Society Section Award
1981	Monsanto Thomas and Hochwalt Award
1982	American Chemical Society Award for Creative Invention
1996	The Organic Reactions Catalysis Society Paul N. Rylander Award
2001	Nobel Prize in Chemistry

ABSTRACT

William S. Knowles' oral history begins with his childhood, attending boarding schools in Depression Era New England. Knowles excelled as a student at the Berkshire School and Phillips Academy, Andover before attending Harvard University to pursue chemistry. Knowles' academic career allowed him to avoid the draft during World War II and, instead, attend Columbia University to study steroids with Robert C. Elderfield. Completing his Ph.D. in only three years, Knowles then moved into industrial chemistry, going to work for Monsanto, at which he would spend the rest of his career. His work there began with basic studies of vanillin and other chemical compounds. Knowles was sent on a leave of absence in 1951 to complete a post-doctorate on total steroid synthesis with Robert B. Woodward at Harvard, an experience that would alter his career path forever. Following Knowles post-doctorate, he moved into studying pharmaceutical chemistry. Throughout the oral history, Knowles discusses the many projects he worked on through his years at Monsanto and how they led to the work that would garner him the 2001 Nobel Prize in Chemistry. Additionally, Knowles gives interesting insight into the challenges and opportunities presented by being a scientist in an industrial setting; and life as a Nobel Laureate, examining the prestige, politicization, and downside of winning the world's most well-known academic honor.

INTERVIEWER

Michael A. Grayson is a member of the Mass Spectrometry Research Resource at Washington University in St. Louis. He received his B.S. degree in physics from St. Louis University in 1963 and his M.S. in physics from the University of Missouri at Rolla in 1965. He is the author of over forty-five papers in the scientific literature. Before joining the Research Resource, he was a staff scientist at McDonnell Douglas Research Laboratory. While completing his undergraduate and graduate education, he worked at Monsanto Company in St. Louis, where he learned the art and science of mass spectrometry. Grayson is a member of the American Society for Mass Spectrometry [ASMS], and has served many different positions within that organization. He has served on the Board of Trustees of CHF and is currently a member of CHF's Heritage Council. He currently pursues his interest in the history of mass spectrometry by recording oral histories, assisting in the collection of papers, and researching the early history of the field.

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LOCATION: **St. Louis, Missouri**

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GRAYSON: So, you were going to show me some information?

KNOWLES: Yes. These are things you can keep.

GRAYSON: Sure, go ahead.

KNOWLES: This is from *Angewandte Chemie*, which is much the same thing. This is my bibliography. It's pretty much up to date. It's what you had. Plus some old stuff.

GRAYSON: Very good.

KNOWLES: The old stuff doesn't plunk out on the computers very well.

GRAYSON: I see, OK.

KNOWLES: I think you go back, like you plunked it out on the computer.

GRAYSON: Right. I did a search with SciFinder to try and get your publications.

KNOWLES: You get some of it, some of these '50s publications. That much gets you a chronology.

GRAYSON: Good, this is great. So, there were a number of publications that came out prior to the work on the asymmetric hydrogenation

KNOWLES: Yes. -- had nothing to do with that.

GRAYSON: Very good.

KNOWLES: Absolutely nothing to do with that.

GRAYSON: I was curious about that.

KNOWLES: Well, I think the history of the prize, I'm … If you want to look at it, I'm kind of a fluke on the Nobel Prize, because first of all you know it isn't given to industry very much. And, I was 100% in industrial labs. And, the great contributions of industry over the past 50, 75, 100 years are usually not awarded the Nobel Prize. It's an academic prize.

GRAYSON: Well, that could be changing though.

KNOWLES: Mostly. Well, in chemistry where I speak mostly. The last one was Pedersen at duPont about '87. For crown-ethers as they call it. And, then you get back pretty far if you go back to almost Irving Langmuir. At '32 and Carl Bosch. This is in chemistry.

GRAYSON: Oh, yeah, yeah, right.

KNOWLES: Physics, you've had a little bit with the, you know, the …

GRAYSON: Solid state?

KNOWLES: The solid state … But, in chemistry. And, then, of course, Fritz Haber the famous one in World War I, he was sort of straddled between industry and academia. So, it's very limited to go to industry and perhaps this one was only chosen because of it's relation to life sciences -- to the field.

GRAYSON: Yeah. So, over all three winners in that year had kind of the same influence in that their chemistry led to an evolution or development or exposition of the life sciences.

KNOWLES: Yes, solution of a stereo chemical problem that was, I mean, life invented chirality. The invention was to be able to make chiral compounds, just like enzymes have been doing for a billion years. And, this is a man-made type catalyst. Now, the origin of this was kind of interesting.

GRAYSON: This is your commentary article in the Accounts of Chemical Research.

KNOWLES: Yonkui Sun at Merck called me last summer.

GRAYSON: Can you spell that for me?

KNOWLES: S-U-N is his last name. And, it's Y-O-N-K-U-I. I might be wrong on that.

GRAYSON: Y-O-N-K-U-I, Yonkui Sun, OK.

KNOWLES: Sun, at Merck. He asked us to make some editorial comments for the *Accounts of Chemical Research* that was having a special issue on asymmetric hydrogenation and closely-related hydrogen transfer reactions. So, he asked us to do this. Well, I sort of put it off. And, then I didn't really contact Noyori. He's in Japan.

GRAYSON: Noyori is the other fellow that …

KNOWLES: He's the other hydrogenation. Well, two of us, three of us got it. One for oxidations. The other two for the hydrogenations.

GRAYSON: Right. And, that's N-O-Y-O-R-I, Noyori.

KNOWLES: N-O-Y-O-R-I, Noyori is the one. And, he's kind of a grand old man and he followed the field after we were almost out of it. But, whatever. He wrote something on his own, which he just really pulled out of his file. It was totally inappropriate. It was just a paper summarizing his work. But, they couldn't tell him that. So, they said, "You tell him that." I said, "Wouldn't something joint be better because for a commentary …"

GRAYSON: Sure.

KNOWLES: "… you don't want a commentary by me and a commentary by him." So, I suggested that to him, but he said he was too busy to do anything. And, I said, "Well, I have time." "And, I'll take your ideas and my ideas and consolidate 'em in one paper." And, he finally said he agreed to do that. So, I did that. And, that's what this is.

GRAYSON: OK.

KNOWLES: And, he insisted on adding all those references.

GRAYSON: OK.

KNOWLES: I would have added two references on Nobel Laureate lectures. [laughter] That's all. You don't put references much in a commentary, but he insisted on doing that. And, he just pumped it out of his files.

GRAYSON: So, Noyori, is he still currently doing research, do you know?

KNOWLES: No, he's out of the research area and he's head of this Riken Institute in Japan.

GRAYSON: Riken?

KNOWLES: OK. That's the same as Max Planck in Germany.

GRAYSON: OK.

KNOWLES: It'd be the big government supported research organization; and he's head of that now. And, he's lost touch. And, we've both lost touch. This field has moved so fast.

GRAYSON: Oh, sure, yeah, yeah.

KNOWLES: We both lost touch. And, this gives you a little idea of just the general

terminology.

GRAYSON: Yeah, OK, great.

KNOWLES: I spent a lot of time last winter, I guess, it was a year ago on it. Plunking this off and using his ideas, certainly half of his ideas in there.

GRAYSON: Try and get something more appropriate for a commentary.

KNOWLES: Yeah. That's right. And, they were very happy with that. It's in *Accounts of Chemical Research*.

GRAYSON: Has it come out yet?

KNOWLES: It's come out.

GRAYSON: OK.

KNOWLES: Accounts of Chemical Research.

GRAYSON: I can get that off the web and find out.

KNOWLES: Yeah, it's out now. *Accounts of Chemical Research*, volume, there it is, right?

GRAYSON: OK.

KNOWLES: No, it isn't on here yet.

GRAYSON: OK.

KNOWLES: I'm sorry.

GRAYSON: So, it's pretty recent then?

KNOWLES: Yeah, I got it out of the galley proof. That came off the galley proof.

GRAYSON: Sure, OK. You did get my form by the way with regard to the oral history program and the release form and all that?

KNOWLES: Yeah.

GRAYSON: OK.

KNOWLES: I think so.

GRAYSON: Yeah, OK.

KNOWLES: Did I sign that?

GRAYSON: Yeah.

KNOWLES: Here it is right here. Should I sign that?

GRAYSON: OK. Yeah, why don't you? If you're willing to go along with this exercise. And, if you want to sign it.

KNOWLES: I'll just sign this right here.

GRAYSON: OK.

KNOWLES: It's the 30th, isn't it?

GRAYSON: Yeah, today's the 30th. The month has zipped by.

KNOWLES: Yeah. Quickly.

GRAYSON: So quickly.

KNOWLES: I know it. That's the one thing that happens. Time and things go faster.

GRAYSON: OK. Yes, yes, yes.

KNOWLES: How long have you been retired?

GRAYSON: Well, just started at the end of last year.

KNOWLES: Yeah.

GRAYSON: So, it's a new experience for me. I'm going to hopefully be able to devote more time to this type of activity, because I think it's important. I enjoy doing it. It's a nice way to meet people.

KNOWLES: Mm-hmm.

GRAYSON: So, why don't we start more or less at the beginning of the process. And, I think the first part relates primarily to your early years, your childhood, education, and things that happened to you that kind of formed your world view, your interests, before you knew it was happening. So, my understanding is you grew up in the New England?

KNOWLES: Yeah, I grew up in southeastern Massachusetts in New England and …

GRAYSON: So, is that on the coast?

KNOWLES: Yeah. It's right on the … in sheltered waters on the coast. It's in Buzzards Bay. It's a great resort and sailing area and all this stuff.

GRAYSON: So, that's buzzards as in buzzards?

KNOWLES: Yeah. But, my family were – my father was very much a businessman. And, as I pointed out, for him, the highest achievement, would be to be a good business salesman. He was on top of a business organization most of the time, selling his cotton. We had a cotton, he had a cotton mill.

GRAYSON: Cotton mill?

KNOWLES: And, spun thread. Made thread, sold thread to people and usually in New York in the garment industry.

GRAYSON: I see.

KNOWLES: And, so, he …

GRAYSON: So, all that cotton had to be imported from the south, I guess, right? I mean, you didn't …

KNOWLES: That was, well, that was the way it was done in those days. And, it's an interesting aside, but cotton can't be spun unless the humidity's over 50% because of the fire danger. You understand that cotton fibers and static electricity was hazardous.

GRAYSON: Oh, oh, I see.

KNOWLES: Well, in the old days, they didn't know how to make artificial humidity. It was not an easy thing to do, but it was easy on the seacoast.

GRAYSON: Oh, OK. So, that's where it was a natural place to do this. Which was a fire hazard.

KNOWLES: It was better in New England and the pricing was better too. But, that changed, of course, after World War II and the whole industry moved down to where the cotton was. And, so, the mills were all closed.

GRAYSON: And, so, I guess that import came primarily by ship up the …

KNOWLES: I don't know how it came.

GRAYSON: OK.

KNOWLES: Trained to New Bedford from Boston.

GRAYSON: It's kind of interesting, I was reading the history of south Texas and apparently in Mexico during the Civil War, there were a lot of shipments south of Brownsville moving cotton and whatnot trying to bypass the American ports because of issues with regard to the Civil War.

KNOWLES: Well, I was brought up in a textile family. And there was no emphasis on science whatsoever.

GRAYSON: Did you have any siblings?

KNOWLES: Yeah, I have two brothers.

GRAYSON: OK. So, you did have your brothers.

KNOWLES: But, they went in the mill. And, I said, "That's not for me."

GRAYSON: So, how did you fit in the ages?

KNOWLES: I was the youngest.

GRAYSON: You were the youngest, OK.

KNOWLES: My father didn't object to that. He liked to have the boys go into the mill, you know. That was always what you did. And, I could have, but I didn't want to go into the mill. I didn't want to do that.

GRAYSON: Well, OK. So, that's fair enough. So, then, I mean, when did you know that you didn't want to do that? Was that …

KNOWLES: Oh, I was just probably from the beginning. I think my mother would have had me go to medical school, for some reason or another that didn't turn me on. I don't know why. Maybe less courses or something, you know. But, I could have gone to medical school perfectly readily, but I didn't.

GRAYSON: So, then your early education was a typical eight grades of grade school?

KNOWLES: Yeah, I went to school in New Bedford, Mass. I always went to private schools. We were reasonably well-fixed during the depression. I think sometimes those that were reasonably well-fixed during the depression lived better than we've done ever since. We had everything done, everything …laundry, cook, anything. And, because of phenomenally low wages, and we always had somebody living in the house, you know? And, because people were glad to have a place to live. And, so, this is …

GRAYSON: This was in the late 20's then?

KNOWLES: Yeah, 30's, yeah.

GRAYSON: Early 30's.

KNOWLES: Yeah. I was born in '17. And, so, I went about eight years to a place called Friends Academy, which was probably started by the Quakers, but it didn't have any Quaker influence at all when I went there.

GRAYSON: Friends Academy.

KNOWLES: And, that was not particularly challenging. I didn't do any science there at all. Just the standard reading, writing, and arithmetic. And, then I went to a prep school in western Massachusetts called Berkshire after that. Connection A was my father went there in its first year to cram his way into Harvard. He wasn't a very good student. And, the then headmaster of Berkshire had about ten boys that he was cramming to get into Harvard. And, he succeeded and my father got into Harvard, but he only stayed one year, I think.

GRAYSON: So, the headmaster was more interested in getting students into Harvard?

KNOWLES: That's how he started the school. Take boys that weren't doing too well and help them out and get them into college or something like that. And, that's what this guy did. And, then he's since developed the school and my father sent my middle brother and I to that school and we went there and that was a good experience for me, though. It wasn't very challenging for me. I was, as I pointed out, I led the class every year. It wasn't a very big class, ten to start with maybe, 20 by the end of the time. Something like that, but I was able to lead the class every year in academics. But, I was a terrible, terrible athlete. And, the emphasis was on athletics.

GRAYSON: Ah, OK.

KNOWLES: And, I've used this story many times that once I received the usual book prize at commencement, you know? I was walking out and I overheard the captain of football saying, "At least Knowles can do something." [laughter] That's the typical thing I ran into. But, then I was a little younger than most of the members of my class. I stayed there five years and Headmaster Buck decided I oughta go to a big prep school like Andover before I went to college. I was admitted to Harvard. But, he thought I was socially too young. And, that was a good suggestion.

GRAYSON: How old were you?

KNOWLES: I spent a year at Andover. I was about 16, I guess, 17 maybe. But all my friends were in classes below me at Berkshire. 'Cause I wasn't emotionally as mature as they were. But, I was academically perfectly able to keep up. So, I took a year off by going to Andover. They do it differently now but I went to Andover and that was what Andover still does. The senior class doubles over the other classes.

GRAYSON: Oh really?

KNOWLES: Yeah.

GRAYSON: Even today?

KNOWLES: I think so, even today.

GRAYSON: That's interesting.

KNOWLES: They've become -- and Exeter's the same way -- they've become a place where you've gone to high school for three years. And you want to go to a -- it's almost a junior college -- but it's something a little more college-like. And, you go one year there. And, so, all the associations I made there were with all the one-yearers. We all got in there together. And, the others had already had their cliques and so forth. I didn't know how to meet the others. And, the class swelled enormously. And, so there were about 20 of us went to Harvard from there.

GRAYSON: So, at Berkshire, was that a boarding school?

KNOWLES: It was a boarding school, yes.

GRAYSON: OK. As also Andover is.

KNOWLES: Yeah. And, that's the culture in Massachusetts, much more if you can afford it, they go to boarding school.

GRAYSON: I see. And, you went home for the summers then?

KNOWLES: Yes. I was home in the summers and away in the winters. And, I guess it was expensive. It sounds cheap; but, it was probably an expensive thing. So, I had kind of the best in education, I think that way.

GRAYSON: Andover, then also the idea there was they wanted to get kids into the best schools.

KNOWLES: Yes. Well, it wasn't hard to get into the best schools if you got decent grades. We just took college board exams. It was very simple in those days. You took college board exams and if you couldn't pass them, you couldn't … you weren't accepted.

GRAYSON: So, this was a little bit like the English system where you get to a certain point and then that determines whether you're going to go on for education there or not.

KNOWLES: Yeah, that's right. They had these regular standing college board exams, which we took and I was able to pass those all right, so, I was accepted. If I didn't pass those, I wouldn't be accepted. I could wait till July and then apply some other place that would accept me.

GRAYSON: So, just by virtue of the fact that you passed the college boards, you could go to Harvard.

KNOWLES: That's exactly right.

GRAYSON: But, if you wanted to go someplace else, then you could.

KNOWLES: Yeah. Well, in my family, the culture was that's the only place I even applied to. There were a group that would apply to Yale and a group would apply to Princeton or Dartmouth or Cornell or so forth.

GRAYSON: Ah, I see.

KNOWLES: It's not anything like today.

GRAYSON: Today where there's kind of competition between the students and the colleges.

KNOWLES: Not very much, yeah.

GRAYSON: Yeah, that's interesting.

KNOWLES: But, they did weed out the ones that couldn't make it by the college board exams, which they had one in, you know, English and sciences and the various subjects and history.

GRAYSON: So, during that high school experience, were there some things that got you turned on to chemistry?

KNOWLES: Yeah, well, I would say that I was turned on to physics. I only took physics at Berkshire and I was turned on there a bit to physics. And, I liked numbers. Physics and math. Because I … you could feel more comfortable pushing numbers around than people around, really. I was always more comfortable doing that. And, I still am more comfortable doing that.

GRAYSON: I see.

KNOWLES: But I never did take any chemistry there. They had chemistry, but I didn't take it. I took physics. And, I took math or just algebra and I guess a little trigonometry probably. And, then, I took the language requirements and the English requirements and so forth.

GRAYSON: So, for language, would you have Latin?

KNOWLES: Latin, lots of Latin. For me, it was a mechanical thing; I was good at it because it was mechanical. It was like solving a puzzle on a thing. You had a subject to and a predicate and you learned to get around the structure of language. And, you get a feel for Latin and then I took three or four years of Latin there.

GRAYSON: I guess they don't do Latin much anymore.

KNOWLES: Not much. But, I didn't ever do the typical sentence structure that some places do.

GRAYSON: Did you do any other modern language while you were there?

KNOWLES: I did French. French, yeah. And, then, I went to Andover where I took more French which was just a disaster, but I took it. And, there I did take chemistry. And, I got fired up with chemistry there I would say mostly. I liked that it was a little more qualitative than physics. I don't know. I did get fired up over it there. And, that was I would say the first place.

GRAYSON: So, was there a teacher that influenced you there or …

KNOWLES: Well, yeah, there was a teacher. I called him Bushy Graham. His name was Graham. But, he had a beard, that's all I know. And, we called him Bushy Graham.

GRAYSON: Bushy Graham.

KNOWLES: Yeah, he was pretty good at just general chemistry. There was more competition there. There was probably 15 or 20 in the class or something like that.

GRAYSON: OK.

KNOWLES: And, then at the end of the class they had a prize in chemistry, which you had to take a competitive exam to get the prize. And, that was the first thing I won. I won a $50.00 prize called it the Boylston Prize and they still give it. But, you didn't get it just by getting the highest grade in the class. The good students in the class took this competitive exam.

GRAYSON: Mm-hmm. So, this is B-O-Y-L-S-T-O-N, Boylston, is that it?

KNOWLES: Yeah.

GRAYSON: OK. So, is he …

KNOWLES: A name they had given a building there sometime back. And, probably a science building.

GRAYSON: So, this was your first "prize"?

KNOWLES: Yeah.

GRAYSON: And, this was competitive. And, how many other people were in the field?

KNOWLES: Oh, I don't remember how many it was. The fact is my relations with the family weren't … I don't know that I ever told them about the prize or not. I'm not sure if I ever did.

GRAYSON: So, the idea that you were interested in the sciences wasn't anything you needed to kind of enforce back on the home front?

KNOWLES: No, they didn't pay much attention to that. That's the one thing when you went to boarding school, they didn't worry about what you did, as long you were passing.

GRAYSON: As long as, yeah, as long you passed.

KNOWLES: As long as they got good reports home, they didn't care.

GRAYSON: And, you were there to stay.

KNOWLES: Yeah, I always got good reports home. So, that didn't bother me. I think the first ability to get into science is probably some ability to take care of numbers. I took math. I took physics, chemistry, biology. You gotta handle numbers somehow. You get into numbers. The first place I probably showed any proclivity was just doing adding, subtracting, and dividing at Friends Academy. My family did give me a nickel every time I had 100 in arithmetic. And, I got nickels quite a bit. And, a nickel bought something in those days.

GRAYSON: Yeah. This is interesting, 'cause my wife is a math teacher and she's actually retired from that, but she's tutoring a student now. This student doesn't know his addition and subtraction tables and he is in college. And, it's like what went wrong here? I mean, I just can't imagine that someone gets to that level of education and they can't even – they don't know their basic addition and subtraction tables.

KNOWLES: Well, you can't do much even in the life sciences and biology without numbers.

GRAYSON: Oh, yeah, yeah.

KNOWLES: More now than you ever did. And, even in those days, you had to have that.

GRAYSON: Oh, yeah. Well, she's incentivizing this fellow. She has challenged him to do 20 addition and subtraction problems in like two minutes and then she won't charge him for his next tutoring section. Because she knows how important it is for him to know this stuff. He can't do any simple problems …

KNOWLES: Yeah, even with the calculator, you gotta be able to do the simple problems.

GRAYSON: Yeah. It's kinda silly.

KNOWLES: A lot of, we were taught a lot of drill. We just had a whole list of things to add and subtract and multiply and divide and you had to do 'em.

GRAYSON: I guess that's something they don't do nowadays.

KNOWLES: Yeah, no, I know that. But, a certain amount of that is good. But, that's where I probably first showed an interest in science, was numbers. Just in numbers and then if I had taken chemistry in Berkshire, I might have gotten turned on by that. I don't know.

GRAYSON: So, you were into physics when you were in high school?

KNOWLES: But, I'm good at math. So, any advice I got was to do physical chemistry. Because that's where the two marry. And, that changed in college really. So, I went to college determined that I was going to major in chemistry.

GRAYSON: OK. That was already a plan when you went to Harvard?

KNOWLES: Well, it was my plan.

GRAYSON: OK.

KNOWLES: I mean, they didn't care at Harvard freshman year. I took a chemistry course and math course and then I was advised since I was good at math that probably physical chemistry would be my thing. And, that would be a natural.

GRAYSON: So, they had an advisor system for the incoming students to help them …

KNOWLES: Oh, yeah.

GRAYSON: OK.

KNOWLES: Every college does. And, I had to take another language at college, take German because of its relationship to science.

GRAYSON: Sure. When you left – just before we go on forward – when you left high school, you got a diploma from what the Friends Academy was it?

KNOWLES: I don't know if I got a diploma there. If I did, I stayed eight years.

GRAYSON: OK. So, when you got out of high school, you got a diploma from high school.

KNOWLES: Yeah. And, I never went to so-called kindergarten was the reason that I got a year ahead. And, I was always in the same class with a cousin of mine, a first cousin, who was a year older.

GRAYSON: OK, OK. So, your birthday was when?

KNOWLES: June.

GRAYSON: June, OK. So, that's quite an advance to go first grade if you were born in June. Our second son was born in October and there was a question whether he should go, you know, at age five or six. And, our pediatrician did a little test and she was opposed to advancing him, but after he did this test, he said, "He should go to school." So then Andover was kind of like a little finishing-type arrangement.

KNOWLES: Yes, that's right. It was more of a college environment a little bit. And, there were … I would know a gang of people going into college. So, Andover was a primary Yale school. It would send 20 to Harvard and 100 to Yale or something like that.

GRAYSON: Oh, wow, OK, crazy.

KNOWLES: So, and they didn't send people to many other places in those days. Now they do of course. So, about 20 of us went to Harvard. So, I didn't go there not knowing a soul.

GRAYSON: Yeah, that's good.

KNOWLES: Which would have been difficult for me because socially I was a little shy.

GRAYSON: Sure.

KNOWLES: I was a nerd.

GRAYSON: OK.

KNOWLES: A nerd. [laughter]

GRAYSON: I understand.

KNOWLES: No, question about that.

GRAYSON: But, you did – I read the prize lecture – you did take off that summer in between, before Harvard?

KNOWLES: Between Andover and Harvard. Yeah, well, I had this friend, Eddie Seaver, in New Bedford, who …

GRAYSON: How do you spell that? I'm sorry, the name is? Eddie?

KNOWLES: Eddie Seaver, Eddie's …

GRAYSON: S- …

KNOWLES: He wasn't a very good student. So, he didn't go to any of the colleges.

GRAYSON: Oh, OK.

KNOWLES: But anyhow, he got me interesting in taking this boat trip to Europe that summer. And, I think he got a cheaper rate because he got me in too, you see. But, that was all right. This was the kind of a trip that a landlocked family might be worried having their son take. But, my family were very seafaring …

GRAYSON: Oh, sure.

KNOWLES: … my family didn't worry sending me off in a windjammer and no motor.

GRAYSON: Oh, wow.

KNOWLES: And, no connection with the outside world really until we got to Europe. We could receive time signals to keep the chronometer running right and that's all. And, that was it, just ping, ping, ping.

GRAYSON: So, this ship was a fairly large vessel?

KNOWLES: The captain owned it. And, it was an old German they called a pilot schooner. It was the kind of a schooner that they sailed around outside of key ports with pilots that knew the way. And, they didn't want to use fuel, so it just had sails. And, the pilot would get in the long boat and row over to the big tanker or whatever coming in and guide them into the harbor.

GRAYSON: I see.

KNOWLES: They'd have a dozen or so pilots on there and they'd supply these …

GRAYSON: So, the big ship would just follow the …

KNOWLES: And, all they would do is sort of heave to with one sail and go back and forth across the entrance to one of the big harbors, like London or Antwerp or something like that.

GRAYSON: So, this was a fairly small …

KNOWLES: 75-foot.

GRAYSON: 75-foot, OK. And, so, it was two masted or …

KNOWLES: That's how he made his living, he bought this ship for probably nothing and he made his living taking college kids on trips.

GRAYSON: Hmm.

KNOWLES: And, so, we took a trip from Gloucester to Norway in this, to Stavanger, Norway. And, that was quite an experience. These were, most of these kids were going to some college or other. They were just about 18 then. There were a couple that were older.

