

Chapter 29

NATHAN (NATE) E. TOLBERT

Okemos, Michigan

July 19th, 1996

VM = Vivian Moses; NT = Nate Tolbert; SM = Sheila Moses

VM: Here we are in...how do you pronounce it?

NT: "Okky-mos".

VM: ...Okemos in Michigan near East Lansing talking to Nate Tolbert on July 19th, 1996.

I notice from reading last night the chapter you gave me for *Advances in Plant Physiology* — that you were an undergraduate in Berkeley.

NT: That's right.

VM: In chemistry?

NT: In chemistry .

VM: Can you tell us how it happened and whom you knew there relevant to the Calvin and the photosynthesis story?

NT: Actually I did my, started my chemistry undergraduate work at Idaho and went to Berkeley in '37, at the time of the World's Fair on Treasure Island, and it was a great, impressive show for a farm boy from Idaho. I was a chem. major, primarily an organic chem. major with, as I said in that paper, a B+ complex and that meant that I never was good enough to really be the top dog and I was always struggling. But I took the regular courses in chemistry: I didn't know any of the professors personally very well. In that chapter I pointed out that when I was taking organic chem. lab. Ruben, who was doing photosynthesis research, the beginning of the carbon dioxide testing programme, was killed because he made phosgene in the sink and it got out into the lab. The other Assistant Professor, who had just arrived there the year before, was Calvin and he took over the photosynthesis project then. That was probably...I graduated in '41...

VM: You went there on a 4-year chemistry course, the regular undergraduate...?

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NT: The regular 4-year chemistry course. I graduated in May of '41 so that could have been the spring of '41 or it could have been in the '40s. I never knew Benson because he really wasn't there but his and Ruben's names are on their first paper.

VM: So you knew Ruben personally?

NT: No, I did not know Ruben personally and I also did not know Calvin at all. I knew the old teachers: F.C. Stewart for Organic Chemistry; my senior thesis was with Randall, a physical chemist. As I pointed out in that paper I was getting close to my future because I picked all of the papers on photoactivation of silver, which has a light phenomenon, and that got me a commission in the Air Force.

VM: But at that time you had no special biological interest, had you?

NT: No. In fact I didn't have any biological interest except that I was raised on a farm and any time you are raised around a botanical environment you then have a biological interest, I would say. But out of curiosity, I took the general course for medical students which medical students had to get a B in to get into Med. School. I took that course with no preparation, no idea about biology and pulled a C and I was crestfallen because I didn't know anything about biology let alone about biochemistry. So, as I said in the chapter, I was challenged so, I'll be darned, I went to Graduate School then in biochemistry. The general pecking order is math, chemistry and biology...

VM: I know; that's right.

NT: ...and I was sliding down the scale when I took that course in biochemistry. And my chemistry professor said, "Oh, no, don't do that!" They opposed that.

VM: So where was the biochemistry course given?

NT: Down in LSB, down in the Life Science Building — that's a beautiful old building. And you know, I don't think Arnon was there yet, I don't remember. I didn't know the botanists at that time.

VM: So you graduated in '41?

NT: I graduated in '41.

VM: And the next thing in your career was in the military?

NT: No, the next thing was I went to Davis. At Berkeley, in the Chemistry Department, when I graduated, it was automatic — everybody went down to Shell Oil Research Lab.; they sent all their students down to Shell Oil. They were really booming because the war was coming on and they were worried about oil substitutes and Calvin later got involved in that. We *had* to go there and that's where we *had* to have a job. They wouldn't recommend you anywhere else. I didn't want to do that. I took a job, instead, at Davis in enology and viticulture, actually. The guy in charge of their brandy research programme...

VM: That sounds a very attractive way of spending time!

NT: ...had just been called up and I took over his research programmes.

VM: Although you actually had no research experience at the time?

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NT: I had no research experience but he had a big programme going on the change in the pH with ageing and the change of the tannins and analysis of the tannins and he had a big cellar of brandy stored and made and I watched over the whole works. As I said in the chapter, I had been a teetotaller up to that time and had never tasted even beer. In the States we're pretty strict, you know, particularly in Idaho where I came from — that's Mormon country.

VM: And your parents were teetotallers as well?

NT: My parents were teetotallers and we had nothing but anti-Mormon jokes, actually, but we also were very strict in the sense that we didn't smoke and we didn't drink. We were Presbyterians.

VM: But I am pleased to see both you and your brother have graduated beyond that stage.

NT: We quickly graduated. I corrupted the rest of the family; my going into the wine business then brought them along. I helped establish many of the wineries. There was no Sonoma Valley then. We planted the Beaulieu Vineyard almost physically by hand down in Santa Cruz.

VM: Do you mean, when you say "we"...

NT: Myself...

VM: And colleagues from Davis?

NT: ...and colleagues in the Department of Enology, in this department. Up until almost the war, this country was also teetotal, during prohibition, and this had wiped out the California wine industry. There were no students, nobody with know-how, so we had to teach, we had big courses and I taught in that. We taught wine tasting; we used to go to France and bring back cases of wine, and to New York and bring back cases of their wild grape wine, and teach the students blindfolded how to taste for sulphite and acetate and where the wine, in general, came from.