GRAYSON: Most of them were young college students?

KNOWLES: Young college kids, yeah. And, most of them were very athletic. I always run into that. Seventeen of us went on the thing.

GRAYSON: And, you actually were the crew?

KNOWLES: Yeah, we were the crew. And, it was luxurious because we had four hours on, eight hours off. Which is a lighter load than crews usually take. And, so, when you have plenty of help

on a boat you can do it and if you have any heavy wind or something, we could all come on deck at any time. It was an interesting experience.

GRAYSON: I can imagine.

KNOWLES: I think that being on the ocean was the most interesting part of it. Three weeks on the Atlantic. Because you were on your own there and, and we didn't have refrigeration for instance. We just lived off canned goods. See, we didn't have any power at all.

GRAYSON: Wow.

KNOWLES: We had a little, uh, I guess a generator to make lights. That's all, just for lights. You had a little light by your bunk.

GRAYSON: Hmm, weird.

KNOWLES: And, that's all that you had. For drinking water, we had a keg on deck. And, there was one outlet in the galley, which no one could use except the cook. They hired a cook and someone would help him. We took turns with it. We just handled the sails.

GRAYSON: Mm-hmm. So, this is two-masted, the ship?

KNOWLES: Two masted.

GRAYSON: OK.

KNOWLES: And, some of the boys were – I was never very good on the heights – I did go aloft when I had to but I avoided it. Some of the others just went around the rigging as though they were monkeys. [laughter] And, we didn't need to go aloft much on it. But, some.

GRAYSON: So, this was like a square rigger?

KNOWLES: No. It was a fore and aft rigger.

GRAYSON: Fore, OK, fore, OK.

KNOWLES: Yeah, two, main sail, fore sail, two jibs and it had some extra sails that we put up at the right time.

GRAYSON: Yeah, so, took you three weeks to go from Gloucester to where did you end up?

KNOWLES: Stavanger, Norway. We went around the north of Scotland.

GRAYSON: How do you spell that, Stavanger?

KNOWLES: S-T-A-V-A-N-G-E-R. It's near the famous place of Durgan, but that's – Stavanger is on one of the fjords of Norway. Then we spent the summer cruising the Baltic. We spent a week in Stavanger. We went to Copenhagen. We went to Talinn. We went to Helsinki and Stockholm.

GRAYSON: Oh my.

KNOWLES: And, and then all of us at college went back to college. No, my friend Eddie Seaver, he didn't go to college. Maybe he did, but he didn't then. And, he sailed with the ship back. And, they were very short-handed and they had problems.

GRAYSON: Hmm. So, how did you get back?

KNOWLES: I came back on the Kunosholm or whatever the Swedish liner was.

GRAYSON: Oh, OK. Swedish basically steamship?

KNOWLES: Yeah, we came back on a steamship, yeah.

GRAYSON: And, that was fairly – how long was that passage?

KNOWLES: Oh, that's five to six days.

GRAYSON: OK. Close to a week. A little less than a week, yeah. So, you basically you spent almost the whole summer then …

KNOWLES: I spent the whole summer and then came back on the steamship to go to college.

GRAYSON: So, did you ever have any exciting experience weather-wise while you were on the schooner?

KNOWLES: No, we didn't have too much. We had one all hands on deck. We blew out one of the sails. But, it wasn't real very trying. They had very trying circumstances going home, but they were short handed. Short handed is the hardest thing on boats. You're up all the time, don't get time to sleep, and all this stuff. We had no problems that way because it was four hours running the ship and then eight hours off. We ran around the clock. And, it was cold. You …

GRAYSON: So, this would have been like in June when you …

KNOWLES: Yeah, but north Atlantic's cold. You needed a sheepskin coat at night and …

GRAYSON: Oh, wow.

KNOWLES: … and your oilskins were wetsuits …really foul weather gear all the time.
But, I'd had quite a bit up here in sailing. I'd never sailed that kind of stuff before, but I'd been in some coastal sailing a lot. And, my family always had some kind of a sailboat.

GRAYSON: So, they were comfortable with you doing this?

KNOWLES: Oh, yeah. They were very comfortable; another family might not have been comfortable.

GRAYSON: Yeah. This was an idea that you cooked up with your friend? It wasn't something your parents suggested or?

KNOWLES: No, well, no. He suggested it and I asked them and they thought it was a good idea, 'cause they thought a young man oughta have some travel experience before he settled down and this sounded like a good one for me.

GRAYSON: So, how was your then visiting these European cities? And, this would have been 1930- …

KNOWLES: '35.

GRAYSON: What was – this was just before Europe started to go down the tubes?

KNOWLES: That's right, yeah.

GRAYSON: So, what did you observe there?

KNOWLES: Well, we were treated very well, because it was cheap over there, but in Stavanger there was certainly communist activity. We were fascinated by it. I can remember there was some guy named – I even remember his name, he did happen to mention it – it was Lars Berensen.

GRAYSON: How do you spell that?

KNOWLES: I don't know. B-E-R-E-N-S-E-N or something. He was a well-to-do, well-off Norwegian and he saw us being fascinated by this communist demonstration. And, invited us into his house.

GRAYSON: Oh, wow.

KNOWLES: To get us away from it. He didn't think we ought to get involved in that. [laughter]

GRAYSON: So, he was a kind of an establishment fellow?

KNOWLES: Establishment fellow and he wanted to get us away from that.

GRAYSON: He didn't want you to be a communist.

KNOWLES: So, he invited us into his house, which was very nice, but we were, of course, fascinated by the demonstrations that were going on. And, I didn't run into any of it in Copenhagen. Our ambassador in Copenhagen came down and took us all out to dinner one time, made a special thing of it. We were docked on the main dock in town. So, they made a big deal of us and we spent a week there, and a very long bike ride. That was the first long bike ride I ever took.

GRAYSON: Oh.

KNOWLES: I was never so tired in my life. [laughter] It was a 50-mile, but it was flat. But, those bikes weren't as good as you have today. So, they were just clunkers. But the other guys were so athletic, they had no problem. I was trying to, coming home, I was trailing I remember I had to keep up and I couldn't keep up. [laughter]

GRAYSON: Yeah. So, well, how about the language issues? I mean, you knew French enough to get by.

KNOWLES: There was English everywhere. In the city and the country.

GRAYSON: I know it's common to get English spoken in Europe today; but I was wondering if it was common then?

KNOWLES: Well, there wasn't much of a language problem. Then we went to the coast. The only really uncivilized old farm town was Talinn Estonia. Some of the people went there; I didn't, it was, uh, Leningrad in those days. It's St. Petersburg again today. But, some of them went there. But, you had to get special permits and everything and two or three of them went to St. Petersburg. It's only about 100 miles south of the line. I stayed in Talinn.

GRAYSON: Now, Talinn, how do you spell that?

KNOWLES: Talinn. It's the capital of Estonia. It's a medieval-type town. And, I guess the most exciting thing; we got arrested there and had to ride in the paddy wagon. They picked us up. I think they thought we were smugglers. We were all at the dock. It was a very rough area of town, which didn't bother us a bit. But, we were tearing around the dock and …

GRAYSON: Just kind of being exuberant 18-year olds?

KNOWLES: Yeah, that's right. And, so, they put about six or eight of us in this paddy wagon and drove us off to the police station and put us there in a room, which was kind of funny, they put us in this room and locked, presumably locked, the door. And, then, left us. They couldn't speak English.

GRAYSON: Oh.

KNOWLES: And, presumably they were gonna go get an interpreter. And, we stayed there about 20 minutes or a half hour. And, somebody said, "Well, maybe the door's not locked." We opened it and it wasn't locked. And, there was not a soul in the office or anything. They just realized their error and just vanished. [laughter]

GRAYSON: Didn't want to stay around to find out what was going to happen?

KNOWLES: They didn't want to do anything. I don't know what would have happened, but I think they were looking for smugglers. That's what it was.

GRAYSON: Or, maybe they just wanted to quiet down the pier. [laughter]

KNOWLES: I don't know what they were doing. And, then we went to Helsinki and that was just across the water. And, we went to a Finnish bath. That's all I remember of Helsinki, but that was an exhausting bit. And, we did stop at a place called Mariehamm, which is part of Finland, where the huge grain races to Australia start. That's where they headquartered. There were two or three of them in there. These were these big clipper ship. They were still using those. And, they were mostly just Naval training ships. They figured if you took one of those, you learned about the lore of the sea and so forth and they used to race between Australia and England to see who got the high price for the grain.

GRAYSON: I see.

KNOWLES: The one that got there first got the price. Then it was done, 'cause the one who got there last got the low price. It was called grain racing.

GRAYSON: Grain racing.

KNOWLES: It's what people called that. When they started out, they didn't know whether they were going around the Cape of Good Hope or around South America, the captain made his decision on the way. It was about the same distance.

GRAYSON: I see.

KNOWLES: It depended what he thought the winds were gonna do and so forth. And, so you really didn't see who you were racing with. But, to get to England first was a …

GRAYSON: So, you start out in Australia with a load of grain? And, the first guy there gets the bucks.

KNOWLES: Yeah, I guess that's it. So, they named it grain races. Then there got to be a big lore behind it. And, then you have to pay to crew it. The crew go for the glory of it, you know. And, they had enormous crews to run these big sails and everything.

GRAYSON: Sure, yeah. The square-rigged …

KNOWLES: Yeah.

GRAYSON: … three-masted boats, I imagine.

KNOWLES: That's right. And, we climbed all over those when they were in dock, there were several of them.

GRAYSON: So, that was really a great experience.

KNOWLES: There were a few tall ships left. They come around and they would buy a lot of stuff.

GRAYSON: We were up I think in New York a while back and they had a couple of tall ships in harbor or whatever, but they're kind of neat.

KNOWLES: Yeah, those were big ships. They were about 300 feet long. And, they hold a lot of grain. And, they'd go pretty fast, relatively, water speed, you know how they go. 15-18 miles a hour, you know, knots I think it was.

GRAYSON: Knots, so, your passage on the schooner was probably what more like 12-15?

KNOWLES: Six or eight.

GRAYSON: Six or eight?

KNOWLES: Yeah. Maybe we could do ten.

GRAYSON: Oh, wow, OK.

KNOWLES: Ten would be the maximum we could do. It's like the old Reynolds numbers and pipe flow.

GRAYSON: So, that would be the only way you could get it?

KNOWLES: Yeah. Is the hull speed. Depended on size. And, so, it takes a lot of energy to push it much faster than that.

GRAYSON: So, then basically it was about six weeks, three months, in Europe before you came back?

KNOWLES: Thereabouts. Three or four weeks. I probably came back in August, yeah. I don't remember the date, but …

GRAYSON: And, then it was Harvard.

KNOWLES: And, then I went freshman year at Harvard, yeah.

GRAYSON: So, what was Harvard like in 1935?

KNOWLES: Well, it was fine. I didn't take the advice as I should have. I was told by Mr. Buck, don't worry about the course, get the man (good lecturer). And, I think the same applies to universities today probably. Get the good lecturers. Well, I got some. But, I didn't get others. And, I was a little disillusioned when they gave us a graduate student to teach German, but I can see how that happens.

GRAYSON: Yeah.

KNOWLES: In a university a bunch of guys have to have a German requirement so they give you somebody that's majoring or trying to get a PhD in German.

GRAYSON: Sure.

KNOWLES: They get someone in German studies to give it to you. So, you didn't get that even in a great university. You didn't always get the top teachers. And, a few things like that. But, that was a requirement I had to have and I never was a good linguist. And, I did get a reading knowledge of German good enough for chemistry. Never anything from ear. It was all in the eye.

GRAYSON: Sure, yeah.

KNOWLES: My French was … I could read French fine for technology but not for literature. I can't read Balzac and I can't understand it but I didn't have to. That was the way it was taught in those days. I think one of the flukes at that time, I took a college board in English and English wasn't my cup of soup. So, I studied like mad in order to get by the college board in English, since English was not my thing. But, I ended up getting honors in college board in English. And, so, I didn't have to take freshman English. 'Course I should have taken it 'cause it was a good

composition course. But, that shows you could cram for these college boards if you really felt you were a little weak in them. And, so, that was where I was weak. So, they just had a standard 'cause there's only so many units you could take. You have to learn two or three Shakespeare plays pretty cold, what you're going to say about 'em and so forth. So, that was a fluke but it did enable me probably to take more science quickly.

GRAYSON: So, then these college boards were I guess would be equivalent to what the SAT's or ACTs are today.

KNOWLES: They had an aptitude test too, which they never showed you the results. I don't know what they did with that. Statistics probably to see something about the class. But, they called it a scholastic aptitude, which is really a vocabulary test. Essentially. And, that wasn't my particular forte either. [laughter] That's interesting how that works.

GRAYSON: So, they advised you to go into physical chemistry, right?

KNOWLES: That's just an obvious thing because I got very good grades in math in college and I probably spent quite a lot of time tutoring. I had a roommate in college that his father made him take math and that wasn't his thing at all. His thing was literature and so forth. He got through because of my help [laughter]. And, there was another guy named Chandler Hovey who's father had a cup defender. He promised me if I'd get him through math, he'd get me to sail on his father's ship, but I never did get that. [laughter] But, I got him through math, I think.
So, I really did better in math than I did in chemistry, I think, I was very good on that. And, I was even thinking of majoring in math, but I didn't.

GRAYSON: So, who were your influential chemistry teachers at Harvard?

KNOWLES: Well, I would say that the first one was in the second year of college, I took organic chemistry with Louis Fieser.

GRAYSON: OK.

KNOWLES: You've certainly heard of him, I think.

GRAYSON: He's Fieser …

KNOWLES: He should have been a Nobel Laureate.

GRAYSON: He's Fieser of Fieser and Fieser.

KNOWLES: Fieser and Fieser. That is right. And, he was the type of guy that the Nobel committee has trouble with. He's a skillful man in a field, in a whole broad field all his life, you know what I mean? All I was was a spot invention kind of thing. But, he he was one of the great lecturers. They were all premeds in the class. And, they got very good grades, but they didn't like the stuff. You know what I can't imagine I've talked to doctors and they say, "Oh, God," they had to get through that organic chemistry and couldn't stand it. So, really we who liked it were a minority. The others got good grades. Plenty of competition 'cause they crammed and they must have taken a special … you could get all kinds of tutoring courses there.

GRAYSON: Yeah.

KNOWLES: And, I'm sure these premeds took that, 'cause they had to do well. They had to get As. So they went to these tutoring schools. You could go to them. And, all they would do is use all the previous exams and there's only so much variety you can give them. And, so, you can really bull your way through. But, premeds had to get good grades 'cause they wanted to get in a good medical school.

GRAYSON: So, how large were the classes?

KNOWLES: Oh, they were big, 200 in Fieser's lecture class. But, he was a bit of a clown and he gave very good lectures and he was very interested in chemistry -- organic chemistry as opposed to physical chemistry.

GRAYSON: OK. So, had he written his book by then?

KNOWLES: No, he had a textbook in chemistry. I think I have a dog-eared edition of it. But, no, he hadn't started his Fieser and Fieser series. But, I didn't know him then. I got to know him later at conferences and meetings. But, I never did meet him much then. He was a professor and then some section man took the individual sections. And, you discussed the matter in detail then. But, he did do very good lectures in organic chemistry and that I'd say got me turned toward organic chemistry and even perhaps away from medicine.

GRAYSON: So, was that in the junior, the sophomore year, or freshman?

KNOWLES: That was sophomore year. Yeah, I took general chemistry the freshman year.

GRAYSON: Did you take additional chemistry courses later on in your college?

KNOWLES: Oh, yeah, you had to … to major in chemistry, you had to take a lot of physical chemistry. I took a lot of physical chemistry. And, I didn't hit it off with the professors as well in physical chemistry as I did in organic and I took advanced organic. Oh, Harvard gave you a good smattering of chemistry, much more than you would probably get at other places.

GRAYSON: I see. So, it had a reputation for that.

KNOWLES: Yeah, so that when I went to graduate school, I was almost a year ahead of the other chemists when I went to Columbia. 'Cause they came from small southern schools, a lot of them, and places like that that just had a couple of chemistry courses. So, they had to make that up. I didn't have to do that. And, no, I had a very solid chemistry education here.

GRAYSON: You went the whole four years there?

KNOWLES: Yeah, I had Fieser's, yeah, organic chemistry and then advanced organic with Bartlett, which he since went down to Texas when he retired. He was not as good as Fieser as a lecturer, but he was good. I mean, he was solid. And, the laboratory, they really had an awful lot of laboratory. So, I didn't have much time in the afternoons. Like, I roomed with two guys that majored in humanities. And, they had most of the afternoon off, you know. But, I didn't. I was in the laboratory most of the time.

GRAYSON: So, these were like three-hour like chem labs?

KNOWLES: Well, you could take till you got it done rather than anything else.

GRAYSON: However much time it took.

KNOWLES: I remember that you were there from noon till 4:00, 5:00 or something like that usually every day.

GRAYSON: You had to get it done, yeah.

KNOWLES: 'Cause the classes were all in the morning.

GRAYSON: Yeah, OK.

KNOWLES: We had eight o'clock classes or something like that. But the laboratory was usually always in the afternoon. We had a guy named … they had the big names. I remember. T.W. Richards was the first Nobel Laureate in chemistry for isotopes. He worked on the atomic weight of lead. He did that. And, showed that these battery acids, or something like that, that the lead was different. Didn't have the right atomic weights, you know, so that's kind of the way the isotope thing got started.

GRAYSON: So, he was doing isotopes by wet chemical methods?

KNOWLES: He was a wet chemist. And you had to be a real stickler for everything. I had a disciple of his called Baxter. And, he didn't ever do it with me, but we had white tile desktops. white tile, 'cause that's awful hard on your glassware. And, once the glass is full of water, then you set it down, it didn't matter. But, anyhow, you scrubbed it before you started. We did a lot of barium sulfate quantitative and you want to show how accurate you could be. But, he would come up to this guy next to me named Lambert and he looked at us and says, "Your desk doesn't look very clean. You're not ready to start." And, he said, "Well, I just cleaned it." So, he cracked an egg, he said, "Eat that egg." [laughter] "See, yours isn't clean enough." He was a clown that way.

GRAYSON: What was his last name?

KNOWLES: Baxter.

GRAYSON: Baxter.

KNOWLES: Yeah. He was a strong disciple of T.W. Richards, I'm sure of that.

GRAYSON: OK.

KNOWLES: And, he carried on in quantitative analysis.

GRAYSON: Hmm.

KNOWLES: So, they really gave you a good going in quantitative analysis. We had the barium sulfate and get every damn last molecule out of your beaker onto the thing and ignite it and weigh it and, you know, and all this stuff.

GRAYSON: Pretty tough stuff.

KNOWLES: Tough, oh, yeah. It's very, very demanding on your technique. And, so, they went into that. And, Fieser was very demanding on technique in the laboratory. When he did one of his favorite lectures was how not to do a crystallization.

GRAYSON: Oh really?

KNOWLES: He loved that. He did that every year. How not to do one. And, did all the wrong things.

GRAYSON: To show how it didn't work.

KNOWLES: Yeah. He was a great stickler for laboratory technique. I don't think they do as much of that today.

GRAYSON: Well, yeah, I don't think they do either. But, those details are important.

KNOWLES: They're very important, particularly when you counted chemistry as quantitative that's the only way you could do it until physical chemists and physicists came along and did it.

GRAYSON: This is about the same time that Al Nier did a post-doctoral appointment at Harvard in the physics department.

KNOWLES: Who?

GRAYSON: Al Nier, N-I-E-R.

KNOWLES: I didn't know him.

GRAYSON: He worked for a guy in physics called – I can't think of the name now, but it'll come to me. But, at any rate, he did a post-doctoral tour of duty there in the mass spec business and I think maybe he had some interactions with Baxter

KNOWLES: Yeah.

GRAYSON: Because there was this issue with regard to lead isotopes that the mass spec people were able to extract, get some information very quickly. And, I think Baxter actually prepared samples for him to test him to see how things worked. So, you spent four years at Harvard and then came out with a basically a …

KNOWLES: Bachelors.

GRAYSON: … Bachelors.

KNOWLES: They were calling it Bachelors of Arts.

GRAYSON: BA.

KNOWLES: Because I had Latin. I took Latin at Andover to the extent of Virgil and I think if you've been that far, you got an AB. You could get a BS and be in literature as far as I could see if you didn't have Latin.

GRAYSON: Uh-huh. That was crazy.

KNOWLES: It was a hangover from the old days but they called it an AB but it was more a Bachelor of Science. I had to take courses outside of my field, my major. I took a course in the Bible as literature, which I really got more out of. but I didn't do well in it. I think I only got a C, but I got a lot out of it. And, that was one of those famous lecturers they had for that. So, that was a very impressive course to me. And, we read the whole damn book, which I think most people haven't done.

GRAYSON: Yeah, I don't think a whole lot of people have read it.

KNOWLES: No, no, that was the assignment. You had to read the whole thing, cover to cover.

GRAYSON: Well, that's interesting.

KNOWLES: And, he gave fascinating lectures, particularly on the Old Testament. He was an interesting guy. There were 200 in the class or something like that. And, he rented a sailboat and took Paul's journey through the Middle East.

GRAYSON: Oh my.

KNOWLES: He went to all the ports and everything. He really got the feel for the thing.

GRAYSON: Well, that's one way of doing it.

KNOWLES: That is.

GRAYSON: Yeah, that's pretty neat. You know, well, Paul did quite a bit of traveling.

KNOWLES: That's right.

GRAYSON: It's hard to think of the range of traveling he did given the facilities he had to get around. They were not that good.

KNOWLES: But, he was much better on the Old Testament and the Old Testament stories. He was fascinating and he could go on those forever.

GRAYSON: That's neat.

KNOWLES: And, but, it was just as literature. It was a literature course. And, well, then I had to take a course in the novel, which really about a half year course or something just to spread out my course load. I didn't ever take much history. Probably should have. Everybody else did. But, I didn't ever get off to take history much. Been immersed in history ever since.

GRAYSON: Yeah, I think the summer, the time abroad helped a lot in developing …

KNOWLES: Yes.

GRAYSON: I wish that more young people today could travel abroad for part of their education, because it's an experience. Fortunately, three of my four sons did travel abroad during their college years. And, I think it's a great experience that is educational in a really fundamental way.

KNOWLES: Yeah. Well, I think one thing that is awfully good for young people that you can't do today very easily that was done in the old days. When a young person didn't know what the hell he ought to do and he's about 18 or 19; stick him on a ship. He's stuck with it and he can't quit. A lot of them did quit in the west coast. When it went around the horn, they didn't want to go back. And, so my name is much more common on the coasts than it is in St. Louis. If you look in the Boston telephone book, the Knowles there's a whole stream of them. And, you look in L.A., it'll be the same way. But, out here (St Louis area), there aren't a whole lot of them.

GRAYSON: So, what does your family think about . . . I mean, basically as soon as you got in your professional career, you left New England. You came to the Midwest and you never left the Midwest.

KNOWLES: Well, they thought I'd just probably come back after a while. They thought it'd be a good experience. 'Cause that was …

GRAYSON: But, you never went back?

KNOWLES: A lot of factors and, yeah, I started here and just stayed here. I don't think going back is a very successful thing anyhow. You really can't.

GRAYSON: Yeah. Well, I don't want to get too far ahead of the story. So, then basically did you know ahead of time that you were going to Columbia?

KNOWLES: No, I didn't know that. That was something new.

GRAYSON: That was something that you had to work up to?

KNOWLES: It didn't bother me. I just finished college and then I worried what I was going to do next. I was going to graduate school, see.

GRAYSON: Did you know that for sure?

KNOWLES: I felt for sure I was going to graduate school or something.

GRAYSON: But, you didn't know where.

KNOWLES: And, I talked with the guys at Harvard and they strongly advised me not to go there.

GRAYSON: To Harvard?

KNOWLES: Yes. They said, "We've done all we can for you. You need to get experience elsewhere."

GRAYSON: I think that was good advice.

KNOWLES: Now, I wasn't as good a chemist as quite a few in the class. I mean, I was a strong B. But, there were quite a few A students that were … what they really called hotshots. And, I think the difference between an A and a B is the ability to take exams, 'cause that's the way you measure progress.

GRAYSON: Your advisors though, even though you say you were a strong B, they still felt that you were good material for graduate school?

KNOWLES: Yes.

GRAYSON: OK. So, they didn't dissuade you from going to graduate school?

KNOWLES: No, no, no, no. As I say, I didn't really probably get much advice or play around a little bit at that age, the teacher's the enemy. So, I didn't really get to know the teachers as well in college as I now look back on it and should have.

GRAYSON: So, there was kind of like a divide between the students and the teachers.

KNOWLES: Yeah. Well, I had A.B. Lamb assigned to me and he was kind of a physical chemist, but he was mostly interested in the *Journal of the American Chemical Society*. He was on the editorial board of that. And, I think that was his love. I know he had a graduate student that stayed with him for 15 years without getting a doctorate. But, he just ran his whole program, his research program. And, Lamb did was editorialize for the journal. And, so, I never saw Lamb more than once or twice a year.

GRAYSON: So, was this guy at Harvard or …

KNOWLES: Yeah, Harvard, yeah. That was my advisor.

GRAYSON: Advisor at Harvard.

KNOWLES: I was assigned that, but I didn't really think he was much … gave me much advice anyway. One course I did take there that was interesting. Since I was strongly motivated to go into industry. Mainly because of my family's business experience. And, their feeling was there were two places that you shouldn't go to, universities and the government. They weren't going to do either of those things. I had a cousin who had a textile mill. And, he had a rule, "Never Do Business with the Government." He had to violate that rule during World War II.

GRAYSON: Oh, yeah.

KNOWLES: But, he just would not accept a government order, he wouldn't do business with them.

GRAYSON: Oh, my my.

KNOWLES: He was pretty handy guy though. Until he had no other customer. Then, during the war, he had to succumb.

GRAYSON: That's interesting.

KNOWLES: So, nobody told me that. But, there was a strong feeling you would go into business or industry or something. So, I took a course in industrial chemistry. They had one guy come in and he wasn't, as a chemist point of view, very intellectual. But, he planned trips to a number of local plants around the area. We went to them all. And, it was kind of cute. 'Cause they had Radcliffe in those days. And, they were separate. So, he'd give us a lecture one hour. Go across the street and give the same lecture to Radcliffe. So, we wouldn't be contaminated. And, then they went on the field trips too. But, we had to write reports. They didn't. The girls didn't have to do that.

GRAYSON: So, this would kind of be like chemical engineering.

KNOWLES: Yes.

GRAYSON: Would be the closest thing that you would have had at that point.

KNOWLES: That's right. There was no chemical engineering at Harvard. I had a contemporary that I since met at Monsanto. He majored in chemical engineering at Harvard, but he had to take courses at MIT to do it. I don't know that they do that today. They may not today either.

GRAYSON: Could be, I don't know.

KNOWLES: I don't know. But, he took courses at MIT to make it fit. He took math and stuff of course.

GRAYSON: So, at the time Radcliffe students were taking this industrial chemistry course as well. That's interesting.

KNOWLES: They took that as well. But, they did not have to write reports. But we did. Anyway, it was kind of interesting. You went to a woolen mill and you went to whatever Monsanto had, sulfuric acid plant, and an alcohol plant, I think. It always interested me how things were made in plants. Even to this day, I like to get inside a plant and see what's going on. And, I've always taken occasion every time I get a chance to do that to get inside some of these plants.

GRAYSON: Sure.

KNOWLES: See actually what was being done. 'Course, you don't see much in a chemical plant except a lot of pipes sometimes.

GRAYSON: Right.

KNOWLES: And, so, you see more in the mechanical end and the packaging.

GRAYSON: So, why did you decide to go to Columbia? How did that come about?

KNOWLES: Well, let's see, I went to Lamb and thought about graduate school. And, he suggested the University of Illinois at Champagne. And, what was his name? Oh, God, I can't remember that fellow's name. The guy ran it for years and years and years. (Roger Adams)

GRAYSON: So, it was a Harvard graduate that was at Illinois.

KNOWLES: His name just slipped me for a minute. So, I applied there. And, I applied to … and, I got actually turned down.

GRAYSON: Oh.

KNOWLES: They only take straight A students. Now, if I'd gone to West Podunk in the middle of Ohio or something, I would have had straight As. And, they would have accepted me.

GRAYSON: Right.

KNOWLES: I was always amused at that. But, they said, "You've got to have straight As. It was just a rule. We can't take anything but straight A students."

GRAYSON: So, they didn't care, yeah, what chemistry department you came from. It was just you had to have the grades.

KNOWLES: Yeah.

GRAYSON: That's funny.

KNOWLES: But, I had competition. See, the premeds kept the straight As because they had to get 'em. And, they must have … I don't think they knew the chemistry. So, I think that they must have taken these tutoring courses. 'Cause they were available.

GRAYSON: Well, they just wanted to get a grade so they could move on.

KNOWLES: My roommate in college took one in French. He had to get a French requirement. He was terrible at French. And, so, he took one. He told me about it. I had the same French course he was in. And, so, we got into it. He took the exam and in the exam was a question about Cyrano de Bergerac's play and there were some French puns in the thing. And, God that threw us modest students completely. He knew the answer to those 'cause he'd taken the tutor course in French. [laughter] And I think that's the way that these med school students got through the synthesis in chemistry. They must have, I mean, I just, looking back, that's the only way I can figure. I don't see how these medical students got those straight As.

GRAYSON: They studied the tests.

KNOWLES: But, they got the As.

GRAYSON: So, Illinois turned you down even though you had a nice Harvard degree. I like that!

KNOWLES: I got the forms to apply to Minnesota. Now, this is a typical teenager. My family didn't have anything to do with this. They didn't worry about it. And, I got the forms, but I lost them. I was too embarrassed to write them again. So, I was with this other friend of mine, Harold Ferber at Harvard, and he was looking for some graduate school to go to. And, we were in New York. So, we drove up to Columbia together. And, interviewed them together. And, he got turned down and I got accepted at Columbia. And, he later went to Cornell and I went to Columbia. And, I said, "Well, that sounds like a good place," and New York seems like a good place to be in these years. Things were moving. It was '39; The war years and so forth. And Harold Urey was the chairman of the department then. He was the hydrogen isotope man.

GRAYSON: Right, right.

KNOWLES: And, they gave us a good smattering of physical chemistry too. And, I could handle that. But, that meant we had to go through the Debye-Hückel theory, which I never want to go through again. I'll never read Isaiah and Jeremiah and Ezekiel again either. [laughter]

GRAYSON: What were those outfits that you weren't going to read anymore? That you said you didn't want to read?

KNOWLES: Oh, I say, the three long books in the Bible.

GRAYSON: Oh, oh,

KNOWLES: Isaiah, Jeremiah, and Ezekiel. [laughter]

GRAYSON: Jeremiah. Once is enough, huh?

KNOWLES: Except if it happens to be in assignment. And, but anyhow, I took a good smattering of physical chemistry, but I did go with Elderfield. There were two professors I had to consider, Elderfield and Marston Taylor Bogert. But, Bogert was sort of half retired. He was a great orator. He loved being in oral exams and things like that.

GRAYSON: Oh, man.

KNOWLES: So, I took Elderfield.

GRAYSON: So, how do you spell Bogert's name?

KNOWLES: B-O-G-E-R-T. I don't know, might be two G's, I don't know.

GRAYSON: E-R-T, OK, Bogert.

KNOWLES: He was kind of a grand old man type and he taught there for years. When he introduced your talk, his speech was longer than yours. [laughter]

GRAYSON: So, then you went for this Elderfield character. What was his specialty?

KNOWLES: His specialty, he'd been with Rockefeller Institute with a guy named Jacobs. And, he specialized in steroids. But we started off with a non-steroid project. See, I could start right away in research, 'cause I'd already had the advanced organic chemistry and that stuff.

GRAYSON: So, you had a leg up on most of the other students.

KNOWLES: And, they had another qualifying exam, which was mostly balancing equations. God, I'd never be able to do those damn equations now. But, we balanced equations like mad and so forth. And, you qualified but I was able to qualify quicker than the ones who came in first with me. Also, I didn't do any teaching. I had a little grant from my grandmother, $1,000.00 or something like that. And, that got me comfortably through. So, I didn't bother with doing any teaching.

GRAYSON: So, that was kind of nice of your grandmother …

KNOWLES: Well, when she passed away, she gave us each that.

GRAYSON: Oh, OK, that's nice.

KNOWLES: And, in those days, $1,000.00 got you a lot of graduate studies.

GRAYSON: Oh, yeah. That would barely buy the books today.

KNOWLES: But, I say I didn't live in fancy facilities. I lived right off 115th, it was on 116th Street. I lived on 115th Street in a very modest facility when I think of it, back then. But, I didn't spend any time there. All I did was sleep there. So, I didn't give a damn. I was over there in the library or over there with the things and ate out with the kids every, the students every night and so forth. So, I didn't need much. But that was during the war year and it was interesting. What happened was that I had a friend at college who flunked out freshman year, Roddy Madden, who went to Trinity. And, he joined a fraternity there. And, Columbia had a the same fraternity. It was a Delta Psi or something. And, I never had anything to do with a fraternity at Harvard. They didn't have them anyhow much. And, they were hard up 'cause during the war they didn't have anybody to live in the fraternity house and they wanted somebody paying some rent. And, so one of their people came around and said, Roddy Madden said you were taking graduate school here and that you might need a place to live. And, so, I joined this fraternity to have a place to live. They didn't usually take graduate students at all.

GRAYSON: Sure.

KNOWLES: It was for undergraduates, but there weren't enough undergraduates 'cause they were all in the service in those days. I was deferred 'cause my draft board never dealt with someone going into graduate school in sciences. That's the way they thought in New Bedford.

GRAYSON: Mm-hmm. So, your draft board was back in New Bedford?

KNOWLES: New Bedford, yeah. I knew them. They were close friends of my family, and were on the draft board. My family wasn't on it. And, they deferred me because they'd never had a PhD – and I wasn't a PhD then, but later was. They'd never had one. Nobody went to fancy schools from New Bedford very much. See, there's no college locally. So you had to go to Providence or Boston. And, in those days, they considered it quite a ways away. One was 30 miles and the other was 60 miles! A long ways to go to … So, most of the people graduating from high school go to work, you see. So, I was an exception, and they deferred me. But, I got through graduate school faster than I would have otherwise because they told them 'Either you graduate this guy so he can get in industry or we'll draft him'.

GRAYSON: Right.

KNOWLES: So I got out close to three years in graduate school.

GRAYSON: From Columbia. So, you never did serve in the military, though, right? Yes. My first problem in graduate school was to try to find the active ingredient in locoweed. Professor Elderfield had gotten a whole big stash of locoweed from some guy out in Montana, or someplace. It was one particular kind *Astragalus wootoni*. Animals ate it and got sort of ill coordinated and would go a little crazy. And, that's why they called it locoweed.

GRAYSON: But, this is like an analytical problem?

KNOWLES: Yeah, well, no. He wanted me to isolate the active ingredient and determine the structure. That was what he was hoping for. He was hoping to get the active ingredient, an alkaloid hopefully and then he would get the structure of it, you see? And, then the deal those days, remember structure took a long time.

GRAYSON: Oh, yeah.

KNOWLES: It might have taken three or four PhD students. But, whatever it is, we got this locoweed and we extracted it with phosphotungstic acid. And, they had some chemical engineering equipment. He and I ran it, Elderfield and I ran it personally to get it to work. And, he had a test that a previous student of his had found, that if you fed this locoweed extract to cats over about a five or six-week period, they would lose their coordination. They couldn't jump off this table and land on the floor.

GRAYSON: They couldn't land on their feet?

KNOWLES: They couldn't land on their feet. They'd go flop on their face. And he had somebody up at P&S in the medical school that was studying the brain, what the changes in their brain were. don't think anything of it came of all these studies. But, anyhow, they were interested. And, so, we had four or five cats and I was trying to get a concentrate of the active ingredient. You first precipitate with phosphotungstic acid and …

GRAYSON: What was that acid again? How do you spell that? The phos-

KNOWLES: Phosphotungstic … that's a standard P-H-O-S-P-H-O-T-U-N-G-S-T-I-C. Phosphotungstic acid.

GRAYSON: That's got a tungsten in it?

KNOWLES: Yeah. That makes a complex with the tannins and everything and it makes it precipitate.

GRAYSON: OK.

KNOWLES: And, you filter it off. And, we did that on a fairly large scale, an engineering scale, 'cause they had a fuller press out in the engineering department at Columbia. And, I remember he and I just went out and ran it. But, then I took this extract and tried to fractionate it into active ingredients. Now, it wasn't a very quantitative test in the first place. And, that never did any good on the thing. I did isolate a number of products out of the thing. And, these were sugar derivatives and things that crystallized out in ureas -- I had to get a crystalline product out of it.

GRAYSON: Yeah.

KNOWLES: But, these happened to be known. And, I spent quite a little bit of time on that. But, we weren't getting anywhere. So, we abandoned that and went over to his steroid project where he was interested in making the cardiac aglycones like digitalis and strophanthidin that have a five-membered ring side chain. And, we were going to try to put that on simpler ring systems so that we could see if it was active. I mean, he had somebody at Eli Lilly that had a test for that. And, so, I got over to that, synthesizing simple analogs for the cardiac aglycones of which the whole thing would be strophanthidin and digitalis.

GRAYSON: OK.

KNOWLES: Digitalis is the standard one that's used even today for heart problems. Well, this K.K. Chen at Eli Lilly had a good test for this. And, so, we would make compounds and he would test them. Actually, my work was purely synthetic. It was putting this five-membered lactone ring on simpler ring systems and we used indene and naphthalene and things like that. And, we did this and we didn't get any activity either. It didn't turn out to be a lead and we put it on some other things like cholic acid and so forth. And, I don't think anything came of that either. But, it's interesting. K.K. Chen was a little aggrieved with the output Elderfield's lab was giving him the

compounds to test. So, he said, "I'm going to do some isolation of my own." And, this is sometimes when fools rush in and you get into danger when you get into other people's fields. So, he was doing this isolation. Everybody was isolating natural products in those days.

GRAYSON: Mm-hmm.

KNOWLES: He isolated two natural products. I can't remember what it was from. He got two sets of white crystals. And, they didn't have a melting point. They just charred. And, they were soluble in water. And, they were different. I don't remember what he, how he even showed they were different. And, he published them. He called one alpha erlene and the other beta erlene. And, then later, you know what they turned out to be? Glucose and sucrose. Which most any plant that he took, if you fiddle around isolating, you could find them in.

GRAYSON: Sure!.

KNOWLES: I think maybe there isn't a plant that you could find that wouldn't have glucose and sucrose in it. [laughter] But, this is so embarrassing when you take a guy who is really a pillar in his testing. He had wonderful pharmacological tests for all of these activities and things, but when he got involved in chemistry, but these didn't have a melting point. Glucose of course will just char on a melting point test. I don't know about his analyses, I don't know what happened on that; 'cause it should show up on the analysis pretty quick.

GRAYSON: That's pretty inconvenient.

KNOWLES: I don't know how he got off on that. But, he did actually get out a preliminary publication and name them.

GRAYSON: Erlenes. E-R-U- …

KNOWLES: Well, I'll always remember alpha and beta erlene.

GRAYSON: Yeah. How would you spell that?

KNOWLES: I don't know. E-R-L-E-I-N or something like that.

GRAYSON: OK. Some spelling.

KNOWLES: But, that's just a cute story on K.K. Chen. And, I think he would be very embarrassed if his forbearers were aware of it. [laughter] But, even that was interesting because a big name in organic chemistry was Wieland and way back in the steroid chemistry, he was one of the ones that got a Nobel Prize for the wrong structure of steroids and then the history later on, the X-ray people came in and showed him that it was a linear structure not a …

GRAYSON: How is that spelled? Ree-, is it Reeland?

KNOWLES: Wieland, W-I-E-L-A-N-D. He got a Nobel prize and nobody begrudged him. He was a grand old man of steroid structure. But, anyhow, he had published a paper that I found had a mistake in it -- which is something you shouldn't find that the great Wieland had a mistake. It was just purely an analysis error. It was a triacetyl cholic acid and it was only a diacetyl cholic acid. But, it threw me off for quite a while. I finally found it actually in the paperwork. And, this happens with literature -- FINDING a mistake. But, he was such a deified figure. To find that the great Wieland had a mistake in one of his papers was something.

GRAYSON: Yeah, well, you know, people do make mistakes.

KNOWLES: Well, yeah, and the literature's got a lot of mistakes if you look for it. But, I just remember that one.

GRAYSON: So, you then switched to the steroid project …

KNOWLES: Yeah.

GRAYSON: … and that's what you worked on for your degree.

KNOWLES: I finally switched over to that and worked on it for my degree, yeah. And, most of the other Elderfield students were doing similar things. Not all of them were on steroids, but quite a few were. He was very busy during the war. He was never there. And, he was always off on committee work and so forth. So, he had a senior man, Gus Fried, who was at Chicago for years and years and he's since deceased.

GRAYSON: F-R-I-E-D?

KNOWLES: And, Gus Fried ran his program for him.

GRAYSON: How do you spell Fried?

KNOWLES: F-R-I-E-D. And, he was a steroid chemist and he really ran us.

GRAYSON: So, how big a group did he have then?

KNOWLES: Oh, I don't think more than eight or ten or something like that. I could try to add them up but … And, most of the time, since if you couldn't get it crystalline, you couldn't find out what it was in those days. You really couldn't. That was the main thing you were trying to do; get something to crystallize.

GRAYSON: Sure.

KNOWLES: You were going around scratching tubes and doing this and that and …

GRAYSON: Needed a purer compound.

KNOWLES: Yeah, that's right.

GRAYSON: So, if you got it, then you had to do the structure determination.

KNOWLES: Even the steroid work, you had to get, if you ran a reaction, you had to get crystals to get the damn thing out pure. You didn't care if you didn't get a good yield, but if you could get crystals, then you could purify it. And, that was very much more important than it is today. It's very important then to get crystals 'cause look at this. The only reason Watson & Crick were able to do that (DNA structure determination) was because Rosalind Franklin had some crystalline in DNA. And, that's damn hard to get.

GRAYSON: So, your work then was successful enough to get a degree.

KNOWLES: Yes. We got a few publications in the JOC on the subject. And, as far as the medical end, it all bombed out. You couldn't get that digitalis activity without the whole molecule. And, maybe that still holds. I think pretty much. And, I really don't know what's happened to the *astragalus*, what was the active ingredient in that? I proved it wasn't selenium. That was the only thing. There are some forms that selenium causing that.

GRAYSON: Oh, the mad cow?

KNOWLES: Yeah, the mad cow thing.

GRAYSON: I didn't really mean to say mad cow. Locoweed.

KNOWLES: Locoweed.

GRAYSON: What was the astro, astra- …

KNOWLES: *Astragalus*. A-S-T-R-A-G-A-L-U-S, that's the general field of locoweed. This was labeled *wootoni*. I don't know how the botanist that collected the sample. He collected, oh, maybe 100 pounds of stuff.

GRAYSON: Oh wow.

KNOWLES: And, sent it to Elderfield and we, I guess, ground it up with water and …

GRAYSON: Tried to do this extraction.

KNOWLES: .. get the extracts out of it, yeah. I don't remember exactly what we did. I had one experience with the cats that was kind of funny. Well, we had the cats out in the lab. And, there was a famous chemist at Columbia called Schoenheimer -- he was a biochemist. He might have gotten a Nobel prize. I don't know. He did radioactive studies on the gut, how things went through the gut. And, he was quite famous for this. But, his wife also indulged in chemistry. And, she had mice they were doing some tests on. And, they were in the same room. What I did was you could

feed a cat and go away for the weekend. Just feed it enough and it would just ration itself. And, you could leave it two or three days without feeding. And, my cat got out of the cage and killed one of her mice, reached in and killed one of her mice and spoiled her experiment. And, I don't know, you ever have a woman mad at you, but this woman was so mad at me. I got thrown out of that room pretty quickly. But, she was … she sounded off. I didn't know what to do. I just sat there and trembled. She was so mad, because Schoenheimer was such a big name. He got rid of this stupid graduate student real quick. And, that was kind of an amusing experiment. But, later on Schoenheimer shot himself.

GRAYSON: Oh, really.

KNOWLES: So, I don't know. At the peak of his career, it was one of these suicide things. You never know what started it. Maybe the wife had something to do with that. I don't know. But, I never knew Schoenheimer and I only knew Schoenheimer's wife once.

GRAYSON: Yeah. And, you didn't want to know anymore.

KNOWLES: I've never seen anybody just get off on such a diatribe at me, screamed and yelled at me.

GRAYSON: And, the cat was the guy that did the thing.

KNOWLES: Well, I know it. Well, I didn't take care of my cats. Well, he just got out.

GRAYSON: Yeah. The mouse wasn't too smart to be close enough for the cat to grab him.

KNOWLES: Well, I don't know. I never did see the mouse. But, that's what she said happened anyhow. But, that was just an aside.

GRAYSON: So, despite this debacle, you end up getting a degree from Columbia.

KNOWLES: I got a degree, yes. And, I do think it was accelerated a little bit by the thing. Of course, as I say Elderfield was working on committees. Most professors were. And, he would just come through sometimes, you know, and go off on his committee work. So, Fried was there all the time. And, he was an interesting experience for me, because he was a German Jew and he got out

of Germany, he bought himself a Polish citizenship for $50.00. And, that was how he got out of the thing.

GRAYSON: Oh, OK.

KNOWLES: He became a Polish citizen. That was one of the tricks that Poland was using to collect funds then. He said it cost him $50.00, well, $50.00 was more then, but anyhow. He bought himself.

GRAYSON: So, basically, he looked like he had Polish papers when he left Europe.

KNOWLES: That's right.

GRAYSON: And, then he was able to get out.

KNOWLES: That's exactly right.

GRAYSON: Now, at that time, Poland was probably occupied.

KNOWLES: Well, I don't know if … I can't, I haven't got the chronology exactly of what he did and so forth. But, he was interesting, 'cause he was very steeped in German culture. He claimed that the only thing the English speaking people had done that was worthwhile was pyrex glass and William Shakespeare. [laughter] There were two things that were superior to what the Germanic people did. That's so funny how they were brought up in that Germanic culture that rejected them. Einstein was the same way. He wanted to be sure that German physics was top in the world. And, they rejected him too. Rejected him completely. Anyhow, this guy was interesting. He had such a totally different background than anyone I had ever run into before.

GRAYSON: Do you know what part of Germany Fried came from?

KNOWLES: I don't know.

GRAYSON: OK.

KNOWLES: Now, there was another guy there that I later got to know, Nelson Leonard. He had been a professor at Illinois, University of Illinois in Champagne for years and years afterwards and he went out to Scripps in the west coast for retirement; he's deceased now. But, he was working on an alkaloid problem. And I got to know him. But, he was pretty much in those days pretty much straight shooter. He would never take a drink or anything. And, I liked to go out and drink with the boys and so forth. And, he was very much a straight shooter. But, we had pretty good *joie de vivre* with the graduate students there and so forth. Though it was still a little fun. We had one black graduate student. In those days, it didn't sound right, but he couldn't eat lunch with us at the west end. In New York? I mean, that sounds absolutely crazy. I mean, he never made a problem of it. But, when we went to lunch, he just didn't go.

GRAYSON: Do you know …

KNOWLES: His name was Len Hawkins and the only place that he could get a job, and he did very well and he went to Bell Telephone when he left. And, he left a little before us. He was an earlier vintage.

GRAYSON: So, he got a PhD.

KNOWLES: He got a PhD with Elderfield and he went to work for Bell Telephone. I don't know what he did there. I think he survived there as far as I know. But, he couldn't find a place to get a job another place. There was a lot of prejudice then. I remember the biggest thing was when Hitler signed the pact with Stalin – do you remember that famous day? That had all the Jewish groups completely disillusioned. I came in that morning and they were just, Fried and all the rest of them, were so completely depressed because Hitler had signed a pact with Stalin. See, they were pretty pro-Stalin, it was just … that was the big, that was the end of the world.

GRAYSON: So, explain a little bit more about this … the German Jewish population. This was the late 30's, early 40's?

KNOWLES: I graduated in '39. It was about 1940, yeah.

GRAYSON: OK. So, this would be before *Kristallnacht*?

KNOWLES: I'm not sure when … what the date of *Kristallnacht* is. 'Cause when it occurred, we didn't hear much about it.

(Note added by Grayson: *Kristallnacht* was in November of 1938)

GRAYSON: Right.

KNOWLES: So, do you know when the date is?

GRAYSON: No, I don't know the date.

KNOWLES: I don't either.

GRAYSON: But, at any rate, so, the German Jews were very depressed by the alliance between . . .

KNOWLES: Hitler and Stalin. Because they thought Russia was pretty good about things. They weren't, actually, as it turned out. But, they (German Jews) thought they were at the time.

GRAYSON: So, they felt that the Jewish situation in Russia was better than it was in Germany? And, by this time, they knew the situation in Germany was pretty bad.

KNOWLES: Oh, yeah, they knew that. And Fried had gotten out. A lot of them had gotten out. But, they had to use one shenanigan or another to do it. But I hadn't had much experience with anybody from other countries if you know what I mean? It was kind of interesting for me to do that.
But, it's still amazing that the little west end restaurant, which is a two-bit place, wasn't anything fancy, it was a bar and a place to eat. And, we went there a lot and but they wouldn't allow blacks in there. It's just amazing to me to think of it.

GRAYSON: But, I think that was standard for the times. This was 1940.

KNOWLES: I know it. It was standard for the times.

GRAYSON: As a matter of fact, it would seem, from my understanding of the time, it would be unusual for a black person to be doing graduate work in chemistry …

KNOWLES: Yeah, it was unusual then. But, we would sometimes go out in the evening and Harlem was real cheap. We couldn't afford to go to the fancy places in New York. But, Harlem was cheap and they just loved you to come there.

GRAYSON: Oh, really?

KNOWLES: Oh, yes. They'd put you at a front table and everything. Of course, it was all black entertainment and probably on the standards of entertainment was very good. But, no, Harlem was something. I didn't go there very much, but a couple of times we went over there.

GRAYSON: Sure.

KNOWLES: And, you didn't feel unsafe or anything at all. You just went in and all these nightclubs that were quite inexpensive. And, 'cause that's where the New York intelligentsia sort of went for a late fling in the end of the evening. But, it was safe. I don't know why it was safe, but it was.

GRAYSON: Yeah, that's kind of crazy.

KNOWLES: Oh, it is crazy.

GRAYSON: Now, so you're graduating from Columbia. You have your PhD. How do you figure out where you're going to go to get a job?

KNOWLES: Well, then, I was influenced quite a bit by Elderfield. But, first of all, my father decided, "Well, I've got a few connections for you." He had one at American Viscose, which did a little chemistry and so forth. And, so, I did interview a couple of his customers, so to speak.

GRAYSON: So, these were people he knew through his textile business.

KNOWLES: It would be textile chemistry. And, so, he had me interview a few of these. But, it didn't seem like very much to offer. So, I did sign up then for the usual interviews. I signed up with DuPont and I signed up with General Electric for trips. And, it was an interesting time to interview, because this was in '44. They would tell you, "You're hired. Now, we're going to show

you what you're going to do." They would take anybody that was sight unseen. Particularly if you weren't black. And, they even preferred you not to be Jewish too. Though Merck took Jewish a lot. But, a lot of the places wouldn't – DuPont wouldn't take Jewish.

GRAYSON: Really?

KNOWLES: No. So, I interviewed DuPont and Hercules and General Electric in Pittsburgh, that was plastics, and I don't remember who else. Doesn't matter. And, then I tried Monsanto because Elderfield had some dealings with Thomas and Hochwalt Laboratories on the anti-malarias or something. I don't know what he was dealing with. He was a wheeling and dealing and he thought that was a nice informal place, maybe you'd be interested in that. And, so, I interviewed Monsanto. They interviewed in St. Louis. So, I was interviewing for Dayton Laboratories. And, Dayton didn't do their own interviewing and they let St. Louis do it all. And, part of the incentive to go was to take job furthest west. I got offered every place I went. So, as I look back on it, I probably took the … I thought the one further west sounded more exciting. And, so, I thought it would be interesting to get out of my niche. I had really never been west at all much until I did take a trip west in college. My two roommates and I took one of my family's cars and drove it west in '36. That was the only western experience I had had at all.