VM: But not, presumably, when you were there because the war was on.

NT: I was there the first two years of the war; I was there '41 and '42.

VM: But you couldn't get to France at that time.

NT: You're right. I guess we had French wine; it was shipped in. No, we didn't go to France, that's right. Later on they did, I didn't.

VM: When you say that you recreated the vineyards, weren't these commercial vineyards?

NT: No, they were all wiped out. The only grape that was left after prohibition in California was Zinfandel. That was only by a few Italians who moonlighted and made bootleg wine. The Californians, at that time, '41, were bringing in, let's say, the Cabernets to be planted and most of them didn't know how to make wine, didn't know what grapes to select, or anything.

VM: So you spent a couple of years in Davis.

NT: I spent two years there and then I went into the Air Force — I got called up, so to speak.

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VM: How many years were you in the Air Force?

NT: Oh dear, from '42ish to the end of the war (be '45) — 3 years. This did not involve the Berkeley group at all, but my brother, who was one year underneath me in age, stayed right in the Rad. Lab. — in the Radiation Labs., so to speak — and took his Ph.D. degree under the Atomic Energy Commission's umbrella running the Rad. Lab. and he actually worked for his living up on the Hill at the beginning of that programme and we would go back there.

VM: So you had contact.

NT: So we had contact. And in fact, I went from San Francisco to the Philippines on the first big 4-engined plane that could fly the route. The point I want to make was that even then we would go back. And I had a sister who got her Ph.D. degree down in LSB in biochemistry and nutrition. So that I would be back in the lab. a lot. And actually, for some reason or another, I guess it was only Donner's Lab. that I remember at that time.

VM: Well, Calvin didn't have ORL.

NT: No.

VM: No, that came later.

NT: Bert was up on the Hill, that's right.

VM: Where were you actually based during the war years?

NT: All over, but actually overseas — do you want me to tell you everywhere?

VM: Well just...you weren't based in California?

NT: The first and biggest base I had was I was in charge of the photo labs. in the New England area. In other words, they had one big Air Force photo lab. I had about 25 people in it and we went out and took pictures of every airplane that crashed and we ran pictures of the photographic development of the CEO so his wife would have pictures and I got my next promotion quickly because of that operation and so forth. And then I went into photo intelligence where you look through that stereo thing and looked at...

VM: See whether it's done any damage.

NT: ...installations in the Netherlands and so forth and from that then I went to briefing pilots and navigators back in California at Muroc (*spelling?*) Air Force Base, which is still the experimental base where the shuttles land. From there, then, I went to the Philippines and in the Philippines I was in the headquarters group in an intelligence group. And our purpose was to be on the ground and get in and take pictures and evaluate things that were of interest to the Air Force, particularly before the GI got there. Once the GI got there, he took everything for souvenirs so we had to beat them in, which meant we had to go ahead of the troops oftentimes, which was dangerous and that's when I got shot because we were out in front of the occupation troops.

And then after the war, I was down recovering in Australia when the Japanese surrendered and then I flew almost directly to Japan and was in charge of picking up all Japanese aerial cameras before the GIs got there. In other words, again we took Japanese officers and transportation and went out to the Air Force fields before the

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GIs took them. This was exciting because we got terrifically welcome receptions and big parties and stuff like that. We took all these cameras and put them in big trucks and shipped them back to the United States. We were particularly interested to see whether the Germans had provided the Japanese with any research developments in aerial photography. They hadn't, that we could find. I have pictures of myself with great big aerial cameras that they had but they were very poor and had nothing we could see of value. But I wrote a big report and took lots of pictures of Tokyo right after the Americans got there and sent it to the *National Geographic*. They didn't quite accept it. They said they had other people that were writing and I suspect my writing was not so good in the end. But anyway, then I became lastly...I went and inspected Air Force bases as we were closing the bases, from Japan all the way back across Indonesia, Egypt, Morocco and so forth. I did that because that caused me to end up in Washington, DC. The name of the game at the end of the war for the American GI was to get back to the States. That took about a year for most of them but I got back in about 3 months by going through that inspection programme. Once you were in the states you just were issued out.

VM: So when did you leave the military?

NT: I don't really remember for sure. I think it was the spring or summer of '45 — when did the war end?

VM: August '45.

NT: Then I got out the next spring.

VM: And what did you do?

NT: I had already had a fellowship from Wisconsin that had been granted just as the war started, in biochemistry, and I simply wrote and told them I would like to come again if they would take me. And, of course, they took you because you had your own money.

VM: This was the GI Bill?

NT: GI Bill.

VM: So you went there the fall of '46?

NT: I went there, probably the summer of '46 and at that time Bob Burris, who was my major professor, had just moved from microbiology primarily because of the *Azotobacter* and the nitrogen-fixing bacteria. He had taken his degree in bacteriology and he had moved into biochemistry. It's complicated but anyway he became the plant biochemist of that department.