GRAYSON: How far west did you get?

KNOWLES: We got all the way. We went to Yellowstone and Oregon and the Oregon coast. We did the circuit of the country.

GRAYSON: That took a while.

KNOWLES: Yeah, that was the summer of '36, it was probably that, and it was an interesting trip because you couldn't cross the country on a paved road then. That's what's amazing when you think of it. You went awfully fast on dirt roads and you wore tires out fast too. We had tire troubles quite a little. And, so forth. And, we often slept just out and sometimes in motels when we wanted to get a shower or something and eat over a cook stove. So we didn't use a lot of money on lodgings and we also stayed with friends wherever you could find them. So, that gravitates where you go a little bit. We had somebody in Eugene, Oregon. So, we went across to Eugene, Oregon. Had somebody in Minnesota. Yeah, I guess it was Minneapolis/St Paul, so we went there. You know, I mean, you worked out the thing. But, we went to Yellowstone Park and we went to Yosemite and so forth. We did the circuit.

GRAYSON: So, let's see, those were the parks, Yosemite, Yosemite's parks had just recently been made into National parks, I think.

KNOWLES: Oh, no. Well, they were all. Those two were parks then. But, that was a good enlightening trip. No new technology.

GRAYSON: So, you got to west coast, Frisco? Or did you go to Frisco or LA or …

KNOWLES: We didn't get to LA. We got to San Francisco.

GRAYSON: San Francisco.

KNOWLES: And, we did the Yosemite.

GRAYSON: Uh-huh, sure, yeah, that's close by.

KNOWLES: And, crossed Death Valley and so forth and came back and went up through Texas, San Antonio, 'cause we had friends there. So, we stopped there. It was interesting.

GRAYSON: So, how many people were in this car trip?

KNOWLES: Just two roommates from college. They weren't in science. They were in humanities.

GRAYSON: So, this is the three of you.

KNOWLES: Yeah, three of us took the trip.

GRAYSON: That's kinda neat.

KNOWLES: It was in my family's car.

GRAYSON: What did you drive then?

KNOWLES: It was a Chevrolet.

GRAYSON: A Chevy. Took the old Chevy.

KNOWLES: The main problem was the tires, the tires.

GRAYSON: Really?

KNOWLES: We had tire problems.

GRAYSON: Did you end up having to buy tires or did you just check to make sure …

KNOWLES: We ended having to buy one, yeah, and we patched them whenever we could.

GRAYSON: 'Cause they had tubes in them too then?

KNOWLES: Yeah, one time we had to patch them with a band aid. We got 40 miles on that tire, though. We had to pump it up every ten miles. [laughter]

GRAYSON: [laughter] Oh, I like that. So, finally, you decided, 'I'm going to move as far west as I can' when you decided to get a job?

KNOWLES: That's right. Well, I thought it would be more exciting and Elderfield had met Thomas and Hochwalt. So, he recommended them highly. He thought it was an informal place to work.

GRAYSON: So, when you came here for that interview, was that by train?

KNOWLES: I took a train. Yeah, they said they'd fly you if you could guarantee that the extra cost was worth it, but for a student it wouldn't be worth it. So, no, I took the train out.

GRAYSON: So, then you interviewed here in St. Louis? Would have to be in the city someplace, I would think.

KNOWLES: Yeah, when Monsanto was down on Second Street.

GRAYSON: Second Street, OK. And, it was then they offered you the job?

KNOWLES: Yes.

GRAYSON: Did you interview other places or …

KNOWLES: Yeah, I interviewed. DuPont and Hercules and General Electric and …

GRAYSON: So, they all offered you the positions?

KNOWLES: Oh, yeah, everybody offered you. And, I think that was all. Maybe not.

GRAYSON: So, when did you end up starting? Would have been in the fall of …

KNOWLES: In '44, yeah. I guess it was fall of '44. I didn't bother to go to my graduation for the PhD. I know the PhDs, they don't often go. I didn't go.

GRAYSON: Yeah. Now, at that time, the war was still on in Europe?

KNOWLES: It was very much on. I went to Dayton. I was in the Dayton Laboratories. That's where I sort of interviewed Monsanto. I wanted to go to the Dayton. So, I was about a year and a half in Dayton.

GRAYSON: Were they doing the war effort thing in Dayton?

KNOWLES: They did war effort. But, it was interesting. Most of the guys that were on the war effort were ones who's draft boards were breathing down their necks. Now, mine never bothered me. 'Cause they couldn't 'cause of the fact that they only had one PhD, see, in New Bedford a PhD was a rare commodity. And, so, I stood out. And, they didn't ever make any argument about that. And, so that I wasn't used nearly as much as I could have been for the war. I did some on the war effort.

GRAYSON: OK.

KNOWLES: But, most of it was not very interesting and particularly in Dayton it wasn't much at all. Though they had a war program. They had a very active one on rocket propellants. And, they even had a fatality that occurred there. But, I didn't have anything to do with that. And, they were very secretive about what it was, but it was solid propellants they were working with and those were rather hazardous. I look back on some of the stuff they did then and I don't think they really knew what they were doing.

GRAYSON: Well, I know that many of the people I've interviewed did get or seemed like were drafted into the war effort, even though they were in science or chemistry or mass spectrometry even got drafted into the war effort or into some aspect of it anyway and it was a grind. You know, it was really a 24/7 type deal.

KNOWLES: Right. Well, anyhow, I wasn't bothered that way. At Dayton I was almost a physical chemist there. I did work on one project, which was related to the war effort. It was purifying hexamethylene diamine, which is a product of formaldehyde and ammonia. It's a complex, very symmetrical ring system that was nitrated and made into an explosive called cyclonite. They were thinking of making that. I don't think they thought very seriously about it. But, anyhow, it had to be quite pure for that purpose I guess. So the explosive would be of known sensitivity or something. But, anyway, that was a good explosive. I'm not sure whether it's used today or not.

GRAYSON: I don't know. Speaking of which, in your Nobel background, you said that you suffered a lab explosion once?

KNOWLES: Yeah. Oh, that was in graduate school. One of the key reagents that were used to make this five-membered; or the key reagent; was diazomethane. And, we had to distill diazomethane. We never used it on a large scale. I mean, I doubt if I ever made more than a gram. But, anyhow, diazomethane is rather touchy. And, this did explode on me once. It was in the hood

and the distillation was done, the door was down and nobody was hurt. But, even a gram made for a helluva big explosion. Scared the hell outta me. But it did destroy a bottle of product which I unfortunately had put right beside it. And, that kind of shook me up a little bit. I spent three months making that product and to screw it up like that. But, so what, you make it again, I guess.

GRAYSON: Yeah. It was pretty much down the drain. So, we're back to Dayton then. I just remembered reading about that, though.

KNOWLES: Yeah, well, diazomethane, we were careful with. So, I mean, it would be a great carcinogen, but I'm sure it's a strong methylating agent, they all are. But it was always handled in the hood. And, we distilled it and if you recall with an ether if you were ever got it pure it would sometimes go off. Didn't set a fire at all. Just went off; no solvent fire. Usually the solvent fires follow. But, there were no fires started but boy they were hot. It was just a small amount, that was all. I don't know why. I only made a gram. I it was right in the distilling column.

GRAYSON: OK. You didn't actually tap it or hit it or do anything to it to make it go off. It just took off.

KNOWLES: It just went off. It's very unpredictable. But, that was just an experience that scares you. But, when you think about the entire history of explosives, it's scary when people first made them, they didn't know what the hell went on. But diazomethane is easy to use if you don't get it out of a solution, but you distill it. This had to be distilled for this particular reaction. You couldn't use it otherwise. Unless you made it with the nitroso methyl urea.
Anyhow, I was assigned to Dayton and about the only war project I worked on there was the hexamethylene tetraamine. The other was to … on the vapor phase hydration of acetylene to acetaldehyde. This is a vapor phase hydration. The standard liquid phase is the usual way to get it, but we had catalysts. This was a catalyst study. Acetylene catalyst study really.

GRAYSON: What was the motivation to do that in the beginning?

KNOWLES: Oh, they wanted to get into that and use acetylene as a building product, a basic petrochemical building product. They had an acetylene process that somebody was … I forget, Wolf process acetylene I think it was or something. I don't remember now. I think that's what it was. And, they wanted to convert that to acetaldehyde for which you could go on and make all kinds of things. And, when I look back on it, there probably wasn't any great plan behind it. They just wanted to be in a position to move if that looked like a good thing to do at some point in the future after the war was over. It was really for after the war was over. They were dealing with petrochemicals. In those days, it was still a little bit coal tar chemicals, you know. And, they were thinking of getting into petrochemicals. And, this was one route of doing it and they wanted to

have all the links in place if they wanted to do it. And, so, I built them equipment, just a hot tube and various condensers and scrubbers and so forth. And, Charlie Thomas was a very promotive type guy. He loved to come in and he'd take somebody around the lab and show them this equipment, which looked like physical chemists' equipment, you know.

GRAYSON: What was his first name?

KNOWLES: Charlie Thomas.

GRAYSON: Charlie.

KNOWLES: He later became president of Monsanto. He was very much a promoter. And, he would come in and of asking me to show them what went on here, he said, "Just show me where the acetylene goes in, I'll do the rest." And, he gives a big spiel about what great things were going on and so forth. But, anyhow nothing ever came of that. As I look back on it, nothing ever could have come from it. I don't know what we really were gonna do. I had a guy in the lab there, his name was John Malowon, typical chain smoker. Took just one match a day, he kept going all day. And, he'd sort of wet his lips and the cigarette would hang out there. We had a cracking process to make biphenyl. I guess we were cracking benzene into biphenyl. And, we did it by bubbling the gases through molten lead. He was trying to see if other molten metals would give a more efficient reaction. And, he was a little careless; he was using magnesium, molten magnesium. And, he turned on the thing too hard and air got to it. All I know is the stuff landed here and I was out the door here. Where I was standing was where the thing landed. He said he never saw anybody come out the door as fast I did.

GRAYSON: Magnesium is not the kind of metal you are careless with.

KNOWLES: Things were just very casual in those days. I don't know why he didn't blow himself up or burn us up with the thing. Again, no alarm, just come around and say, "Oh well, try something else." But, I don't know that there was any good reason to believe that any other molten bath was nonreactive and would do it any different. But, they wanted to be sure. Now, they do it in a hot tube.

GRAYSON: Sure.

KNOWLES: Pyrolysis; I think it was benzene to biphenyl. That's right. And, I think they may even still do that. I don't know.

GRAYSON: So, you spent a year and a half there. At Dayton.

KNOWLES: Then I was transferred to St. Louis.

GRAYSON: OK. Was that something that you opted for or was it …

KNOWLES: Well, a little bit of each. It sounded a little more pharmaceutical oriented and so forth and fine chemical oriented and that would be better, I thought. And, so, that turned out to be where

GRAYSON: Well, eventually the Dayton operation was shut down, wasn't it?

KNOWLES: Yeah. Oh, eventually it got shut down, yeah, eventually. But, it was quite a while after that. It was maybe another ten years before it got shut down. And, both Thomas and Hochwalt came to St. Louis.

GRAYSON: So, when you came to St. Louis you were on Second Street then?

KNOWLES: Yes. And, got involved in plasticizers first, which was a fairly big product with Monsanto at the time.

GRAYSON: So, this was like late '40s, no, '48?

KNOWLES: No, no, no, it was '45. See I was, '44, let's see, I came, I think it was '45-'46. It was about '46. And, I was married here in St. Louis.

GRAYSON: OK.

KNOWLES: When I came from Dayton, a bunch of bachelors lived in a house on Maryland Avenue.

GRAYSON: So, where did you meet your wife?

KNOWLES: We had people coming to parties in that house.

GRAYSON: Was it in Dayton that you …

KNOWLES: No, here. (St Louis)

GRAYSON: Oh, OK. You met your wife when you moved here.

KNOWLES: Yeah.

GRAYSON: OK. So, plasticizers were a big item then. Where did they end up going?

KNOWLES: Well, plasticizers going to polymers like vinyl, mostly vinyl. They modified the properties of vinyl to make it flexible.

GRAYSON: Yeah. So, there was a big market in vinyl?

KNOWLES: Oh, yeah; car upholstery, all kinds of things. I don't know if designers started that early or not; probably. You can't work vinyl without some plasticization.

GRAYSON: So, what kind of plasticizers did you work on then?

KNOWLES: Phthalate esters mostly. They were working on phthalate esters and phosphate esters. The phosphate had some fire-retardancy properties and so forth that were favorable. And, I would say that I started in phthalates, but moved over to more of the phosphates. And, mixed phosphates.

GRAYSON: So, these were usually added in small amounts, right?

KNOWLES: Yeah, we had tri cresyl phosphate. Oh, no, no, no, no, no, they'd added sometimes as much as 50%.

GRAYSON: Oh, really?

KNOWLES: Oh, yes.

GRAYSON: Oh, wow.

KNOWLES: Plasticizers in vinyl, yeah, it sops them up. It's like a perfectly good flexible solid. A flexible piece of vinyl I may have 50% plasticizer in it.

GRAYSON: Oh.

KNOWLES: So, it's a bulk market. It's a tank car thing.

GRAYSON: OK. So, there was a real market for these things.

KNOWLES: Oh, yes. And, it makes the vinyl plastics possible. There were other places that it was used, but it was mostly vinyls. Poly vinyl chloride.

GRAYSON: Sure, wow. That's interesting.

KNOWLES: It's a brittle solid. I don't know that it's ever used by itself. It may never be. I don't really know.

GRAYSON: So, where did that chemistry come from. 'Cause somebody figured out that you had to add these plasticizers to vinyl.

KNOWLES: Well, the first plasticizer was camphor in cellulose nitrate, I think. Camphor was the first plasticizer I know of. They make the toothbrushes out of it. Cellulose nitrate, yeah, I think it was, cellulose nitrate. But, I think it was camphor they used first. But, that was back in, God, the 1900's or something like that. So, plasticizers have been used to modify the property of polymeric

materials; and vinyl became the real market so we got into these phosphate esters that use tri cresyl phosphate, which is more flexibilizing than tri phenyl phosphate. And, is a cresyl with methylphenol that was mixed with isomers of course. We had a mixed phosphate that we worked on. It was 2-ethyl hexyl alcohol was made from acetaldehyde and that was usually 2-ethyl hexyl diphenylphosphate. That was one. And, then, of course di-2-ethyl hexyl phthalate was one where they sold their patent rights. They sold their patent rights on that. That was a big volume item for Carbide.

GRAYSON: So, the work that you did, was this developing synthetic routes, better ways to do it?

KNOWLES: Yes, improving the process. It was purely process chemistry. And, then another product, more in the fine chemical line, we got into was vanillin, synthetic vanillin. Monsanto made synthetic vanillin, but they wanted to get a better process. So, we had better processes, but that had to be interrupted because of the war. But, after the war, they did that.

GRAYSON: So, this is for cooking vanilla?

KNOWLES: Vanilla, yeah. That was, I mean, now, these small competitors are small beans. But, at that time, the company's size, it was big beans. It was one of the more profitable items was vanillin.

GRAYSON: Hmm, that's interesting.

KNOWLES: That was Monsanto's reason for being in the fringes of that business. Because they were looking for uses for vanillin. See, if you have a flavor use, you can make a little bit more and you don't need to have very much, and it expands your market a lot. You see what I mean? And, it's always good to have something other than flavor uses for the product.

GRAYSON: So, what would your vanillin be used for besides flavor?

KNOWLES: Well, that was why we got interested in L-dopa because the basic starting material was vanillin.

GRAYSON: OK. So, it's kind of related …

KNOWLES: You can always turn out a little more vanillin, you see? But, anyhow, it was all flavor in those days.

GRAYSON: Well, were you competing with flavors and fragrances houses? There were fine chemical houses that do that kind of stuff.

KNOWLES: Yeah, well, somewhat yeah. But, they were a bulk supplier of vanillin. And, we didn't sell to the guy that puts it in the ice cream. We sold it to some intermediate. Monsanto was always an intermediate producer. They never sold it directly. And, they made aspirin the same way. They never sold aspirin as a pill. They'd sell it to Schering-Plough or somebody, you know.

GRAYSON: So, aspirin was developed in Europe wasn't it?

KNOWLES: Aspirin first originated by Bayer about in 1850. But the process was vastly improved with the Kolbe synthesis about the turn of the century. And, so, it was easy and cheap to make and it's still a big bulk item. Monsanto in those days was just purely a bulk producer of chemicals. And, they let somebody worry about the formulating and selling. They sold in bulk.

GRAYSON: Like a wholesaler operation.

KNOWLES: Yeah. At that time anyway we were getting involved with vanillin and which way to make it. See, we had lignin vanillin coming along in the wings. This was making it from lignin waste from the paper industry.

GRAYSON: Mm, OK.

KNOWLES: And, they eventually ended up making lignin vanillin. But, in the beginning it was kind of traumatic and I was assigned to the chemical end. So, I was always pushing that end. You know, you don't forget where you're assigned. We had to have a better process, so I worked on several vanillin processes; to put the aldehyde group on 1-2 dihydroxy benzene. That amounts to catechol. I played around with a number of different processes in the lab. And, we had one that was going in the plant, but we wanted a more efficient one. Also in the wings was another group. They would have been on the west coast, trying to push lignin vanillin, but at first they didn't get the smell out of it and so it didn't smell like vanillin. Which is what you're selling; so we didn't think they could ever solve that, but they of course did solve it. It was a big controversy. And, then Edgar Queeny, the head of Monsanto, finally said, "Well, we'll just go into lignin vanillin period, boys." And, so, all the synthetic vanillin was shut down and we went with lignin vanillin.

And, they had put in a plant out on Puget Sound there. It operated for a great many years and then, of course, it got sold to somebody. And, I don't know whether they still make it that way. Probably vanillin is still made from lignin. But, that's the kind of thing where you got a free raw material, but you get a hellishly low yield, and you process a lot and you bring in a barge of lignin and you end up with a barge of lignin waste that you've got to do something with. And, I thought if you can get rid of the effluent at some cost, put it on a road or do something …I don't know what they ended up doing. But, you gotta do something to handle all that carbon. 'Cause you can't just stash it up.

GRAYSON: Right, yeah.

KNOWLES: But, it does make the BOD factor lower, since you're oxidizing the lignin, lowers it. You've already oxidized it to make your vanillin.

GRAYSON: So, as I see, it's a free starting material, but then when you're done, you still have almost as much material that you have to dispose of.

KNOWLES: Yeah, when you get a 2% yield out of it. It's like extracting the natural product. But, anyhow, Monsanto went into the lignin vanillin eventually. The next thing that came along was this; I'd put on my brochure that I had steroid experience. And, Woodward came to Monsanto, I think maybe first. I'm not sure. He had a total synthesis steroids in the early '50s. And, he was working on it. It wasn't complete then, but it was pretty near complete. He was getting somewhere. And, he got the ring system down pretty well. And, cortisone was very desirable, but you couldn't get any. I don't know if you remember in those days, but when it first came out, it seemed to cure everything.

GRAYSON: Mm-hmm.

KNOWLES: I don't know, take it for the common cold. Take it for anything. It looked like a general cure. So, Monsanto thought interesting to get into cortisone as a long-term thing. They were in a few other pharmaceuticals. Nothing very much, an antacid and aspirin and stuff like that. And, they had a cathartic based on phenolphthalein indicator. And, that was another story. How that got discovered as a cathartic; but it was a very good one and they made that for a number of years at the Queeny plant. And, so they were on the fringes of pharmaceutical and fine chemicals, but not heavy. But, the cortisone looked like it would turn out to be a volume item. They said this guy Woodward had a potential synthesis for it. And that depended on the knowledge of steroid chemistry. They said, "We got anybody in the company who's in the know on steroid chemistry?" I turned out to be the only one, as I put that when I signed up you know, what's your expertise.

GRAYSON: Sure.

KNOWLES: And, I said I was kind of a steroid chemist, though I hadn't done much with it. But, I was familiar with the ring structure and the things that we do and so forth and I knew the structures anyhow. And, so, they asked me to read up on steroid chemistry and get involved in the Woodward thing; which I proceeded to do. Charlie Thomas had an academic leave program, which he thought would be good for his chemists, like a sabbatical. Well, he thought he might use this steroid program as the first instance of this and he put me with Woodward for a year. So, I had a company-sponsored post doctorate with Woodward in '51 or something like that. I went to Cambridge and did that. That was a very exciting period in my life.

GRAYSON: I can imagine.

KNOWLES: And, it turned my chemistry around; 'cause I'd been dealing with pretty much cut and dried mundane things like phosphate esters and vanillin and so forth. So, it really got into more serious stuff. So, I found that a very exciting experience.

GRAYSON: So, Woodward was in Cambridge?

KNOWLES: Yes, he was on the faculty at Harvard. He got real acclaim immediately. He was not one to hide his candle under a bushel basket by any means. I don't know if you know much about him. It was pretty fascinating to have worked with him, because he was a boyhood genius kind of in chemistry; really the closest thing to a genius in chemistry. Although, not in general living outside. And, so, the experience with him was very interesting. I never knew anybody that had more chemical information on his brain; on tap, and loving to show it off. He had that ability. He loved to show off really how much he knew about chemistry. And, he had it all on tap. He said he lost it after he was 30-ish. He was my age exactly. Born in 1917, but in his 20's, he didn't ever keep a file or note. He remembered, he knew everything. "Go to Beilstein, page so and so, you'll find something on that." And, he said he lost that after he was 30. He just couldn't keep it up. He had to keep a file and do a few things.

GRAYSON: Like the rest of us!

KNOWLES: Yeah. But, he could just memorize everything. He got some fame from quinine synthesis that he cooperated with Doering. And, remember quinine was short during the war. And, this was a typical organic synthesis, which was totally impractical. But he had to testify to a congressional committee and all that stuff. They got so excited 'cause we didn't have enough

quinine. And, that's where the big impetus on the anti-malarial program and the other synthetics came along to take its place. And, that's where Elderfield got involved. But, anyhow, Woodward was involved with this steroid synthesis. Total synthesis of steroids. And I was assigned to go to his lab and become well-acquainted in the field. And, I did. That was an interesting experience because Woodward's the kind of a guy that whatever he does is very intense. He never came in in the morning. He gave a course there, but you never knew whether he was going to attend it or not. He had a seminar. It was a fascinating seminar when he ran it. And, people came from all over, MIT and so forth. But, you're never quite sure if he's going to have it or not. You showed up and if he had it, it was fine. If he didn't … He was very independent minded. But, he couldn't get along with Fieser.

GRAYSON: Hmm, Fieser was still there then?

KNOWLES: Fieser was upstairs. Woodward had downstairs and Fieser had upstairs. And, Fieser was very much a lab technique guy. Woodward was "up here" (points to head); couldn't do a thing with his hands. He got a PhD at MIT, but claimed he hired somebody to do his experiments for him. I mean, Woodward really was totally up here.

GRAYSON: In his head?

KNOWLES: Up here, he had his technique. But, he drank too much and womanized too much, did everything too much. He was a typical burn the candle at both ends kind of guy. The obituary was a little too nice to him. It would be more interesting if it was written about the whole person. Because the whole person is more interesting. And, he was the closest thing to a real genius that I ever ran into in the field.

GRAYSON: So, what did he think about you showing up in his lab?

KNOWLES: Oh, he liked that, because he was pushing Monsanto executives. I don't know whether he went to them or they went to him, but he got in contact with the Monsanto executives and he really wanted somebody to commercialize this synthesis. And, the damn guy could get up and write steroid structures in a very methodical way in front of those guys and get 'em to understand it a little bit. He was good at that. Oh, he was a master at that. His lectures in the early days were just something. They were an artistic event, really. He would start out, this is what he wanted to synthesize and he put it up on the board and he'd start down here and he would come around he would come back just to right where the place was. And, there were it was; you could take a picture of it and publish it almost.

GRAYSON: Wow.

KNOWLES: The drawing was perfect. Everything was done in 50 minutes; but he got out of that when he got famous in his old age. But, in the early days, he used infra-red spectroscopy -- that's all we had then was infra-red. And, he could read more into that than anybody I ever saw. I was impressed with what he could read into that. And, he'd be right. And, he gave a course with what you could do with infra-red. And, that was very good. I don't know if it was a course. Maybe it was just a seminar.
But, anyhow, my stretch with him was very interesting. I was there about nine or ten months I guess. But, the first three months I was there, he would come in about, oh, quarter of twelve. That's about when he came in. Said, "Let's go to lunch." And, this guy, Ted Brutcher, who was also a post doctorate with him and I and he would go to Schrafts to lunch. And, we did this every day for three months. And, then I never saw him again. But every day for three months and the lunch menu was full of structures. Was kind of a fascinating experience. We just covered the menu and everything with structures.

GRAYSON: So, you'd just go eat lunch and discuss chemistry.

KNOWLES: Just discuss chemistry very intensely the whole time.

GRAYSON: And, did you bring the menus back with you when you guys left?

KNOWLES: Well, I didn't do that. But, I remembered what was on them. And, I spent quite a lot of time. Brutcher was good. He followed the thing. He had a lot of experience.

GRAYSON: This is B-I-R-C …

KNOWLES: B-R-U-T-C-H-E-R. He ended up at the University of Pennsylvania. He was what you might call a confirmed bachelor. See, I was older than most of them.

GRAYSON: Sure.

KNOWLES: I was older and Brutcher was older too. And, John Herber got his degree with Brutcher. He was the one that you mentioned you had talked to to set up the interview.

GRAYSON: OK.

KNOWLES: Me to you or you to me.

GRAYSON: OK, all right.

KNOWLES: John Herber did get a degree with Brutcher. And, I think Brutcher's deceased now, but he had problems. But, he did get me off on a modern approach to chemistry, 'cause I'd go out drinking beer with him every night. We had a place in Cambridge. And, during the summer, my family were down at the beach and in Rhode Island. And, I would just work about 12-15 hours a day four days, five days a week and go and have a long weekend in Rhode Island. And, then go back and forth that way -- to me, the ideal way to work. Work very intensely for four or five days a week and then take a long weekend and just forget it. And, then go back and do the same thing over again. So, I did that for all summer and then the family came up to Cambridge. We rented a house, which really was a very primitive thing. But, it was right on Brattle Street and right on everything. And, right next to Longfellows house and all the famous things in Cambridge. But, it left much to be desired. But, anyhow, we got by there.

GRAYSON: What was the name of the street, rattle?

KNOWLES: Brattle, oh, Brattle Street is the tourist street of Cambridge.

GRAYSON: OK. B-R- …

KNOWLES: Capp originated there with Little Abner and …

GRAYSON: How do you spell that?

KNOWLES: … and he lived there. What, Brattle? B-R-A-T-T-L-E.

GRAYSON: OK.

KNOWLES: Longfellow's house was on that. That's where everything … well, we were on Brown Street, which is just a little offshoot of that. And, I could walk over to the chemistry

department. I had an old girl's bike that I sometimes just rode over. And, that was a very nice existence and very interesting people that lived on Brattle Street too. The professor of the business school and a banker lived right next door to us. He may still live there. But, Brown Street, and we were living in an old New England house, but it was really rattle trap. It was something. But, it was nice to be very close to where we were going. I just had to cross Harvard Square and I was there. And, so, I found that a very exhilarating experience. And, I say, Woodward was very intense for that period and then he was off on something else. He dealt with his various students. He didn't teach any undergraduate courses. And, then it turned out his total synthesis was a relay synthesis. He synthesized something, which, incidentally Fieser had taken to cortisone

GRAYSON: Oh, really.

KNOWLES: He and Fieser didn't talk. Woodward said "All Fieser needed was a good research director". Fieser gloated and saying, "Well, Woodward needed somebody to complete his synthesis." [laughter] And, they were both probably right. Fieser was a perfect, meticulous on lab technique. He always ran a lot of his own experiments. He was another chain smoker. I mean, chain smoker. Fieser was a chain smoker with less reason to be than anyone else, 'cause he actually isolated benzpyrene, a carcinogen, out of cigarette tars.

GRAYSON: Wow.

KNOWLES: In the '30's. He did that way back.

GRAYSON: Oh. Yeah, well, it's a habit.

KNOWLES: But, he didn't quit smoking till he had a lung removed. He didn't last long after that.

GRAYSON: So, basically after this three-month period, Woodward just kind of left you guys high and dry?

KNOWLES: Well, then I had the students, the graduate students. There was Franz Sondheimer and Dave Taub and Ted Brutcher, who I was rather close to, there. And, we kicked chemistry around and we had his seminars. We always went to his seminars. That was enough of him, and he came to some of them. And, they were good. Nobody's idea was stupid. He was very good on that. The guy had an awful lot on the ball, other than a colossal ego and everything else. And, I think when he thought of a chemical problem, we had him as a consultant for a number of years in the '50's after the steroid thing kind of declined. But, he didn't think about a problem until he was

in front of you. He liked to think in front of an audience. You ask me a chemical question, I like to go over in a corner and scribble around, figure it out and then come back and say, "Well, maybe this would work." But, he wasn't that way. He'd like you to see his mental processes going right in front of you.

GRAYSON: He was a show off.

KNOWLES: Yeah – but he was very good at it. I mean, he's responsible for the *beta* lactam ring in penicillin. I mean, they had the formula for penicillin, but they couldn't figure out the structure, because the *beta* lactam wasn't considered a plausible structure. Nobody'd ever made *beta* lactam. It was a strange damn thing. Nature'd never make it that way. And, he could come up with unusual things like that. And, another one was ferrocene. He came up with this unusually stable product from iron and cyclopentadiene -- ferrocene, the sandwich complex. Well, Wilkinson was at Harvard at that time. But, I attribute that strongly to Woodward to be able to look at things differently. See, this was an unusually stable thing that shouldn't have been stable, like benzene. You know, way back. And, he could always look at things at a little different slant.

GRAYSON: He had a different way of seeing the chemistry.

KNOWLES: That's right. He just could do it. Yeah, differently. As I say, he didn't have to keep a file. The rest of us did. But, he didn't. Until he got older. He was very good on structure determination and he proposed a structure for strychnine. He was involved with the structure of that; these very complicated molecules, which we only had chemical methods to find the structures for.

GRAYSON: Right, yeah.

KNOWLES: It was a very elaborate problem. His point was there was always something wrong with the data. He could put it out on the table right now, everybody's experiment, and try to figure out where that mistake was. And, that's what led you astray. And, of course, the same things in the steroids way back in the '20's when there was something wrong in Wieland's data. You had to pick it out and then you see why the thing was linear and not blocked.
But, it was kind of funny, because when he came out to Monsanto we always had to have a poker game in the evening for him.

GRAYSON: Oh, really?

KNOWLES: And, he didn't have that phenomenal memory for the cards or anything. He played it just like you and I'd play it. It was just recreation for him. He didn't bother with anything. And, I don't really think that he had a good memory for the cards and what's been played could be useful. But, he didn't use that at all there. But, he was a monogenius or something on chemistry. That was his thing.

GRAYSON: But, he had to have this poker game whenever he visited.

KNOWLES: Yeah, well, he had one in Cambridge with the Polaroid group. It was Elkan Blout was in Cambridge and they were all with Polaroid. But, that was truly recreation. And, he also liked to have a Scotch in front of him most of the time. He'd come out on a train – he'd never fly – he always came out on the train. And, he wouldn't fly till he got famous and had to go to Europe a lot. And, you almost have to fly today to go anywhere. So, he finally had to succumb to flying.

GRAYSON: Pretty crazy guy.

KNOWLES: Yeah, and he used to have parties out at his house and there was very much booze at those parties. But, he would talk chemistry though.

GRAYSON: He did?

KNOWLES: Oh, he did at parties. Sure, he did, sometimes.

GRAYSON: So, did he ever get married or …

KNOWLES: Oh, yeah, he was married, divorced, I don't know maybe two or three times.

GRAYSON: Oh, really?

KNOWLES: I can't keep track. After he was married and divorced once anyhow. And, his home life was very erratic. I tell you, he was impossible. And, he was a night person. He always stayed up all night. And, we had trouble with him. He'd go to the East side (East St Louis Illinois) when he came here after the poker game.
Note. East St Louis has always had a reputation for a rough place to go, offering a variety of 'entertainment' not available on the Missouri side of the river.

GRAYSON: Oh, really?

KNOWLES: Some of the Monsanto people went with him. I never went with him over there.

GRAYSON: That was kind of a risky.

KNOWLES: Yeah, when I first met the guy, we had an ACS Convention meeting here. And, it was in our convention center, which is now the hockey rink, but, he was giving a lecture there. So, I thought I'd go hear him. I'd never met the guy. I hadn't seen him before. And, so, I went into this lecture room and it turned out that the clocks were bad. And, so, I got in there way early. There was this one man sitting in the front row and no one else was in the lecture room. And, I said, "Gee, I must have made a mistake." So, I sat down beside this man. And, I said, "Well, doesn't look as though anybody's coming to this lecture. I feel sorry for the lecturer." He says, "So do I;I am the lecturer." [laughter] And, then it turned out everybody came but it was ten minutes late. For some reason, my clock and the clocks at the conference were quite different. But, he says, "I am the lecturer." Another funny one with him was we went to these Gordon Research Conferences up in New Hampshire. And, one time he was the keynote speaker on Thursday night. And, he was very famous for his very Mr. Cool lectures at Harvard and every place. Didn't ruffle a thing. Never bothered. Completely Mr. Cool. And, you didn't think he thought a thing about it. Came in and gave this perfectly fine lecture; completely adlibbed. You'd have thought he didn't have a note completely adlibbed. Well, I was with him and he gave one of these world-famous lectures at the Gordon Conference. And, before the lecture, they'd had a big dinner, you know, and everything. And, so, I asked him to have a drink with me afterwards. And, he said, "Sure," we went to the place and had a drink. And, he called the gal, he said to her, "Bring me a hamburger, in fact, bring me two hamburgers." And, I said, "Well, didn't you like the lobster we had at dinner? Didn't you eat tonight?" And, he said, "Oh, before I give a lecture, I can't ever eat."

GRAYSON: Oh, wow, that's interesting.

KNOWLES: That kind of thing doesn't get in the obituary. And, various things that I don't think detract from him.

GRAYSON: No, I mean, that makes him … it humanizes him and …

KNOWLES: Yeah, that's right.

GRAYSON: … you get more of the inside story on what kind of a guy he was.

KNOWLES: Yeah. Well, a lot of those very good lecturers spend quite a bit of time before them. I don't think he's alone in that.

GRAYSON: Yeah. So, then at the end of the year …

KNOWLES: Well, then cortisone went by the way when it was discovered that … the problem with cortisone, I don't know if you know the steroid structure is, well it's Ring "C". You have A, B, C and D. Ring "C" has a hydroxyl on it. And, most of the steroid syntheses in the natural product steroids don't have this oxygen in Ring "C". All the natural steroids that are in soybeans and so forth don't have it. Well, Upjohn discovered that using, I think it was *Aspergalus niger,* that damn organism would put oxygen in Ring "C". And, so that made all the soybean steroids and diosgenin in the Mexican yam all available to make cortisone. See, before that it's a very difficult problem and here's a saturated ring. No way you could get oxygen in Ring "C". Now, with the synthetic process, we had a double bond there we could put the oxygen in Ring "C" easily. Just epoxidize it and open it. So, we had an easy way. So, that part was no problem. But, then they turned around and did this oxidation with the *Aspergalus niger*, which is a pretty common fungus I think, and they found that that would put that oxygen in Ring "C". So, that knocked the bottom out of our toluene 36 steps you see. That was too many steps. It knocked the bottom out of any thought of that; so, they got out of it.

GRAYSON: You started out with toluene?

KNOWLES: Yeah. We started out with toluene.

GRAYSON: Then go 36 steps to …

KNOWLES: Yeah, but we cut it down. It was 50 steps originally. And, we cut it down to about 36. I think a few more steps would have been cut out of that, but not a lot. Because, in the total syntheses of steroids, you're better off putting two halfs together than build it up succession wise. So, anyhow, that doomed the thing to failure. I have to admit that we chemists on the job were so interested in doing all this chemistry that we didn't tell management it wouldn't work, but we didn't discourage them if they wanted to support it. You see what I mean? I didn't do anything to discourage them. Woodward remained a consultant for, oh, five years or so afterwards during the 50's. And, I do think he had an unusual way of looking at things. There is another one that, at

least I wouldn't have thought of it, but I would have liked to have thought of it. Nothing to do with steroids or anything else. But, we were in the caffeine business.

GRAYSON: Mm-hmm.

KNOWLES: And, actually, we were having trouble with Coca Cola. They didn't like to buy our caffeine. It was made from urea. And, Coke, which is the big customer, was afraid that somebody would get onto that that we were making our caffeine in Coke from urea. Sounded too much like urine, you know what I mean? And, this would really kill them. So, they said, "We can only buy natural caffeine." Well, the Germans, they said, "Our supply is a natural caffeine." Well, I had been on a trip to Germany and I told our management I did not think that the Germans were doing that. I think they were mislabeling it. They were making it from methyl urea. This was my particular guess. I didn't know for sure, but it looked as though they were not making it from that. And, but Coke said, "But they're labeling it that. If you will label it natural caffeine, we'll buy it." And, Monsanto, and good credit too, they would not mislabel it. They would not do that. And, so, we said, "Well, how can we prove that the German is not natural?" Well, Woodward said, "Well, it's easy. We'll send it up to Libby and have him carbon date it." And, sure enough it came out of coal mine, dead.

GRAYSON: Oh, wow, sure.

KNOWLES: You can't get it except out of a coal mine if it's dead, can you?

GRAYSON: Yeah, yeah, interesting.

KNOWLES: Didn't need to have an accurate date on that at all.

GRAYSON: No.

KNOWLES: I think there might have been a little bit of alcohol used in the synthesis so that it wasn't completely dead, but it was so near dead.

GRAYSON: So, this was Woodward's idea that the carbon dating would show that it was synthetic.

KNOWLES: Send it up to Libby and have it dated and it was practically dead. So, that proved it. So, we went back to Coke and showed them this. And, then in the meantime, Sanka coffee had come into being. That was what killed our caffeine business, because they took the caffeine out of coffee and just put it right back in Coke. And, then they lowered the caffeine content in Coke. Coke had a lot more caffeine in the 30's. And, they cut it back, because the young were drinking it too much. So, that's how synthetic caffeine went kaput because of the rise of Sanka coffee. Now all the caffeine needed for soft drinks is gotten out of decaffeinated coffee.

GRAYSON: Taking it from one place and putting into another.

KNOWLES: That's exactly what's happening and I'm sure today it's a huge amount. But, I did work for a while and I had a guy working on a synthetic caffeine process; we were starting with methyl urea, and it's a little better than when we started from urea.

GRAYSON: Oh, let me see. Maybe we oughta stop for lunch.

KNOWLES: Sure, OK. I think probably. Now, do you want to have a bowl of soup here?

GRAYSON: Well, it's up to you. I mean, I'm more than willing to treat you to lunch.
Note: Dr. Knowles warmed up some soup and we ate at his home.

[END OF AUDIO, FILE 1.1]

Note: During lunch, Grayson restarted the recorder. The conversation centered on Woodward.

KNOWLES: But, that was the way he (Woodward) was.

GRAYSON: So, he's really very good intellectually but he couldn't really do anything in terms of making things. He would be good as a director.

KNOWLES: No, he was no good. I mean he got through his PhD at MIT very quickly because he didn't bother with the undergraduate. In fact, I think he was purported to say, "Well, I didn't want to take any of the courses because I know all of this stuff." And they gave him the exam. He knew it all. I mean he was a prodigy.

GRAYSON: Mm-hmm. Apparently, he enjoyed life too.

KNOWLES: Oh, yeah. I think he took terrible care of himself though. But, he was way above it as far as these other professors around that you run in to; way above it.

GRAYSON: Great-tasting soup.

KNOWLES: You didn't do much teaching at Washington University?

GRAYSON: No. No, my ... I was just a staff guy. Basically, the Director, the PI on the grant needed someone to pick up the paperwork end of things there and carry that for him. So, I'd been working at McDonnell-Douglas Research Labs prior. So, I had a feeling for dealing with paperwork.

KNOWLES: That was your first job with … Where did you go to school?

GRAYSON: I went to St. Louis U and then the University of Missouri-Rolla.

KNOWLES: OK.

GRAYSON: I actually, got a masters in physics at Rolla and then, well, my graduate education ended there. I never went on to a doctorate but was able to get in to an area that was fun and interesting. And, so, I don't think it really hurt my career that much in terms of doing fun stuff. But, nowadays it's (a PhD) almost … really it is a requirement. More and more.

KNOWLES: Much more, isn't it?

GRAYSON: Yeah. Actually, I got in to mass spec by working for O.P. Tanner (who was at Monsanto during the '60's through the early '90s.) In the S building over in Monsanto. And, the guy that hired me was … That was when I was doing undergraduate work. I was part time. There was a guy by the name of Bill Cave who was over in the S building.

KNOWLES: Did you ever know Gucci at Washington U when he was there.

GRAYSON: No.

KNOWLES: He retired and went down to Texas, Austin.

GRAYSON: I mean we've got Jake Schaeffer.

KNOWLES: Jake Schaeffer, I know him.

GRAYSON: He used to be at Monsanto.

KNOWLES: He was an NMR (nuclear magnetic resonance) man.

GRAYSON: Yeah, NMR man at Monsanto. He's at Wash U now.

KNOWLES: Mm-hmm. Is he still active?

GRAYSON: Yeah, he's still doing research.

KNOWLES: He was doing solid state NMR. I don't know whatever became of that.

GRAYSON: Well, it's like all these analytical techniques, they've become so sophisticated. They have all these new methods of obtaining data and plotting it and extracting more information and getting better ideas about structure and so on and so. Very good soup. We might have to get the recipe. I cook soups.

[END OF AUDIO, FILE 1.2]

GRAYSON: When did Woodward die?

KNOWLES: Oh, the 70's.

GRAYSON: Oh, so, he really burned himself up.

KNOWLES: Yeah. I think '78 or so. I didn't see him any of the last years. Since 1960, we didn't see much of him. He stopped being a consultant and so forth. Gone off on these very glamorous things. He spent a lot of time in Switzerland going back and forth.

GRAYSON: It was a great experience for you.

KNOWLES: Yeah, well, it was a great experience. Hi.

[MRS. KNOWLES ENTERS]

MRS KNOWLES: Hi there.

KNOWLES: Can I help you with anything?

MRS KNOWLES: No, I just got back from my shopping.

KNOWLES: OK.

GRAYSON: So, let's see, at this point, you had explored this steroid thing up to the time that yams showed that it wasn't going to work.

KNOWLES: Yeah.

GRAYSON: I just was curious about management at Monsanto during this period. My impression is that after the War in that period the people that reached the upper levels of management and came up in the industry were trained in chemistry. And, were chemists primarily. But, then, later it evolved to where you got more and more business people to the top and you didn't have people with sound chemical understanding at the higher levels of management.

KNOWLES: Yeah, I think you could say that. That's true. Edgar Queeny, who was in power the whole time didn't have a chemical background but he had a number of people around him that had chemical backgrounds. He had Gaston DuBois and he had other people. And, then, Thomas and Hochwalt had quite a bit of chemical background. But, after that, there was none. And, I think I ran into that problem later. I mean it's very easy to describe the Nobel thing (What Knowles did for the prize.) to anybody who's had any basic chemistry but if they haven't, it takes a lecture.

GRAYSON: So, in this 1950's period, there were still chemists who were more in charge.

KNOWLES: There were some there, not all, but some.

GRAYSON: Now, you elected to go up what they call a technical ladder?

KNOWLES: I never went up any administrative ladder at all. I just didn't want to do that, so I didn't.

GRAYSON: Sure.

KNOWLES: And, I think you would make more money if you did that.

GRAYSON: Oh, yeah.

KNOWLES: I know I'd made more money, but I didn't. That wasn't the primary concern. And, I was getting to be a fairly senior man so I wasn't bothered by a lot of nitpicking.

GRAYSON: So, you had shown your value to the company and they had recognized that?

KNOWLES: Yeah, well, one project, I don't the dates of it that we played with. We were always interested in getting around to the commercialization or synthesis of chloramphenicol, which is an antibiotic. Chloromycetin, that'd be the other name.

GRAYSON: OK, very good.

KNOWLES: No, Parke-Davis had come up with this. And, this had two features in it. It was a simple chemical but it had two features in it that were unique. In natural product chemistry it had a nitro group and a dichloro acetyl group. Well, I go involved. I can't remember when. It must have been a little back in the late '40's or something, putting the dichloro acetyl group on. We were using pretty much Parke-Davis' stuff. And, there was a resolution. It was an optically active material and you had to resolve it. We had to run a resolution and so forth. And, others did that. And, I put the dichloro acetyl on. And, I prided myself that I was able to shorten the route that Parke-Davis had considerably. It made it much simpler. And, it was very easy to put it on. We made 14,000 pounds of it. And, then, it had a problem. There is a disease called aplastic anemia, which is pretty damn often fatal. And, there were a few cases. I mean, they probably had already millions of prescriptions out there. And, there were a few cases of aplastic anemia. And, then, the other ones, the terramycine and chloromycine came along and they do pretty much the same thing. So, it didn't get banned but it got very much pushed back and so we got out of that. Otherwise, we would have probably gone in to the manufacture of that for Parke-Davis. But, that is still around and it's still the best thing for typhoid fever but who was the last one you ever heard of having typhoid fever? I think it's still the antibiotic of choice for that. And, I've still got a bottle of it in my medicine cabinet. I had a dog at the time that had some fungus or something that wouldn't cure very easy with the ones the vet gave. I just threw in one of those ointments, mixed in chloromycetin in. It was gone like that. But, it was a very good antibiotic but it did have out of a few million cases, two or three cases of aplastic anemia. Well, if you call that a military operation, you'd consider that enormously successful.

GRAYSON: Right.

KNOWLES: So, that was another one that involved making an optically active compound, chiral compound just by a difficult resolution method.

GRAYSON: When did you actually get into the asymmetric hydrogenation?

KNOWLES: I didn't get into it until later. First of all, I went in to kinetic problem in the plant about the late '50's. This was a very simple rubber chemical intermediate, para nitro phenetol was made into para phenetidine, which was the rubber chemical intermediate and it was also made into some other things. But, that was the key in the media. By scrutiny of the kinetics -- and I didn't even get the kinetics. Our analytical lab got that. With just scrutiny of the kinetics, we were able to double the production by short reacting and recycling and reacting back. It was that kind of a study, but we were able to double production without adding much capital. Hardly any capital. So, from a point of view of economics, that was much more important than most the other things I did. And, I spent quite a little while on kinetics. It was successive, secondary reactions, which gets pretty complicated. And, I'd forgotten my math. I had to go back and learn it a little bit again, which was kind of fun. And, there was one physical chemist that helped me with the math to get back in that. Math's the kind of thing that's easy to forgot how you differentiated and all those

kind of things. But I did get involved with kinetics for two or three years. And, next I got involved with some straight hydrogenations. We were hydrogenating using a nickel catalyst, mostly nitro groups over at Krummerich Plant. And, one of them was this para nitro phenetol. They were reducing it to the amine, the nitro group to the amine and they were using a nickel catalyst. The problem with that is that their source of hydrogen was intermittent. They had cells, caustic cells and you got hydrogen as the byproduct. And, if you shut the hydrogen off, then the catalyst poisoned. Condensation products covered it up and you had to re-catalyze and start all over again and it was a big nuisance. They were worried about that problem and they had some corrosion problems. Well, my suggestion was very simple. I had them use palladium on carbon. That sounds like just nothing now. But, anyhow, it was more then. And, they used a nickel catalyst, which they actually made or something. Well, palladium on carbon didn't have these bad properties. And, they said, "Well, palladium is much too expensive." When actually, you use less dollars with the palladium than you do with nickel to get the job done. But, I couldn't get them to do it in the plant. And, it wouldn't work in our pilot plant, because we'd had so many poisons in the autoclave there that we couldn't hydrogenate anything in it with these heterogeneous catalysts. And, it turned out that one of our guys found out that England was doing this hydrogenation on nitro phenetol. And, he talked them into trying it; with palladium on carbon - this big plant unit that had been using nickel. And, of course it worked just fine, they never did turn back. And, so, then, they had us all shifted over to it, which was much cheaper, even throwing away the palladium, it was cheaper, but you didn't filter if off and send it back for recovery. It never got more than 75% on that.

GRAYSON: So, the plant in England, was that a Monsanto plant?

KNOWLES: That was a Monsanto plant. And, it was just one of our people that I was talking to said well they're trying it, why don't we talk to them? Maybe they'll do it. Well, they weren't so conservative and decided they'd try it.

GRAYSON: So, the whole idea of using palladium just scared people away because of the price?

KNOWLES: It scared them away. It was too expensive. You didn't need to use very much but I couldn't demonstrate that on a pilot plant scale, because you couldn't get by with that little layer because of the fact that it was eternally poisoned. And, to get the pilot plant clean would have been - I don't know. They had to really boil everything and caustic and blah, blah, this and that and so forth. So, anyhow, there was a little politics in that. It took a little while because of the hydrogenation group, which wouldn't move 'cause they said we've got to solve the corrosion problem. And, I said, "Well, you won't have the corrosion problem if you use this." Oh, no, we'll solve that first before we can do this. So, we went ahead and finally got England to do it.

GRAYSON: You kind of did an end run.

KNOWLES: That's right. And, sometimes it takes that in a plant. I got involved with engineering. I never was an engineer, but I got involved with engineers.

GRAYSON: Yeah, it sounds like you're kind of getting in the chemical engineering side of things here.

KNOWLES: Yeah, well, the kinetic job required putting in a continuous distillation. And, I did have a very good rapport with this one engineer named Davis, I think. I don't know what his name was. He'd just come out at lunch with me everyday and we worked it out and so they were able to throw together. It had to be a continuous recycling back of the reactants. They were reacting out the starting material and that was taking them forever. Two or three times as long to get … you can get to 90 % conversion quickly with successive second order reaction which tails off fast. And, so, we'd go to 90% and recycle the 10 back. We had a very simple test that all we had to do . . . The recycled material had chlorine in it so we could run Beilstein test and that's what we did, it was that simple kind of thing. Now, the plant would have the fancy equipment and blah, blah this and that. This just had a little room with a flame and a guy would test it. And, if the flame was negative he'd cut the still off. But, we had to do that continuously. And, this guy put it in and had all the equations for in-use installation and all of this. I got acquainted with that at least. But, anyhow, I did get into the hydrogenation using noble metals. That was the first venture toward things that you can use in very expensive metals if you don't use very much of them. We always were in dispute as to how much palladium we recovered. I'm wondering, still whether some of that palladium was solublized into the nitro phenetol, but we didn't have the analytical devices then that would measure that if we did. I speculate now that maybe that was happening.

GRAYSON: You were losing some of the catalyst in the product.

KNOWLES: Well, when this came along, about the first thing I think I mentioned in there that we were always looking for projects to do and one was lysine, which looked like a good project. And, there was a pretty good route for the synthesis of lysine. The Japanese synthesis from acrylonitrile. We made nylon from acrylonitrile. See what I mean? It's the whole thing of building a family tree. It's very easy to make a little bit more acrylonitrile and make lysine, you see what I mean? So, that's a good thing for us to do. It wouldn't have been interesting at all if we'd had to buy the acrylonitrile. But, we had a big plant making it.

GRAYSON: Right.

KNOWLES: We could expand that plant much more cheaply. And, so, that was a good project to look at. Of course we got racemic lysine, if we wanted to do the process. Everything we'd calculated, you could take the d-lysine and racemize it and cycle it back in the system and all that stuff. But, you end up with so damn much equipment that you really double your costs however you look at it. We just couldn't come out ahead - it was all paper chemistry. I think from one of our engineers and we just couldn't come up with anything unless you could make the damn thing directly and we didn't know how to do that and I still don't know how to do that in that particular one. But, we do really know how but not simply. But, that's - so, that sort of sat fallow just as a problem but I didn't do anything about it. I didn't have anything to do about it. And, then, during the 60's, we had a new research director, Costas Anagnostopoulos - that's a tough one. You don't have to bother about that. He came in and decided that I would be a senior scientist, they called it then, or I don't know, a distinguished fellow. I don't know which it was, but I would get a new man to train. Every time they hired a new PhD, they'd give them to me for a year to train and put him on anything. And, he said "I don't want to know what you're doing." And, so, I figured out - a number of exploratory projects. Some of them were exciting. We had one to extract a flavoring agent out of larch bark. This flavoring agent is called maltol, M-A-L-T-O-L. It's a simple cyclic sugar derivative.

GRAYSON: Mm-hmm. You were trying to extract it from what was it?

KNOWLES: Well, the way it came about was this. Pfizer was making this and it does the same thing to Jell-O products that monosodium glutamate does to meat. Monosodium glutamate makes it meatier, it just gave Jell-O products a special flavor and I think it's being used today. Strawberry Jell-O, those kind of things. And, Pfizer was making it from cogic acid. Well, I don't know if I noticed or one of my people noticed in Beilstein that this maltol existed in the bark - in larch bark. Way back, somebody in Beilstein, found that out.

GRAYSON: This is larch, this is the tree bark?

KNOWLES: Yeah. So, we had learned from our paper operation that St. Regis had a big larch operation up in northern Montana. This was a glamorous trip at least. So, we went up there, there was a little fishing to boot. But, we went up there and took a look at this place and 50% of their intake was larch trees. This was a *tamarisk occidentalis*. It was some kind of larch that they were using. And, so, we got samples of bark.

GRAYSON: How do you spell that tree?

KNOWLES: Larch, L-A-R-C-H. A larch is a conifer that loses its leaves. It has cones just like a regular conifer but in the winter it loses its leaves and they look all dead. And, the tamarisk is the

most worldwide kind. Russia has millions of acres of tamarisk trees. I can't go out and collect it *per se*, but they're already bringing in and debarking these trees. So, it looked as though there was an opportunity here with the St. Regis Paper people. They said, "Well, gee, something you can sell for $12.00 a pound sounds good to us. We'll go ahead and take a look at it." So, we went up there and we got the bark and brought it back and it did contain maltol. And, we were able to isolate it, it wasn't very hard to isolate. We got a lot of bark and chopped it up. I had a little shredder in my backyard, I brought it down to the Queeny Plant and we shredded it and then extracted the bark. And, it was the glycoside, you had to hydrolyze it first. But, we got the maltol all out and we had good maltol and so forth. But, then, it got more complicated later. It wasn't quite that simple because they didn't bring only larch in. And, they had a pond in front of the sawmill and they brought the logs in. And, this guy in the boat would prod and push the logs in various places. The valuable logs would go to railroad timbers. The stud logs, the ones that weren't very big, would go to making studs and so forth. And, he made the decision, this guy, completely uneducated. So, it was just impossible to get him to just only do larch today 'cause they debark them immediately. And, they had this huge pile of bark, which they'd burn for fuel - it wasn't much good for fuel; it's 70% water. But, nevertheless, that's what they did to get rid of it. But, anyhow, it didn't look as though we could just collect the larch bark and the other bark didn't have any maltol. [laughter] So, we ended up not doing much with that but that was an interesting project. That was the kind of thing that I was on. And, the second project which I'd started was one where we were trying to solve -- and never did solve -- was to find a resin system, which when it cured, expanded. And I mean not just with a gas. You could do it with a gas. But, it's a bit like ice freezing. And, this would be very useful in potting compounds; a lot of things. So, the idea was to generate a coil spring molecule to crosslink in an epoxy. We could reduce the contraction but we never did get it to expand.

GRAYSON: The expansion.

KNOWLES: But, I still think if you had coil spring molecule and brought the thing together by polymerizing, the shrinkage would be less than the expansion due to it uncoiling. And, we found some advantage in taking very flexible cross linkers, such as cyclic anhydrides. They would be quite flexible and they can crosslink with an epoxy. Some of them, 10% that shrank, when they're cured.. We got it down to maybe 5%, 4%, something like that. And, that sat that way and I had a publication on that; it's in your list probably somewhere probably. I never did anything with that because these other things came along.
What happened was I read about Wilkinson's discoveries in '66 about tristriphenylphosphine chloro rhodium. This is a hydrogenation catalyst that would hydrogenate simple olefins just like the heterogeneous but by a homogeneous process. Homogeneous hydrogenation was practically an unknown thing. It was around. There'd been one that would reduce quinone to hydroquinone, a copper one back in '39. Generally speaking, that wasn't really effective.

GRAYSON: So, these were just catalysts for opening up the double bond.

KNOWLES: Hydrogenating the double bond. But, they were just to make it saturated. And, they worked not as a heterogeneous on the surface -- they worked in solution.

GRAYSON: OK.

KNOWLES: That's the difference. Wilkinson presumed solution. He made this discovery and he got a Nobel Prize - not for that but he would have gotten it for that. I think he wouldn't have gotten it without that. We'll put it that way. Osborne and Wilkinson did this. I of course, met Wilkinson. I'd met Osborne, and Osborne said, "Well, Wilkinson was never there. I really did it." And, the chronology, this is interesting because Osborne and Noyori were at Harvard at this time.

GRAYSON: How do you spell Osborne?

KNOWLES: O-S-B-O-R-N-E. Osborne and Noyori were both at Harvard at the time and familiar with Wilkinson's work. And, I read about Wilkinson's work first in a Welch Foundation lecture that Wilkinson gave. I didn't go to it. In the discussion afterwards, it was suggested. If you used an asymmetric phosphine, say on a pro chiral olefin you would get an asymmetric synthesis. See what I mean? And, it was decided that this would be a good thing to try.

GRAYSON: This was in discussion of the talk?

KNOWLES: It was in the discussion. And, I guess there were, best I can tell you, there were about five of us that decided that this would be a good thing to try. So we all tried it at the same time. Mostly people just but some chiral side chain on the phosphine and the tri phenyl phosphine and let it go that way. But, we thought the asymmetry should be right on the phosphine because that was where the action was. So, we found out just at that same time, Mislow and also Horner in Germany had discovered that you could make an asymmetric phosphine. You see, nitrogen connected you to three different things. You can't resolve it because it racemizes so readily at room temperature. You could resolve it at minus a hundred and something like that. But, phosphines they thought might be the same but they found out that they were stable at room temperature. Well, I think in 110 degrees they have a half life of two or three hours or something. So, both Mislow and Horner discovered this. Horner did it with electro-chemistry and Mislow did it with pretty confused synthetic chemistry -- which he didn't understand. We had him here and he had to call his student to find out what the hell he did. I mean we never did find out very well. But, he was interested in learning how fast these things racemized with different structures. His discovery was made just at that time so, we decided that we'd make a chiral phosphine and namely the one that Mislow made and try it in this synthesis. So, we made the one that Mislow made which is methyl propyl phenyl phosphine. And, that has four different things attached to the phosphorous and,

that's resolvable and we did get it. He never got it completely resolved and probably we didn't either. We had pretty good 80 and 90%.

GRAYSON: So, when you say resolved, that means separate out the enantiomers.

KNOWLES: Yes, we need the chiral one. Then, we used that instead of tri phenyl phosphine. And, we had to choose a what we call a pro chiral olefin And, the simplest one we could choose was alpha phenyl acrylic acid. That was the simple one, alpha phenyl acrylic acid. And, this main problem was it took six months to synthesize the phosphine and had all kinds of troubles doing it. This new guy came in with me … Well, first of all, the first guy that I wanted to put on this project to make phosphine said he didn't want to do anything that fancy. I mean with low chances. So, he wanted to do something else. Maybe he went over and did the larch bark. That's what, he went over and did the larch bark project, he was much happier on that. And, this other guy, Jerry (M. J.) Sabacky, he'd just come from Illinois and was very good on NMR, which we weren't incidentally. I didn't know anybody that did NMR, but Illinois had them really trained there, organic people, they really know it. So, we were able to use his skill on that because you couldn't have made phosphines without that. It was very stinky. He was very unpopular, because that the trimethylphosphite stunk terrible. And, the whole series stunk all the way through. It took him five or six months to make it. He started in January and it was June before he had a phosphine. And, methyl propyl phenyl phosphine - this is the one that Mislow had already made and Horner had already made. But, they didn't have descriptions of how to make it really. Oh, they had some fancy electro chemistry. Mislow never published details. He just said he made it. We knew the secrets and reactions but we had to work them out the same as he did. And, so, we ran that; Jerry ran it four or five times to be sure we got a chiral effect, not much – 15%. And, we hadn't really done anything that no one else had done. The only substantial effort in this direction had been a Japanese group since 1955, they'd tried to empirically absorb chiral agents on heterogeneous catalysts and do it that way. And, they'd got perhaps, up to 15%. Purely empirical and they had one good result with palladium on a silk fibroid, which they said they couldn't repeat. And, we weren't going to try it that way. That was a heterogeneous catalyst and we liked this because it was homogeneous. And, we had to establish that we were in fact homogeneous and that there wasn't any material plated out on the reactor or something; we had to go to some trouble to prove that.

GRAYSON: Yeah.

KNOWLES: But, then, we did get that first publication out. And, that was traumatic because the patent department doesn't like to hurry. But I knew - I kind of knew we had something here and wanted to get a communication out on it.

GRAYSON: Yeah, the first paper is pretty important.

KNOWLES: It wasn't worth anything. And, so, that kept them happy. They weren't disclosing anything that anybody could make a buck out of. And, so, I finally talked them into filing a very poor case 'cause they really didn't know what to file. So, they filed a case about it. They had to file a case before they would let you publish, and I got it published. And, we beat Horner to the draw by a month.

GRAYSON: Oh, wow.

KNOWLES: And, then, he was a little mad at us.

GRAYSON: So, you were saying, before you could do the publication, you had to get the patent department to get the patent process going.

KNOWLES: To file a patent. They always have to do that. So, they filed it. That took from June to September. We did it in June but we didn't publish - we got a *Chem Communications* publication out in September. But, we were the first even so, to publish in this field. And, the one thing I didn't notice at the time -- Gilbert Stork pointed it out much later. He was at Columbia, he was actually at Harvard at that time - we got to know him.

GRAYSON: What was his last name?

KNOWLES: Gilbert Stork. He's an old-time professor now at Columbia. He was kind of an associate professor or something at Harvard. He didn't get tenure and so he went to Columbia.

GRAYSON: OK. S-T-O-R-K, Stork?

KNOWLES: Right. He mentioned that the main thing is we made the prediction in this original publication that given time we would very rapidly be able to find something that would give acceptable yields. And, nearly everybody says this on their breakthrough publications. Stork said this is the only one I ever read that came to pass.

GRAYSON: That's funny.

KNOWLES: That's kind of funny right there.

GRAYSON: Yeah, you made a prediction that worked.

KNOWLES: Yeah, we made a prediction but that's what happened. It works much faster than we predicted. So, what we had to do was to find a phosphine that had a suitable structure that would give us acceptable results. I mean we're not doing the impossible because nature can do this with enzymes. But I wanted to get something far short of the complexity of an enzyme. And, so, to make a long story short, phosphine number six was acceptable.

GRAYSON: So, basically, you took it and just changed the substitutions on the phosphine? So, the phosphine has the three different groups on it.

KNOWLES: Right - three different groups and we wanted to put different ones on there. So, we - this is methyl propyl phenyl. We decided that the ortho anisyl group would be good, that has a steric hindrance and would withstand the rigors of the syntheses. It requires Grignard reactions and Grignard reactions won't just run on anything, they're rather reactive materials. So, the ortho anisyl group was just great for that. So we took the ortho anisyl group and made methyl ortho anisyl phenyl phosphine. That gave fairly good results -- 60% or so. That spurred us on. That's not good enough to be practical. We took the phenyl and made it into cyclo hexyl, and got the methyl ortho anisyl cyclo hexyl. And, it jumped to 80%. Actually, this was good enough for lab preps. We could get it at low temperatures up to 88 but practically 80. That got us very excited but we couldn't really publish that, because that department gets a little hairy about it. We finally did get a communication. One way I got to publish and say something about it was the fact that Throdahl was the vice president in charge of research and was talking with the head of -- what was this magazine called?

GRAYSON: C&E News?

KNOWLES: Not Chem News. Chem Tech or something. It was a sort of a little bit of a 'popularized' magazine. And, so, we ended up getting an article in that 'cause I was sort of lied and said Throdahl wanted us to do that. I told the patent department that. 'Cause this guy wanted to get something and so I showed him.

GRAYSON: Yeah, so how does this man spell his name? Thr- …

KNOWLES: T-H-R-O-D-A-H-L. He was the vice president in charge of research at that time.

GRAYSON: OK. So, you kind of faked that to get the publication out.

KNOWLES: Well, I faked the little announcement there but not much. Then, the other place that I got to go was to give a talk at the New York Academy of Sciences, which doesn't require much of an abstract - not as demanding as the other places. And, they get our sort of a publication, which isn't as demanding. So, I could slip that by the patent department.

GRAYSON: So, over this period of time was the evolution of this catalyst.

KNOWLES: Yeah, we wanted to get some publication out and I could do that into these type of places, which aren't normal for coming out with news. I couldn't get into the *JACS (Journal of the American Chemical Society*) quickly. We were unable to get that because we hadn't published it for them with considerable details. These other places didn't require any experimental like, you know, the New York Academy of Sciences.

GRAYSON: So, your interest here was to get the idea out ahead of other people.

KNOWLES: Yes.

GRAYSON: But, still you had to kind of circumvent the patent department.

KNOWLES: That's right. It's difficult. In the mean time, there were as many as five others who had done similar things and most of them didn't get good results and quit. And, through no particular wisdom on our part, we'd chosen a better starting place. But, Morrison did it by putting a side chain on the thing and he got 15% or something. Nothing special. And, then, over in France -- and this was the first real publication came out; Kagan did this with the one based on tartaric acid. And he was getting exactly similar results to ours. Our original one (catalyst) we called camp, C-A-M-P. And, his was called DIOP, D-I-O-P. Kagan came out with his and he got a communication out a little faster than we did because he was in a university.

GRAYSON: How do you spell his last name?

KNOWLES: K-A-G-A-N. But, he didn't know we existed and we didn't know he existed. When we got to 80%, it was sometime like in June and he came out with his in the following winter.

GRAYSON: So, you were busy trying to publish the fact that you were getting these reasonably high yields of the one racemate.

KNOWLES: Yeah, well, there was another thing happening at the same time. It shows how much luck there is. But, it was probably very important. The discovery had been made that L-Dopa was a very good treatment for Parkinson's disease.

GRAYSON: Right.

KNOWLES: But, you had to have only the L isomer. But at the time they started with the DL mixture since it was so difficult to separate the racemate. It took such massive doses that you were feeding the patient a lot of junk that he really didn't need. And, you were worried about what it might do to him 'cause originally they used pretty massive doses to get a beneficial effect. And, so, it looked look like it could be a fairly big business.

GRAYSON: So, these doses were mixtures of D and L?

KNOWLES: Yeah, this is where vanillin gets into it. Monsanto was in the custom manufacturing business. And, they were custom manufacturing an intermediate for this L-Dopa. And, the intermediate was starting with vanillin. Their motivation was, they told Roche. Roche wanted to just buy our vanillin. And, we said, "We want more of the act. We've got some idle capacity." So, they made this advanced intermediate with Roche's process. And, they were doing this in the Queeny plant. Now we weren't even supposed to even know about this but we learned about it. And, we found out that we didn't get good results with our synthesis with simple olefins. We had to do what turned out to be the intermediate in this synthesis, which is in organic syntheses. Pretty standard synthesis called the Erlenmeyer az-lactone synthesis. It's on page one, collective volume three. That olefin worked much better for our kind of synthesis … for our hydrogenations, than anything else. So, we had gone over -- I should have said it earlier – to use the ene-amide intermediate. We could make it either from the vanillin derivative, which would be dihydroxy phenylanaline, which would just be phenyl, so benzaldehyde. So, I went out and tried to find out what was going on in the Queeny plant because the patent department said well, it was just a secret process. Roche has told us that. And, so we can't tell you what's going on. And, I said, "Well, I believe I know what's going on and I had Organic Syntheses, which is the standard checked out synthesis for organic chemistry." They take the literature and somebody, some professor, confirms that it works. Well, on page one of collective volume three, Erlenmeyer's az-lactone synthesis, with benzaldehyde and, I said, "Is this what they're doing?" And, the guy says, "You mean I signed all these secrecy agreements for something in the public domain?" I said, "You did." Well,

then, he was a little more cooperative. But, so much for the secrecies. It's a funny thing sometimes. The less you have to hide, the more secretive you become!

GRAYSON: Well, I mean there were using something everybody else knew. They just didn't want anybody else to know it.

KNOWLES: I think that's what it is exactly. But, whatever it is, in the Roche intermediate, we could take it and get 80%. And, coupled with it, our separations were very easy in the L-dopa field. We were able to commercialize it. We said let's stop everything and commercialize this. And, that was a very good decision on my part, because no one would criticize me if I hadn't done anything at all and just kept on working in the field. They wouldn't have said boo. But, I said we'll show somebody this work. So, no one really believed it worked. And, there's nobody in the development department or anywhere believed we had any more than just some laboratory gimmick -- just go away. No one really believed it. But, then, we decided to run a 50-gallon scale in the pilot plant. Incidentally, that reactor was poisoned but these things don't poison. These type of catalysts have different poisons. They poison but they don't poison with sulfur. And, as soon as we ran the 50-gallon scale, they perked up and said, well, gee, maybe you have something that works. And, it was kind of funny because there were a few people … see we're still in vanillin and we had the starting material.

GRAYSON: Right.

KNOWLES: So, Merck was in talking about vanillin and so forth because it has dihydroxy benzaldehyde. And, it's very hard to make that specifically for it. So, it doesn't take any great brains to say that's what you're going to start with. And, they were really talking and they came into our lab and their people were congratulating us. And, our people were saying, "What for?"

GRAYSON: I was curious.

KNOWLES: That's an interesting point.

GRAYSON: Yeah, so, it's like a prophet is not well-liked in his own country.

KNOWLES: "What are they congratulating you for?"

GRAYSON: When your competitors congratulate you for chemistry that you're doing in your company, and they don't having a clue as to what's going on.

KNOWLES: That's exactly right.

GRAYSON: Wow.

KNOWLES: But, anyhow, in the basic chronology that we can do later if you think … It came out that we were at the 50-gallon scale and came up with this initial communication. And, that was the only proof we had that we beat him because we beat him by six months. That's about what it took for us to get from the laboratory to 50 gallons. And, nobody bothered about it because there wasn't much expense there. You just put on another man or so in the pilot plant. But, then, after that, we have to find a place to make it and then you start spending a little money. We ran into the problem that you talked about, the top brass not being very cognizant of what's going on. I made a chemical and I couldn't get anybody to back the project. I couldn't get anybody for a while and just got turned down. "You could spend your time on something more important than that."

GRAYSON: So, you were trying to sell the brass into going into L-dopa production.

KNOWLES: Yeah.

GRAYSON: And, you got a way to do it except it would be extremely efficient and profitable.

KNOWLES: Put the other out of business.

GRAYSON: But, they weren't interested

KNOWLES: They didn't understand it. That was the problem. And, then, finally, a guy named Al Heininger was head of a fine chemicals group. He was I a vice president. And, 'cause he had a background in chemistry and he understood it. He'd been involved in the custom manufacturer that Roche was doing all along. And, so, he finally backed it.

GRAYSON: So, how does he spell his name?

KNOWLES: Heininger, H-E-I-N-I-N-G-E-R. He backed it.

GRAYSON: So, you finally found somebody that had enough chemistry background to appreciate the significance of your work.

KNOWLES: Well, that's what you've got to do in a big corporation. You're not welcome with open arms for discovery. It's a fact of life. It changes their way of doing things. They've got all the plans and everything. So when you come up with something new it changes their plans.

GRAYSON: It's not in my plan so that messes up my applecart.

KNOWLES: It happens that way.

GRAYSON: Oh, yeah.

KNOWLES: And, even it happened a little bit with Monsanto's product, Round Up, which is the biggest discovery they ever made in their labs. It happened to be John Franz who did that. He was a little taken aback when he came up with that. And, they said, "What do we want this stuff for?"

GRAYSON: Yeah.

KNOWLES: That's the first attitude but then they finally …

GRAYSON: How do you spell his name?

KNOWLES: Well, Franz, F-R-A-N-Z. he was the inventor of Round Up. That happens a little bit … He's got something in Chemical Heritage.

GRAYSON: Yeah, so, you've got this high performance, 'stable' chemist working for you and he comes up with something and they say -- go away. I'm not interested.

KNOWLES: It's easier to have him come up and say, "You're doing it the right way and there isn't any better way to do it." That's what management likes 'cause the business man likes to deal

with the marketplace and stuff like that. He doesn't like to deal with real change 'cause it upsets everything. That was what I ran into with the hydrogenation thing. It was pretty obvious what to do but it just upset their plans. They had all these scheduled plans and they had groups, which were skilled in hydrogenation and running those damn autoclaves. And, it took a lot of stuff to do it and it takes a lot to get that to work.

GRAYSON: Yeah, it looks like a steamship heading in one direction and you've got to change course.

KNOWLES: Take a new course, that's right.

GRAYSON: So, if I understand this correctly, you certainly knew that what you were doing was this asymmetric hydrogenation was important and something that needed to be in the literature?

KNOWLES: Yes.

GRAYSON: And, you wanted to make sure that you got it in the literature?

KNOWLES: That's right.

GRAYSON: But, the patent department is over here saying …

KNOWLES: Well, yeah, they would say, "Wait a minute. You've got to at least file a case before you can do that."

GRAYSON: OK.

KNOWLES: And, they held up the Round Up for a long time because that was very important to them. This was not important to them. The only reason I got by with it was because it was a side issue.

GRAYSON: So, as far as they were concerned, it was an insignificant development?

KNOWLES: Yeah.

GRAYSON: But, they still had to get their patent control?

KNOWLES: Yeah, oh, yeah. And, once the patent department got into it, they were thrilled with the opportunity because it was a unique filing. Most of the stuff is just a little better way to plasticize vinyl or something. And, you go on endless, infinitum, with little minute changes but this was a breakthrough. And, they patented the wrong thing. They just patented the use of a chiral phosphine. All chiral phosphines don't work. Only very special ones do but they didn't look at it that way at all. And, they said, "Oh, you guys will find the right one."

GRAYSON: So, they do have technically competent people in the patent department to look at these things and understand the chemistry?

KNOWLES: Oh, yeah.

GRAYSON: At least the patent department does.

KNOWLES: They did. I don't know if they do now. Because, they may have canned all those people. I don't know whether they've got 'em now because that's a different ballpark. But, … they must have. They had competent people that knew enough chemistry to proceed and we had a very competent guy do this. One of the things he was able to do on this one was change the original disclosure. The original disclosure was on that 15%. And, you usually only get in a patent, the claims. You don't get any more claims than you make in the first application. They chop off things. You can have three, you can have five, you can have six but you can't add anymore after you once say it. But, the patent department sold his point. It's the only time he ever did it. This is a pioneering invention and he didn't know what to claim in the beginning. He was able to add more claims; he got a whole bunch of claims.

GRAYSON: You really had to broaden the claims at the beginning.

KNOWLES: Yeah, they broadened it as much as they possible can because they can't get any more. And, this was a unique case. He was able to convince the guy that he could do more. This didn't make a lot of money for Monsanto, it made some but not a lot. But the fact that we commercialized it so quickly attracted the Swedish Academy. Because most of the things that they talk about don't get commercialized that fast and it turns out that if we hadn't done that commercialization, we'd have never been heard of.

GRAYSON: Mm-hmm. So, it would have been a neat trick in the literature and that would have been the end of it.

KNOWLES: That would have been the end of it and the Nobel prize would have gone to Kagan and Noyori and Sharpless. Now, that's another thing that happened. This thing got pretty well recognized in the 70's. And, everybody found out that yes we do it with an improved phosphine later that gave 95% efficiency. And, everybody else found there were maybe 100 phosphines that could do the same damn job about the same efficiency; what we call precursors for alpha amino acids and nothing else. That's where it sat the end of the 70's. Now, remember, who was sitting on the stage watching us do all these thing, but was hesitant to make phosphines. I don't know, just picking on Noyori, but he wasn't a synthetic chemist. And, he didn't think it was worth the trouble to make phosphines. And, he was at Harvard at the time with Osborne, who supposedly did invent the Wilkinson thing. The thing was all sitting on the platter there for them to do first. But, they didn't want to bother to do the synthetic work. It was sloppy, dirty chemistry to make those phosphines..

GRAYSON: So, this Sabacky fellow was the guy that got the job.

KNOWLES: He got the job and well then Vineyard came in with me later. We weren't getting too far. And, he had nothing to do with this type of chemistry at all. But, he came in and said, "You need to study the mechanism." And, we did a little bit and found out what the stoichiometry was and phosphine and phosphorous and all that stuff -- made a little sense out of the project. But, we were wise to go ahead and commercialize it with this not too good catalyst; but good enough for that kind of pharmaceutical; because of the fantastic properties of L-dopa to crystallize so readily. We were gonna do that and then a number of phosphines were made during the period of the 70's by all kinds of people and the deal sorta stalled. I pointed that out in this final write up, the deal stalled until Noyori came along and made a very difficult to make phosphine. I don't know why it took so long; he says it took him four years to make it. But, he was doing it with slave labor, I mean, graduate students in Japan – he called it Binaph, B-I-N-A-P-H and that turned out to be a leap forward in the field. It could be applied with another metal. We knew ruthenium was in the act. We tried to use things with ruthenium but we weren't doing any good. We'd get hydrogenation, but we didn't get good results. But, Binaph did great results with ruthenium. So they ended up exploiting the field and it burst wide open in the 80's and 90's and the Japanese commercialized it into a menthol process, a large scale menthol from about 1980-82, something like that. About 10 years after dopa. So, we were first to do the initial prototype by a month; then by about six months on the first good catalyst; and finally, by about 10 years on the commercialization. And, I got the usual awards. Probably the most elegant was the creative invention award from ACS. (American Chemical Society) And, that was in '82 or something. We went to Las Vegas and got that. And, there was a local company had an award that I got. Then, we were pretty much forgotten. But, there was one award from a catalyst group in '95. In the

meantime, Sharpless had applied these kind of reactions, catalytic reactions to oxidations. Not as beautiful and efficient as hydrogenation, but making much more difficult things. And, Sharpless said he was inspired by us. I think that's a fact. 'Cause he stated that in his Nobel lecture. And, that was his first spur to drive on with the thing. And, Noyori exploited the field with a very large amount of graduate school labor. He did explore all kinds of structures that we weren't effective on; but mostly using his baby Binaph. Which is, by his own admission, kind of hard to make. So the Nobel thing sort of came along a lot later. And, I think the first guy they decided they were gonna give it to was Sharpless and then they decided, "Look, we've got Noyori," but there was a Wolf Prize. You know that one? It's an Israeli prize.

GRAYSON: No.

KNOWLES: It has a fairly big stipend. $100,000.00 or something like that. And, that went to Sharpless, Noyori and Kagan. That was the winner of 2001. Remember they got the prize in 2001. That went to them in the winter. The Monsanto community were fuming. Said, "Well, we did that first." [laughter] And, the prizes are all about being first. But, I didn't pay much attention to it and I'm not sure how the sequence got done. And, I'm never gonna know because they (Nobel Committee) don't open their books. But, at least the sequence as I know it, there's Corey and Jacobsen at Harvard wanted to set the historical record correct. In 1995 Monsanto was sold to Pfizer, you know?

GRAYSON: Mm-hmm.

KNOWLES: And, Corey's a consultant for Pfizer and there's a John Talley that was with us. And, I don't know that he had any influence or not. He said this was worthwhile a thing to Corey. And, we did it first. And, this interested Corey anyhow.

GRAYSON: How do you spell Corey?

KNOWLES: C-O-R-E-Y. He used to be at Illinois. And, then he was at Harvard. And, he's still at Harvard. I don't know him well; I've corresponded with him on phosphines. This is the kind of field that he was working in a bit. And, he did it in a very complicated manner which wasn't practical. But anyhow he was very interested in making phosphines. And, I helped him a little bit on that -- back in '84. But, he called me in the spring of 2001 saying he'd like to get some information for his files. He was getting together the chronology of this and so forth. And, so I sent him what I had about making the thing and so forth. And, I had some inkling -- and Talley said, well, he'd put him up to that more or less.

GRAYSON: Talley is spelled?

KNOWLES: But, he'd done a lot of exploiting with the catalysts and made a lot of chemicals for testing that you wouldn't have bothered to make otherwise. But this is so easy to do that he did it.

GRAYSON: How do you spell his last name?

KNOWLES: T-A-L-L-E-Y. He isn't with Monsanto anymore. I forget where he went. So, that went on and then I did hear from a guy from the Swedish Academy. And, he said he was doing a review article in the field for the Swedish audience, and he wanted some CV data -- that's all. So, I sent it to him. I don't know, sometimes you don't really know. This was in the spring and I pretty much forgot all about it. He said he'd send me a reprint when they wrote it up, but it was going to be in Swedish. It was really for the local audience. This is not an unknown thing in these little countries that have a lot of research. Per Ahlberg – he was doing that. And, so anyhow, I didn't hear about anything until a phone call really. Per Ahlberg said they decided by winter that it was gonna be me. But, doesn't make sense to put Corey in there 'cause they didn't do anything till spring. So, I don't know how the situation works. But, the thing is that the Wolf Prize came out in January and that was for Noyori and Kagan and Sharpless -- this discovery was made completely unbeknownst to me.

GRAYSON: So, do you have any at all suspicion or sense that there's this consideration going on about the prize for your work? I mean, prior to it, did you have any inkling of it at all?

KNOWLES: Not too much. I heard, after the fact, I heard some things. But, I didn't really get much inkling prior to the award. I mean, there were those two things. So, at least I knew in the back of my mind, I might have been on the panel to be considered. And, that's all I knew. But, you see the dilemma was that the actual publication -- it's about who's first. I mean, if I hadn't existed, the field would have been in the same place because Kagan came along and did it and he would have done it a little differently.
[phone ringing]

KNOWLES: I'll get that. I don't know, is my wife went out or not?

GRAYSON: No, she came back, I think.

[END OF AUDIO, FILE 1.3]

KNOWLES: Well, I didn't get too much from that.

GRAYSON: So what happens? Usually they call you first thing in the morning here, so it's what, 5:00 in the morning?

KNOWLES: Exactly, 4:00.

GRAYSON: 4:00. Boy, you get a phone call….

KNOWLES: Well, they have a meeting. They have a final meeting at 9:00 there.

GRAYSON: So you get a phone call at 4:00 in the morning.

KNOWLES: Yeah, they tell you that.

GRAYSON: So what do you think when the phone's ringing at 4:00 in the morning? Usually it's a wrong number.

KNOWLES: Well, you get up and answer, and they immediately explain who they are and they make sure that you don't think it's a crank call, because they'd get two guys to talk. Yeah, one guy says that you have won the prize, and then he says, "I'm gonna turn you over to so-and-so," and he talks it too.

GRAYSON: Oh, so they didn't want anybody behaving like they were….

KNOWLES: There are prank calls, because university people, I mean Noyori actually was expecting the thing. He said he had the paper already signed and everything, and it didn't come the previous year.

GRAYSON: Oh wow, so he figured he was in.

KNOWLES: Anyway, in academia they know more about what's going on. I didn't.

GRAYSON: So was your reaction then?

KNOWLES: Well, pretty complete surprise.

GRAYSON: So that was a really pretty exciting thing to happen.

KNOWLES: Yeah, it is the most exciting thing that ever happened to me.

GRAYSON: So this was – how long had you been retired from Monsanto then?

KNOWLES: Oh, '86. Yeah, and pretty much what we'd done there had quieted down.

GRAYSON: Sure.

KNOWLES: There was this one thing in '95, but other than that -- and I had consulted a little bit with Monsanto, and there was some activity there, but they weren't really fascinated with this particular field. The only application was amino acids and naproxen…. these NSAID type alpha aryl acrylics that the pharmaceutical people make for aspirin-like activity. They call them NSAIDs and certainly this kind of synthesis could be used as a way to make naproxen, which is a natural derivative and one of our people was interested in working on that. He didn't get too far along, with it. I don't really know whether naproxen's made this way or not. It can be made this way. It may be. They're doing pretty well with it. It's Aleve, you know. They advertise it a lot, and so it could easily be using this technique.

GRAYSON: I guess….did you just have to sit down after that, or fall down, or….

KNOWLES: They told you not to go to sleep again because you'd immediately get phone calls from the press and everything.

GRAYSON: Wow, so then you get noticed right away.

KNOWLES: You get noticed right away; but the main thing is at Monsanto, remember, we were going through a lot of attrition, so they called Monsanto, and then Monsanto said, "Who's he?" Well, because they were all over the Ag (Agricultural) Division. They didn't know me and then they finally found somebody in the personnel department, Gary Barton, that knew me and he hightailed it over to my house; but it's perfectly reasonable that they had forgotten all about me.

GRAYSON: Sure. This was work done what, 25, 30 years earlier almost.

KNOWLES: That's right, but that's pretty much true with Nobel prizes. They're not very timely. Five or six years is very common. It's pretty hard to do it less than that. The Watson Crick thing was six years, I think, and Woodward was quite a while too. I didn't know that somebody had put me up in 1990 -- he sent me a copy of the thing. It's very easy to put somebody up. You don't have to have a lot of stuff. All he had to do was send in a copy of that Accounts of Chemical Research article I wrote which adds up everything. That makes a nice place to get all the references.

GRAYSON: Right, because everything's there.

KNOWLES: And he just had that one page and that's all that I think Per Ahlberg had. They don't really require an elaborate nomination. Most prizes do, you know? You have to write all the stuff like you'll get in here. They do the digging through others, and they have professors around, and I'm just not sure what went on and Per Ahlberg just told me the timing. He thought I was decided the winner, which doesn't make sense with the Correy contact, and so I'm not sure what's up. The Wolf Prize went differently, and the Kagan people were….. He's a very nice guy. I've known him for years and he's visited us. I haven't seen him much this century, but I probably used to see him once a year or so, and he came over to the company and so forth, and he was definitely an early pioneer. He did it without chirality on the phosphine. He did it with a chiral carbon backbone, which became the way that most ligands are made now.

GRAYSON: I know that being first counts a lot, 'cause there's a controversy in the mass spec field about the prize. I think it was maybe the following year it went to Koichi Tanaka for the development of matrix assisted desorption ionization. What he had done was show the very first mass spec by this method on a large molecule, I think 100,000 molecular weight or so. Whereas there's a group in Germany that had been pursuing the same objective in a very precise, careful, logical step by step way. And most the people in the mass spec field feel that this group in Germany should've gotten the acknowledgement for that, but Tanaka published a paper that was in press first. The reality of it is nobody uses Tanaka's method today. The one that the Germans developed is used today, so being first is really important.

KNOWLES: Well, this whole Nobel thing is about being first. DNA is a famous one where it would've been discovered in two or three months by somebody else, but these guys did it. You might've read the *Double Helix*. They did it mostly with models and things, but it took somebody to get the right pictures, but they recognized the significance of the pictures. That was important. The electron microscope is just like you described. That came out, there were two guys….three guys got it, but there were two guys in the middle '80s who got it, and I suppose it was quite a little while before they did their work, and they didn't notice that the guy who had the first prototype was a guy named Ruska back in 1932, and he made one, but he never did anything with it, but he had made the prototype. He was in Germany, but they recognized that, and they gave it to the three of them, but usually there's somebody left out. I have a book on it. I read a lot about it since it happened, and they said they don't make many mistakes. They did find a mistake they thought they made, but they don't make many, but they do leave out people, mistakes of omission.

GRAYSON: Give it to somebody that doesn't deserve it.

KNOWLES: They said there was one Swedish guy that had done something for stabilizing silage, but it didn't work except for Swedish silage or something like that. Their books are open from 1950 back. This book was on the Nobel deliberations, and they went into Einstein, and they went into why Mendeleev got left out. It was fascinating reading through that, but I think that it has to be about being first. It's something in society that accepts that immediately. If you're the first to climb Everest, who's the second? You don't know.

GRAYSON: Yeah, right [laughter].

KNOWLES: And he may have just as tough a job, but mountain climbing is the worst. But science at least pays off the guys running second a little bit.

GRAYSON: There's a book by this guy that did *The Road to Stockholm.* I don't know if you've read that one.

KNOWLES: Yes, I've got that. I've got that book. Yeah, there's an awful lot of things there, but it's amazing that the Nobel Prize trumps all other prizes. One guy told me, he says, "You've got the one that trumps all other prizes," and it doesn't make any difference what it is. This is the only one that crosses into the arts and everything else. I could paint a picture and get the top prize in that. They'd say fine, you'd have your dinner, and go on with your life. But it doesn't carry over after that. The Nobel Prize doesn't leave you the rest of your life.

GRAYSON: Yeah, there's something it; it's just recognized by everyone. It doesn't matter who you are.

KNOWLES: It's the only prize I can think of that's recognized by everyone.

GRAYSON: Whether you're a carpenter or a high powered executive, or you're an airline pilot, or you're a housewife, Nobel Prize, bang.

KNOWLES: That's right.

GRAYSON: Everybody understands what it means.

KNOWLES: We came back from Sweden and we couldn't make an earlier flight because we didn't know if we'd make it exactly on time, and so we had three hours waiting. Oh, those porters knew all about it. Just show us the medal they put us through security in the front of the plane; just bypassed security and just put us through right on the plane.

GRAYSON: Oh, wow. Just whip that sucker out.

KNOWLES: Show us the medal. No, that's the only prize I can think of that doesn't make any difference. I mean even the Congressional Medal of Honor and so forth, I mean they're great and you have a White House reception and all that. This had a White House reception.

GRAYSON: Oh, really? Okay.

KNOWLES: Yes, we did. Some of them didn't go. I think it was stupid not to go. We went. That was before we went to Sweden. I thought it would've been stupid not to go. It was after 9/11. The place was closed for tourists, but the Swedish Embassy had a very, very nice affair. They had a special dinner for us. They always do that, and that was separate from the White House thing.

GRAYSON: So how long did that kind of celebrity round last? A couple of months, a couple of…a year or what?

KNOWLES: Well, it's never dead. The autograph people….I don't get many. Last year, I'd get maybe a dozen requests for autographs, mostly from Germany. Germany is great on asking for autographs, little old ladies in Germany collecting autographs. In fact, my grandson was surfing the Internet and found out there's a market for these autographs. Mine was $10.00. I don't know where he found that, but he found somewhere that they collect autographs and then they sell collections or sell individual ones so you can get more in your case than others. I'd say that you usually get a stamped envelope, and they just want your signature, or your picture if you've got one. But it's mostly Germany; there's more of a tradition of science there than in most countries.

GRAYSON: But you had gotten recognition prior to the Nobel Prize.

KNOWLES: The interesting part is there was this news item in C&E News. They didn't really do their homework, looking back, because this guy started off his article saying "William Who?" It was a priceless article in C&E news [laughter]. Because he didn't recognize all these other awards. I mean they were very nice things with an award dinner, but people forget it immediately. Oh, you may get on a list of the previous winners so the next year I guess one looks to see who's been there before, but it doesn't affect your whole life. This affects your whole life. And it doesn't stop.

GRAYSON: Yes, well, that's why I am here [laughter].

KNOWLES: Well, I had a conflict today.

GRAYSON: Oh, really?

KNOWLES: A guy wanted me to meet somebody from McCaskill's office today. They're trying to set up a panel to get some science….sense out of science in Missouri.

GRAYSON: Oh, Claire McCaskill, yeah. (Junior Senator from Missouri)

KNOWLES: They wanted to know whether I wanted to sit on the panel, but I couldn't do it today. I don't know, but I kinda shudder at that, but you can cash in on it. Of course, Noyori is younger, he cashed in on it, and he's gotten the top job at Riken Institute. That would be the top research institute -- the Max Planck of Japan.

GRAYSON: Well, it gives you some credibility in your organization.

KNOWLES: Yeah, well Monsanto's mixed up because they didn't exist in 2001. The Monsanto name is gone. First it was Pharmacia bought Monsanto, and then Pfizer bought Pharmacia, and so the Monsanto name was zilch, and one of the executives wrote me and said, "It's too bad the company's gone. We'd celebrate." They put a plaque up finally. The president of Monsanto did put a plaque in front of one of their buildings, but they included in it -- and I'm very happy they did – Sabacky and Vineyard. Which is good because they did the hard part in my opinion.

GRAYSON: Yeah, I was curious about that, I had seen those names in the literature.

KNOWLES: It was a joint effort in the lab. I did start it. There's no question about that, but I couldn't have finished it without both Sabacky and Vineyard

GRAYSON: What about this fellow, Weinkauff?

KNOWLES: Weinkauff?

GRAYSON: Yeah.

KNOWLES: Oh, he's an executive I worked with a lot back in the '50s on the cortisone thing. I love Weinkauff. He was a character. His quaint expressions still remain. We were evaluating projects. He says, "Don't ever look up a dead horse's ass [laughter]."

GRAYSON: Okay.

KNOWLES: I love him in that kind of respect. Woodward, I remember, didn't get to cortisone. We did get to cortisone in the fifties here. We actually made a sample, probably 100 mg of racemic cortisone or something like that. But we used diazomethane to get there, which would've been out of the question, but nevertheless. I don't think anyone wants to commercialize diazomethane.

GRAYSON: So in the New York Academy of Sciences, were you a member of the Academy?

KNOWLES: No, I used that because it was an easy place to publish. That's why I did that, and so I had several things there, and the other place that you could do it readily was the Gordon

Conferences which don't require much of an abstract. They didn't care what you say. It's what you write.

GRAYSON: Right, exactly.

KNOWLES: One thing we feel bad about, we could've written an article for JACS that would've been a classic paper. They occasionally have classic papers and Henri Kagan did that. He wrote the classic paper 'cause he could do it in the academic environment. We couldn't get it out fast enough. A full paper takes too much scrutiny.

GRAYSON: Inside the industrial setting.

KNOWLES: Yeah, that is one of the difficulties, and it's always gonna be in industry. The only other advantage of industry is that you can sometimes see results of your efforts used. I didn't push phenylalanine hard enough. That was another thing I kind of regret. Phenylalanine is a way to make the sweetener aspartame, but you start with benzaldehyde, and that's the key. Benzaldehyde is only used in perfumes. It's expensive, but it didn't need to be expensive. It could be made by oxidation of toluene. The chemistry isn't all there, and in fact the phenylalanine is a much bigger volume thing, but I regret that I didn't push that hard enough. There's a sweetener that's based on that, 'Equal' or aspartame, and they make that by fermentation of glucose, which is fine, but it took them years to do it, whereas this could be done much faster. And aspartame's been made with phenylalanine. It's made by this technique, but we didn't do it. The Italians did and I don't know what they're doing now, but I do know that one of the drawbacks in phenylalanine is that the separations aren't as clean. It forms a DL compound, and doesn't separate out as readily, whereas with 80% of yield you get 80% -- out in hand. But with phenylalanine, you only get about 60% out quickly. You can get the rest, but it's hard to get out. And even 95% is kind of bad, but now they have 100% catalysts, so they report. The guy in DuPont came along '93 or so with Burke, and he came up with a phosphines the same as an enzyme. Now he claims 100%. Whether he's precisely 100% or 99%, but from a factory point of view….now you wouldn't give the time of day to a catalyst that wasn't almost 100%. I think one of the significant features that came out when I wrote this with Noyori, is the resurgence in this century of activity in this field. Perhaps there isn't a week that goes by at Merck that somebody doesn't run asymmetric hydrogenation in their labs, because all pharmaceuticals are chiral now. Either they are making the starting materials, or the finished goods, or something. Usually if you can make them with hydrogen, you're gonna make them with hydrogen, 'cause that's the simplest.

GRAYSON: Sure.

KNOWLES: It isn't like Barry Sharpless's stuff. He can make exotic things, but you won't do it unless you have to.

GRAYSON: Right.

KNOWLES: This one you will try to, and the reason this is so easy is because of the lab supply houses. You don't have to make your phosphines anymore.

GRAYSON: I see.

KNOWLES: I can show you my files. Sigma Aldrich has structures we wouldn't even dare attempt. Some professor has a few students in Pennsylvania; I think it was University of Pennsylvania, and they need a nice Ph.D. problem. You get a good phosphine and it's hard as hell to make. You don't have to make very much of it for the lab supply houses. You buy a half a gram, they're so active. You see these things, back to our old adage, our activities are fantastic. We used, in our plant, 20,000 to one and that's almost throwaway.

GRAYSON: Yeah.

KNOWLES: I could go back and we aren't running the plant anymore. We're out of that field, but I could go back and do 100,000 to one. Noyori found a case….I think it was almost two million to one.

GRAYSON: That's amazing.

KNOWLES: Yeah, that's because it's molecularly dispersed. See, that's the difference on the carrier. You're only getting the catalytic action on the surface. You're talking molecules here. With heterogenous catalysis you have just as active catalysts, but you're only using about one percent of your palladium if that much.

GRAYSON: Yeah.

KNOWLES: Maybe less. Maybe it's a hundredth of a percent of the palladium is being used during a really catalytic job.

GRAYSON: So it's just not the catalyst, but the fact that it's a homogenous catalyst.

KNOWLES: The homogenous catalyst is molecularly dispersed, and that makes all the difference. Enzymes! Nature uses homogenous catalysts. They're all over. So that approaches about as fast an enzyme as you can get. Using a complex catalyst at a million to one, there's a commercial process for making an herbicide dual. That's the biggest scale one I dug up, an herbicide based on diethylaniline and choracetamide. We had one. We called it Lasso. A German variant and it has a chiral center, and they don't get a very good result, but they've got an iridium ferrocene complex and it gives them about 60% to 70%, and they can sell that mixture, but there's only one isomer that's active. Instead of selling a 50/50 mixture, they up their activity -- almost doubled, and so you can cut down the pounds per acre. Now they say it's commercial and I don't know how well they've done it, but that would be the biggest scale commercial thing. I know the takasago menthol is a pretty big volume product; relative to L-dopa.

GRAYSON: So most of this is stuff from your publications and literature. Did you present any of this at the scientific conferences, the ACS meetings, or anything like that?

KNOWLES: Yeah, I did. I went to quite a few conferences and did that.

GRAYSON: How was this type of stuff received in your sessions, the chemistry, the showings?

KNOWLES: Well, there was extreme interest in the '70s in it, and probably the most interest was when we didn't have much out. I think it was just before Kagan had published. We went to a conference in Laboule, France. The family went too. It was a very nice conference on asymmetric synthesis but we weren't on the invited list; neither Kagan or I. A number of people presented things, and they were getting 20%, 15%, and they would say, "Well, if they made the one group a little bigger, that'd come out 20% instead of 15%," so they were getting a gain. Mislow was there, and he was very caustic, he got up and showed the energy differences, and how trivial it would be to get from 20% to 25%, since it's only two kilocalories to get 90%. So he just said, "Anybody who tells me in any speculation as to what's making them go is indulging in pure fantasy." He sat down, but then at the end of the conference. We were asked to say a few words, and we each said we were at 60% or something like that, and that was of extreme interest at that time.

GRAYSON: So you weren't actually giving a paper.

KNOWLES: No, we weren't invited to give a paper.

GRAYSON: But they knew you were working in the field. And they wanted to know what you were doing.

KNOWLES: But then they found out our results, and so they on the last night they had us give a fifteen minute talk. So we gave out our results, which was kind of a thrill, because it was putting us on the program when we were the only ones that had anything….the only ones.

GRAYSON: The invited speakers were low balling, or getting lowball numbers, and here you guys weren't even invited and you were doing much better than they were.

KNOWLES: That's right.

GRAYSON: Wow.

KNOWLES: Well, we got involved in a number of conferences and things.

GRAYSON: Was the company pretty liberal about letting you go to conferences?

KNOWLES: They weren't too bad. They were OK on that. Where they balk is when they have to put lots of money in. They like exploratory research. That doesn't cost very much. It's when you have to make a process out of it. It's an awful lot of competition putting that L-Dopa on the market. You have to have a special file, and one guy's full time on that, just to get it all in. I think there's a master file you have to get for a pharmaceutical, and there's so much red tape getting the thing going, and then we had to adapt it to the saccharin plant, which became available at the right time, actually. We had to do that, and it was a lot of other little things. Monsanto got out of saccharin at that time. It was a combination of a lot of things coming together, so we were able to adapt the saccharin plant. Now the saccharin plant had lead reactors that were really using almost cleaning solution; not very much different than cleaning solution, sulfuric and nitric acids or something like that. Saccharin's a pretty stable compound. But the basic reactors aren't most of the plant, most of the plant is for fine chemicals, crystallizers and fillers and all that, so we could use all that.

GRAYSON: So were you really involved in the plant conversion?

KNOWLES: Yeah, and I was involved with the engineers, and my people were. We added more people at that time, and Vineyard was very much involved in it. Getting the plant started was most of the year. Most of the problems, it's interesting, weren't with the hydrogenation process.

GRAYSON: It was everything else.

KNOWLES: Never had a glitch. We've never had a hydrogenation with a glitch. We ran maybe 15 years and it doesn't show in those nitro reductions that I was talking about earlier. They often….not often, but frequently poisoned for some reason or another, and you've gotta re-catalyze, and start over again, or do something, but this one never had a batch that wouldn't go. One event was when Bill Sherman ran our first large scale batch in a thousand gallon reactor, which is a big reactor. That's commercial size. We were doing fifty in the pilot plant. Well, Sherman was doing the night shift for me on that, and we started it off, and we put in an amount of catalyst based on what we had to use for the pilot plant, which was, as it turned out, way too much, but we put it in. He called me, and said, "Well, I started it up," and I said, "Well, it's gonna take you eight hours. You'd better go out and get some dinner and come back, 'cause nothing's gonna be happening much," so he was out getting a bite, and he came back in about an hour and half and he called me and he said, "It's not taking up hydrogen." Well, that's a real problem. I said, "Oh god, what do we do," and I said, "Well, take a sample and let's find out from the UV spectrum how far we've gone." He called me back in half an hour and said, "We're done [laughter]." So it couldn't maintain the hydrogen pressure, it took it up so fast.

GRAYSON: Oh my.

KNOWLES: Well, it just came from a bank of hydrogen cylinders in the truck or something. We had put way too much catalyst in, so we had to cut way back. But it was the first clean system we'd had. We hadn't had it clean -- and clean meant getting the oxygen out of the reactor. Oxygen in air is a poison, and on a small scale in the lab, we had oxygen in most of our hydrogen cylinders. We later learned to pick 'em so they wouldn't ruin the catalysis. Basically, it's a filling error.

GRAYSON: Sure.

KNOWLES: When you cap the cylinder up, you fill it. It's not very much, but you put so little of catalyst in, it is easily poisoned.

GRAYSON: A little bit of oxygen in the catalyst messes it up.

KNOWLES: Oxygen and phosphine oxide -- and peroxide's the same way. Well, on a large scale, you don't even use the dry intermediate. You use a wet intermediate. You don't dry it. You're gonna put it back in water and alcohol again, so you just filter off the intermediate and put it in a hydrogen atmosphere, and so there's no air in the interstices, the crystals, whereas the dry intermediate has a lot of it, and it takes a long time to get it out, and get it all out in the pilot plant. You have to….by venting and filling, venting and filling with nitrogen and hydrogen, and so that was the first time we were clean on a thousand gallon scale.

GRAYSON: Then it went like wham, all the way over to the hydrogenated state.

KNOWLES: It went wham, yeah.

GRAYSON: Wow, crazy.

KNOWLES: It is crazy, but it's a funny experience.

GRAYSON: So the saccharin plant, where was that located?

KNOWLES: Queeny. Yeah, most of the fine chemical things were done at Queeny. That was the basic thing, and the larger volume things were done over at Krummerich. Phenol and the bigger things, but that's how it goes. I think that this resurgence is interesting how this occurred since 2000 in that this is a natural problem. A guy can say find a phosphine that's better than what's out there. He can do that, and they've improved on our errors that way. These are called hindered biphenyls and they've got hindered biphenyls that are adjustable now. Oh, god! But the lab supply houses -- I wish I'd emphasized that more. I didn't think of it. I wrote that in there, but I should've emphasized it more. They played a terrific role, because it isn't easy to do otherwise. Otherwise you have a chiral compound and you have to make your own phosphine -- you're not gonna bother.

GRAYSON: Yeah, so my sense is the thing that makes it work is this catalyst.

KNOWLES: Catalyst, yeah.

GRAYSON: And the synthesis of the catalyst is the rate limiting step in the process.

KNOWLES: Oh yes, that's the limiting step, and you don't do it lightly. But if the lab supply houses have it for purchase, you buy it; sure it costs you $100.00, but that isn't much. You only need a little bit, like a hundredth of a gram -- most labs perhaps use about 2,000 to one. That is typical, but you can go lower than that. These things are active as all hell -- and you can put the metal in yourself or maybe even buy them with the metal, but we actually made a complex with rhodium in it.

GRAYSON: So now while we're mentioning the metal, I was gonna come back to that. The metal is an important part of the package.

KNOWLES: Yes, it's complex with the phosphine.

GRAYSON: So this is the complex of the metal with the phosphine that makes it work.

KNOWLES: Yeah, that's right.

GRAYSON: And then you have to make sure that the substituents on the phosphine are the correct ones.

KNOWLES: Correct structure.

GRAYSON: For your particular synthetic problem.

KNOWLES: And most amino acids, it's general. It doesn't seem to make much difference. Roche went through an awful lot of amino acids, known and unknown, 20 to 30, and they all came out about the same, so the side group doesn't seem to make much difference. You start with the dehydroamino acid, and it comes out the same, so you do get a lot of successful results with a given structure, even though you don't necessarily predict that you would. Enzymes don't do this. There's an enzyme for everything, practically. But these do have quite a bit of versatility; BINAPH does an awful lot of things with ruthenium.

GRAYSON: So now the metal is also part of the picture, though.

KNOWLES: Yes. Oh, the metal is….it won't work without the metal. If a phosphine complex is with the metal in it, then that's your catalyst.

GRAYSON: Okay, but the metal, are you talking about ruthenium, or are there other metals?

KNOWLES: And iridium, and rhodium, yeah.

GRAYSON: So are they rare earths?

KNOWLES: They're noble metals.

GRAYSON: Noble metals.

KNOWLES: Platinum. Platinum's among them, palladium, and all of these are being used today for various kinds of reactions.

GRAYSON: So it's the metal complex with the phosphine, with substituted phosphine that makes it go.

KNOWLES: That's right.

GRAYSON: Okay, but the metal is important. The selection of the metal is also critical.

KNOWLES: Yes, well rhodium is where everyone gets started, but ruthenium is harder, because your compounds don't make as easily, but it seems to be more versatile. Rhodium's been used. Rhodiums are very dear. It's more dear than platinum and palladium, but you use so damn little. That's the thing. But I think the biggest use of the technology is the labor saving device in the laboratory, other than commercially, because it is a labor saving device, and you can make all these chiral molecules without thinking twice. I can make that happen tomorrow. If I bother, maybe it will give me some good or it may not. That's where Noyori made his gain, he had faith to make the BINAPH. We wrote BINAPH on paper. It's too damn hard to make --compared to the things we made. It is. Much harder to make than what we made. And we didn't think it would be that much better, and it isn't with rhodium. It's good with rhodium, but it's sluggish, but with ruthenium, it's a different story.

GRAYSON: So do we really know exactly how these things work?

KNOWLES: Isn't that interesting? Yes, there's a lot of speculation on the thing, but when you really get down to it, we don't know how any chemical reaction works too well. You know what I mean? We have pictures and models, and they're great, useful, but they all have limitations and I'm not sure that we do know. I've speculated and every time I come up with a theory….that's another story because Halpern would also consult with us on our mechanistic study, and he did quite a lot of studies in the mechanism and added quite a lot to it. Jack Halpern, he's at University of Chicago. He's still there. He's perennial in that respect, but he immediately took up work on the mechanism, and he did elucidate it quite a bit where the chiral thing was taking place and so forth, but the exact structure of the transition state in my opinion remains elusive. I'm wondering how many transition states in chemistry do we know exactly, because when we get down to making formal pictures, that isn't what molecules look like probably.

GRAYSON: Right, you'd like to think of them in those terms . . .

KNOWLES: We think of them in terms of the models we draw, but they're not that way, and the thing is that we're talking such tiny energy differences even to get 90% yield. I always pointed out in lectures that you can get 90% yield, which is considered good. But that is only two kilocalories difference between the two possible chiral forms, and hell, that's a rotation barrier in ethane.

GRAYSON: Wow.

KNOWLES: Yeah, put that out in a rotation barrier in ethane, so it's terribly subtle.

GRAYSON: Yes.

KNOWLES: We had the ortho anisyl group. We never made a good thing without it, and no one else has ever found it did any good. I don't think a single venture since then has ever exploited the ortho anisyl group.

GRAYSON: So when you finally got around to making L-Dopa, did Monsanto essentially have the corner on that market for a while?

KNOWLES: Yes. They had the corner on that market for ten, fifteen years, and this is another thing to amuse you about corporations. One time, an engineer, I think his name was Duggan maybe, was going to meet with me. I think it was about 1978 or '79, and he said, "Well, I'm going

to be late for your meeting this morning," and I said, "Well, I'm sorry. I hope you'll be there," and he said, "Actually we're having a celebration in the L-Dopa department for our millionth pound." I guess I (Knowles) didn't get invited [laughter]. Isn't that funny though?

GRAYSON: Yeah.

KNOWLES: Just the way the corporation are. They wouldn't have thought of asking the inventors to come down and have a coffee and a donut.

GRAYSON: Yeah, they probably didn't know who was responsible for that.

KNOWLES: They never realized they were doing a first for a synthesis. Now maybe that's because I didn't publicize it hard enough, but they didn't realize that was the world's first.

GRAYSON: But then also, the fact that it was applied to a compound that was important to treat a disease state made it worthy of the prize.

KNOWLES: That's right. This chiral thing is basic to the origin of life and the life sciences, and I think if this had been an improvement for a way to make nylon, they (Swedish Academy) wouldn't have been very interested. They'd recognize Ziegler-Natta but they were in universities. See what I mean? That's control of polymerization. Monsanto had a new way of making nylon with electrochemistry but they (Swedish Academy) would never have recognized that. Commercially for them (Monsanto), it was much more important, but this had a connection with life sciences I think, and there's no question that the Swedish Academy was attracted by the rapid commercialization. See, 50 gallons would be commercial for them and that's only six months after we got CAMP. I didn't even think of CAMP as a discovery until I wrote up the Nobel lecture, and then I said, "Well, that's the discovery," and then DIPAP which we called the next one which gave better yields. Just pull CAMP out and put DiPAMP in, and it turned out to be easier to make also. That I thought was a real basic discovery, but it really wasn't when you look at it. It was the first breakthrough was CAMP. Everybody nicknames their phosphines, and they all got nicknames, and there's a whole bunch of them out there now. But even academia quit developing phosphines after the '70s. There were five or six people, and we went to meetings, and they all had phosphines that worked well, but nothing further than what we had, just the same, and Kagan tried to exploit it. He didn't make many other catalysts, so he just exploited his DIOP on all kinds of structures, and he was fairly versatile, but not anything like what Noyori came up with.

GRAYSON: So the Nobel committee, they always very succinctly make a statement about what you're getting the prize for, and so they said it was for their work on chirally catalyzed hydrogenation reactions.

KNOWLES: Yes.

GRAYSON: Is that an accurate….

KNOWLES: That's right. See, that's what it was. We didn't invent a process. We invented a chiral hydrogenation which would be applied to L-dopa. Yeah, that's right.

GRAYSON: Okay.

KNOWLES: And somebody wanted to set the history records straight and presumably that was Corey, I don't know.

GRAYSON: You have no idea what happened?

KNOWLES: I'm not sure because of this anomaly with Per Ahlberg. When I was over there, he said, "You're not waiting for that reprint!" But he said it was decided way before, so I'm just not aware of the details. He said in 50 years they'll open up the files and let you know, but that's not very good! They keep it quiet; but I notice that nearly every prize; somebody's left out. Most of the chemical are joint prizes. There are a few that aren't, but usually the ones that aren't joint are something that's been developed over a long course, like E. J. Corey, of productivity in an area. He's an expert, but he probably hadn't invented a lot.

GRAYSON: So is there a downside to this prize thing?

KNOWLES: I don't know. I guess the worst part is if the guy that gets left out. It certainly gets more acclaim, maybe more than it's worth, because of its history. I've read fairly extensively on the history of the prize, and that was the first time anything like that had been done. They got a few from the French chemical society, but it was barely more than a pat on the back. This was the first time that anybody had contemplated this kind of a thing. It really took a lot of doing to get it set up, and it couldn't be done by a big country. It was better done by a small country.

GRAYSON: And so all the proceeds of that come from this money that Nobel invested.

KNOWLES: And they're very cautious with that. I don't know where that's invested. They'll tell you, but they never spend more than their income, so the prize has varied a lot. They first had it in such conservative investments that it wasn't very much. But most of it started to go into stocks. I don't think they divulge their portfolio to anybody.

GRAYSON: I'm pretty sure they don't.

KNOWLES: No, but they're very international, I'm sure.

GRAYSON: I'm not sure I'd wanna be the guy who manages that portfolio either [laughter].

KNOWLES: And they throw such a gallant ceremony too. Nobody equals the ceremony. It's really quite gallant, and they usually have the king and queen, and they do the whole thing up right.

GRAYSON: So how long were you in Stockholm?

KNOWLES: A week over there. Your time is full. You get treated like a VIP, ….a car, and a driver, and an adjutant.

GRAYSON: Oh wow.

KNOWLES: Yeah, and he takes you. He just says, "At 9:30 I'll meet you tomorrow morning, and here's the schedule, and just go." You don't have to do anything but be there in the morning. We went out once on our own to a restaurant in Stockholm this one night. They had a lot of interesting luncheons, it was a high tax area, so they love expense account luncheons. They had a lot of luncheons around town and they were fine. I liked the luncheons better than the big, formal affairs, but a lot of people didn't attend a lot of the luncheons. I attended the luncheons and enjoyed them immensely.

GRAYSON: So I'm just looking here, because I'm sensitive to the industrial chemist kind of situation. I looked at the organizations that you worked for. In 1968, it was Organic Chemicals Division. In 1972, it was Monsanto Industrial Chemicals. Same in '75, then in '77 it was just

Monsanto Company. In ’81, it was Corporate Research Laboratories, and then ’83 it was Monsanto Agricultural Research Division.

KNOWLES: Yeah. A lot of that’s the same thing.

GRAYSON: Sure.

KNOWLES: The Organic Division, Monsanto divides itself in various ways. The original way they had an organic division, and an inorganic division, and a plastics division.

GRAYSON: Okay.

KNOWLES: And that was probably as good a way as they could get, but every once in a while they have a period of troubles. They change the organizations. For instance, the Ag(ricultural) Divisions came our of the Organic Division, and Ag became big with the herbicides. I spent my final years in the Ag. Division doing whatever I really wanted to do. I didn’t get very far on it, but I had a few things going.

GRAYSON: So then Monsanto eventually disappeared into this buyout thing.

KNOWLES: Into Pharmacia, and then into Pfizer, and Pfizer didn’t want the Ag. Division, so that’s what split off into present Monsanto.

GRAYSON: So they split it off and they just call themselves Monsanto.

KNOWLES: But the culture’s pretty much the same. The corporations all have their own culture, and the culture is very much the same. The big feature of the culture is no nepotism. I bet there’s nothing written on paper, but there is no nepotism. You never have the boss’s or department head’s son working for you. You never do, and they adhere to that even though it’s one of those unwritten rules. It’s part of their culture. Queeny’s son was the only one. It stuck, and so if they said they wanted to go into chemistry, they’d go somewhere else. Now on the union level they didn’t care, but on the technical level, they’ve adhered to that. I’ve had friends at Mallinckrodt and it’s terrible if you have one of the Mallinckrodt kids in your lab. He comes in at 10:00, runs a few experiments, and leaves for a golf date or something. You know what I mean? It’s terrible, but that’s exactly what the Mallinckrodt kids did. I play bridge with a Mallinckrodt group, and that’s one thing that I can see from a few Monsanto meetings that I go to occasionally. Otherwise, the

culture's pretty much the same, even though they're in a different field. They do sell one chemical, Round Up, and a few herbicides, but mostly it's modified seeds.

GRAYSON: Yeah, they're getting into this kind of…

KNOWLES: Genetically modified seeds is 's their business, and they're beginning to make some go of it.

GRAYSON: So I know that's getting to be a pretty big area. I heard a duPont person overview their research a talk. They're heading into this area of genetic modification of things to try and improve the crop yields and so on. That's what the Ag. Division, or Monsanto, which used to be the old Agricultural Division, that's what they're up to now, The name lives on in the same field. So, I guess we'll kind of wrap things up. I was wondering if you had any parting words of wisdom -- philosophical thoughts.

KNOWLES: Parting words of wisdom, I always think that industry doesn't do enough of what I call undirected research, exploratory research, and everything is too budgeted. You don't really get any breakthroughs. As I say, 'Round Up' came out of non-budgeted research, and so did most of the significant discoveries. The electrochemical discoveries to make hexamethylene diamine down in Pensacola came out of -- well, it was a little budgeted, but a little more open ended. You put a guy on it, but you don't tell him what the hell to do. He was goal oriented in that case, but I even think don't have it goal oriented. Let the research set the goals -- but I don't think we do enough of that. We can't do it all that way, and everybody admits that. All these big government programs, they're not gonna get any breakthroughs from them at all, because they don't have enough of totally undirected research. All you can do is to take a man and bet on him. That's all you can do and sometimes you're gonna bet wrong. We've had them at Monsanto. It didn't cost much to do this kind of research. The first part of it didn't cost much. To commercialize costs more money, but the initial part doesn't cost much. I don't know what you do on huge, big things like the Department of Energy does, but I suspect that these huge plants for clean burning of coal will amount to nothing. I don't know that, but I suspect that.

GRAYSON: You don't do research that way.

KNOWLES: The basic inventions haven't been made and one that I still worry about is the battery car. The really good battery hasn't been made yet, and I don't know that it's gonna be made by these people in an evolutionary study. They've improved batteries a lot. God, your lead battery acid now, you can go for years and you don't have to buy a new one. But they don't carry much more energy than they ever did per unit weight. The lithium ones are better, but it's very obvious thing that we need a breakthrough invention; but I don't think it's gonna come from the

battery people. I don't know who it's gonna come from. The same holds for these pharmaceutical cures; it may not come by directly looking for a cure for cancer or a cure for this or that disease. It may come from some totally indirect thing. Monsanto hoped L-dopa would come up with some real uses. The only one I can think of, it did cure some kind of very rare breast cancer. It was very good for that. I read about it once, but it was half a dozen cases a year in the country or something like that. When you get a pharmaceutical like that going, then everybody studies it for everything else, and it's a pretty good deal. Is it worthwhile to bench it? There's a pretty good chance somebody will find some other area where it is very effective, and this is happening all the time. I think that was one of the motivations to keep them (Monsanto) in (L-dopa) for a few years. If this happened, and everything busted open, then they'd also move vanillin; which meant that production costs would then be cheaper, because they could operate at capacity rather than 70% or 80% of capacity, and that kept them going. But now they sold those to an entirely different company. That's the main message I can give you is that we have to find ways to do that. Now in a sense, I credit Costas Anagnostopoulos (Research Director) for finding a way to do that in an industrial lab -- using a training function with a senior man, because in a year with a senior man, he learns the ropes a little bit. Then people can go on to something else where they are better able to fit in. That's the main thing, but I haven't got the complete solution and I don't think anyone has, but it's the old story, this government supported research is pretty well directed.

GRAYSON: Yeah.

KNOWLES: You think this (selective hydrogenation) would have been supported [laughter]? I suspect it would not have been. People had done asymmetric synthesis where you have a chiral agent. In some cases you got some fairly good results, but you usually used a chiral reagent rather than a catalyst. They've been doing this for a hundred years, since Pasteur opened up the field, but they weren't getting much product -- and the catalytic process was getting nowhere. The only thing that Akabori work was purely empirical Still, they improved their results, but they never did get anywhere putting some kind of a chiral agent on a heterogeneous catalyst. They tried everything, and put a lot of manpower into it. What I don't know is what motivated Wilkinson to even take his coordination compound and see if it was a catalyst. I don't know what made him do that and I never did find out. I sat with him at a dinner but I didn't ask that question outright. I don't really know what motivated him to do it, 'cause he wasn't looking for a catalyst; he was looking for unique coordination compounds. Ferrocene was his baby, and he collaborated with Woodward on the structure of ferrocene. He was making oddball coordination compounds of all kinds. He may have thought of this as a catalyst. But there weren't any good homogeneous catalysts before that. There were homogeneous catalysts, but not any huge successes.

GRAYSON: So I was just thinking about this when you were talking about Monsanto a bit. Isn't Solutia the old Monsanto.

KNOWLES: Solutia is the old part of Monsanto, yes.

GRAYSON: Okay and they've had their difficulties.

KNOWLES: They've had their difficulties, that's right, and it's not their own making either, much of it. Much of it is on pollution by their forebears.

GRAYSON: Right.

KNOWLES: They got out of the chlorinated biphenyls which is the culprit. Certainly haven't made any since 1970. We were using quite a lot….they were used as plasticizers at one time. But they are just too durable for the environment. I don't think many people have died because of them, or anybody. But it polluted a bit where they made them, Anniston, and they're being clobbered for this. It's like the sins of the fathers are being visited on their sons. It's all biblical, really it is. They haven't done anything (producing chlorinated biphenyls) since 1970 that would be bad. But they probably did something before; but before, they were probably always playing by the rules. The rules weren't there then. That's the problem. And who is to bear those expenses? I don't know. They'd like to find somebody to bear the cost. This is the only way Solutia has to protect themselves from paying it off, and it's probably hurt some people's real estate, and so forth. I don't know, but I don't really think it's quite just to forever hold a guy responsible. There should be some statutes of limitations. There are on everything else except murder, isn't there? And there should be a statute of limitations for Solutia. Love Canal is pretty much the same way, I'm afraid. Maybe we have to collectively put together something to clean it up if that's what's required.

GRAYSON: Yeah, it does seem to be unfair.

KNOWLES: We had Times Beach. That was the most ridiculous one, because there was a nice place with low cost housing for a number of people. They put the stuff on the road, and if they hadn't paved it over, it would've probably dispersed into the environment with the wind and the rain.

GRAYSON: There was the dioxin thing, wasn't it?

KNOWLES: Yeah, dioxin, and dioxin hasn't killed anybody. I went to a lecture Eschenmoser gave on that and he said, "Dioxin hasn't killed anybody. Well, one person. One person was killed. He was shot at a demonstration in Italy," Remember they had that blow off of dioxin at Seveso in Italy? Now, there are bad things. We had that terrible thing in Bhopal in India. So you can't say the chemical industry is completely scot-free of everything. But I feel dioxin isn't one of the

serious problems. It's associated with a side project I was on. We were making herbicide esters in our lab, 2,4,5 T, that sort of thing. We were making esters to see if they could improve the formulations. You could make all kinds of esters. We were doing that in our lab. Quentin Thompson and I, we had a lab full of those damn things, and there's dioxin. We didn't know about dioxin. That was the in mid '50s. We didn't know dioxin existed then. It hadn't been discovered, so I know we had ppms in all those samples we were playing with. Quentin had the most and he's thriving. And benzene is another one. God, they're scared the hell of benzene. We were saturated with it. God, we used benzene. We extracted vanillin out of the reaction mixture with benzene. It was a good solvent. Hydrocarbons weren't good enough. You needed a more powerful solvent, and we extracted it with benzene. We used lots of benzene, and they didn't pay much attention to it. I don't know how many problems they've had. I never heard of anything unusual. I shouldn't be around anyhow!

GRAYSON: A lot of chemists are long-lived, and they work with these bad chemicals.

KNOWLES: I don't think there's any evidence that chemists have shorter lives than any other people.

GRAYSON: No, I'd say some of them, I think, are longer-lived.

KNOWLES: Well, a few. But I don't think there's any statistical evidence that they are short-lived. I've had a friend that died of lung cancer. He didn't smoke and he worked with methyl iodide a lot. They had an acetic acid process that used a rhodium iodide as a catalyst, and he worked out the mechanism, and so he was using large quantities in the acetic acid process. Presumably that was the cause of his lung cancer, because methyl iodide is -- and methylating agents are -- carcinogens, but he never pursued the issue much. He did die of lung cancer, and at an untimely age. I don't really know if for sure that was it, but it's hard when it's 15, 20 years later. It happens.

GRAYSON: I was actually getting an article out of….I think it was *Nature*, to send to my son, and it just so happened that they had a link on this with this World Innovation Foundation, which is right up here, and I noticed your name there, William Knowles, and I was wondering if you were aware of the fact that you're involved with this organization or not?

KNOWLES: Serious foundation. Maybe I signed something. Oh, WIF. Yeah, I signed something.

GRAYSON: World Innovation Foundation.

KNOWLES: I haven't done much with WIF.

GRAYSON: Well, apparently you're on the Board of Directors.

KNOWLES: I'm not too familiar with WIF, but I remember signing some things. They're trying to get cleaner chemistry and so forth, and slow global warming; things that are dear to my heart. They're using my name. I don't know if it's in vain or not.

GRAYSON: Yeah, well, who knows? I don't know.

KNOWLES: What is it?

GRAYSON: It's the kind of thing that Nobel laureates are subject to.

KNOWLES: I know. You get quite a lot of unusual things. I got one from the Chinese press up in Beijing or Shanghai saying, "China has no homegrown Nobel laureates." and what would I do about this? That's a difficult question to answer.

GRAYSON: It sounds like that business that Hargittai wrote about in *The Road to Stockholm.*

KNOWLES: Yeah.

GRAYSON: The fact that there's a bunch of mostly European American (Nobelists), and there's not many from the Asian countries, so it sounds like they're trying to pick up on that.

KNOWLES: I know. Well, there's plenty of non-homegrown Chinese. There's quite a few, but there's no homegrown, and there's been very few Japanese homegrown. There was a group in the late '90s on conducting polymers, and I think that was a Japanese group. There was a lot of pressure on Noyori ('s nomination for the prize), I think. I don't know a thing about it, but I suspect there was national pressure. In Kagan's case, he didn't mind, but the French were very mad. They wrote some scathing articles to the Swedish Academy about this. It was partly justified.

GRAYSON: Yeah, I think it's a similar thing with this Koichi Tanaka fellow on the MALDI that I told you about. Most people in the field think that it should have gone to Hillenkamp and Karas in Germany, the people who were actually doing it. But Tanaka got it, so I know what you're saying.

KNOWLES: I know. I have this book, *The Politics of Excellence*, and I read that. Somebody sent that to me.

GRAYSON: I haven't read that book.

KNOWLES: Well, it's not a very easy, readable book, but it goes into the physics, and it doesn't bother with medicine, just the physics and the chemistry prizes.

GRAYSON: Okay.

KNOWLES: And it had a whole chapter on Einstein, 'cause that was very controversial, and you remember the Swedish chemist Arrhenius.

GRAYSON: Sure.

KNOWLES: He was the first to follow global warming. He's the first one that made calculations in that direction, and he's a great chemist, and he got the Nobel Prize. He was head of the committee for years, 20 years maybe, and he blackballed Mendeleev, because there were no noble gases on his periodic table. Ramsey, I think came up with the noble gases, and therefore made it complete. But because Mendeleev made some scathing remarks about one of his (Arrhenius') papers Arrhenius blackballed him. [laughter]. That came out in this book. And then the Madame Curie thing was fascinating too, of course.

GRAYSON: Yeah, what's the name of this book? *The Politics of Excellence?* Maybe I'll get it.

KNOWLES: I've got a copy if you want it.

GRAYSON: I'd love to read it.

KNOWLES: I've got a copy right here. You don't need to return it very quickly, because I don't think I'll read it again for a long time. It's about the first 50 years of the prize, and it's from the files.

GRAYSON: That's gotta be exciting.

KNOWLES: The book spends a lot of time on the politics of it, but there are really quite a lot of things in it, and it's interesting thing to read about what went on. The Nobel Prize has become famous, and it has quite a history, but there was a political consideration every time, not just once.

GRAYSON: Oh wow.

KNOWLES: Every time, there have been some political considerations, and I guess each year, they release another file from another year. The second 50 years will be a while. Fritz Haber, of course, was very controversial. He came up with poison gases, but he did ammonia synthesis, and so he got it for that. But Madame Curie of course was up and down, and she was one that certainly wasn't recognized in France, until she finally got the prize, and they said, "We do have this person right in our own ranks? " But they never admitted her to the French Chemical Society.

GRAYSON: Well, there's a woman who does….a story-smith on Madame Curie, and the St Louis Section of the American Chemical Society had her do a performance in Southern Illinois University, Edwardsville about a year or so ago, and it's just fascinating because she basically acts out the first two phases of her life. She does the accent, and she's got all the props and, she really dramatizes this woman's difficulties. You think of a Nobel Prize winning chemist in France as being born with a silver spoon in her mouth, when in fact, she had a difficult, very difficult time, just to get educated. So her performance brought that out; life was not so simple for these people.

KNOWLES: Well, I've really had a cushy problem with education. Perhaps my biggest problems were the divergence of other things [laughter]. In other words, there was no culture of science in my family whatsoever, and there was a strong culture of business, a very strong culture of business, so it was expected I'd go and be a typical business executive. And a lot of Ph.D. chemists, do that, but I don't think I was particularly well cut out for it. However, if you just look at the salary, you get more that way.

GRAYSON: Oh sure, you definitely make more money.

KNOWLES: And I don't know why it's that way.

GRAYSON: Well, we don't want to get off on that subject; why those guys get paid so much money.

KNOWLES: No, I know that, yeah.

GRAYSON: Your siblings, what do they think of your accomplishment?

KNOWLES: It was a considerable air of surprise, surprise on the whole thing.

GRAYSON: What did you do, call up your brother and say, "Guess what? I won a Nobel Prize in chemistry."

KNOWLES: Yeah, well there were people coming to the house all day about that.

GRAYSON: I bet.

KNOWLES: Yeah, and the press comes, ….it's fairly exhilarating to start with.

GRAYSON: Oh sure.

KNOWLES: A month and a half is not your own. There's no other prize that would claim that much of you. The others, it's usually a dinner and speeches.

GRAYSON: Sure. Well, let me get a couple of pictures, unless you have any other thoughts that you want to record.

KNOWLES: Not at all.

GRAYSON: Then we'll go ahead and put this to bed.

[END OF AUDIO, FILE 1.4]

[END OF INTERVIEW]

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