VM: Why did you choose to go there? I mean, when I ask that question it is done in the knowledge that Bert is your brother and Bert was at Berkeley and presumably you knew what was happening in Berkeley. What was in your mind — the thought of going back to Berkeley to do your graduate work?

NT: No, I had never thought about it because I thought I wanted to go into biochemistry. And at Berkeley at that time biochemistry was all down in LSB and there wasn't to my knowledge anything about plant biochemistry.

VM: You didn't know about Hassid?

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NT: No, I didn't know about Barker or Hassid, I really didn't...about the answer to that. You see, I had been in enology and viticulture. I was plant oriented from those two years. I didn't want to go back there and I didn't know about Barker and Hassid so what I wanted was a degree in plant biochemistry so I could come back into, say, viticulture or someplace.

VM: Did you not know — or maybe it was too early — but did you not know yet about Calvin's photosynthesis interest?

NT: No, I had no knowledge whatsoever about Calvin's photosynthesis. At the end of the war, it was at that time that they picked up on carbon-14. Bert has probably told you when he started working for Calvin; it was at about that time and they started their carbon-14 on anything that could be tested or they could use. Andy Benson had been a conscientious objector and had been up in the mountains, which becomes very important to me later because we used to hike the mountains. And he must have come back also at the same time that I went to Wisconsin.

VM: You were in touch with Bert, presumably, so you knew something of the developments going on.

NT: I knew but I don't have any major recollection of anything except that of his role in developing the carbon-14 programme.

VM: OK, so there you are in Wisconsin in the fall of 1946.

NT: Yep, like all graduate students.

VM: Right. What did you do? What was your thesis topic?

NT: The first thing I did was buy a canoe with three other graduate students and we'd row out into the middle of Lake Mendota and study German to pass our German test.

VM: You had to do that?

NT: Yes. And French. And so, research-wise, I started on polyphenol oxidase but I quickly switched after a while onto a new oxidase that Burris and another student, Carl Clagget had just discovered and they were saying, hey, there is another oxidase here. We don't know anything about it. We don't know what its function is. And in that era the phenomenon, we used to say, was a "terminal oxidase", these oxidases were terminal oxidases, that's the role of cytochrome-C oxidation. It's the end of an electron transport chain. And we used to consider the other oxidases, like glycollate oxidases and polyphenol oxidase and ascorbate oxidase as a system just to waste the hydrogens and transfer the oxygen without making ATP. And so that was the concept. That is an important concept for the future of my whole career because although that is partially correct for glycollate oxidase, it really wasn't that direct — take the hydrogens and transfer it to oxygen. Actually to regulate and control such a system you had very complicated metabolic pathways which prevented this from actually occurring.

Whereas many people later, particularly in England and in Canada, pursued the concept that you could oxidise glycollic acid to glyoxylate and turn right around and reduce the glyoxylate to glycollate and that became your terminal oxidase to waste energy. That's in my preparatory chapter in the *Annual Reviews*. As it turns out that has always been true except that it has a major function. It controls net photosynthesis and it controls the ratio of CO₂ and oxygen.

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VM: But you didn't know that at the time?

NT: No, we had no concept; we had no idea. What we had was an enzyme and we set out to characterise it.

VM: And that was essentially what your thesis was.

NT: That was my thesis. My thesis was titled "Glycolate Oxidase."

VM: So, you finished your thesis work in Wisconsin when...in about '51?

NT: No, I finished it, actually, at the end of December, 1949.

VM: That was pretty quick.

NT: Three years — it was pretty quick. I was smart! No, I'm only kidding — I was lucky. I had a good enzyme, I could isolate it, purify it, look at the product. And Bert made carbon-14 labelled glycollates, he made C₁- and C₂-labelled glycollates; I could toss those into the Warburg flasks, look at the products and how much was oxidised and all of those things so we had two papers in JBC and some others fairly soon out of that.

VM: You had your own counting equipment in Wisconsin by that stage?

NT: We had home-made Geiger counters. We actually got the models in part from Berkeley, from Calvin's lab., by golly, and Andy Benson was making these big Geiger counters. You probably remember those, with big windows. We made our own in Wisconsin after the Rad. Lab's. models. And, of course, Bert also was involved in this because he was counting carbon-14 all the time. So I had a lot of things going for me then with my contacts there through brother.

VM: So when you finished your Ph.D. at the end of '49 you were involved with plants, you were an expert in glycollic acid since that's what you had been working with, you had practical experience in the use of isotopes...

NT: Yes.

VM: ...and you knew what was going on by that time in the Berkeley lab. And then what did you do next?

NT: Well, this gets complicated. It was obvious because already Benson and Bassham were saying there was radioactive glycollate on the chromatograms. It was one of the early products they identified. It was obvious that I should go and work on that type of thing in Calvin's group. But in order to do it meant leaving behind in Wisconsin my fiancée and we never did get back together.

VM: What was your fiancée's position in Wisconsin?

NT: She was still a graduate student.

VM: In the same department?

NT: No, she was not. I don't know what she was in — she was in literature or something. We don't need to go into details. Her father was a major General Motors executive and he didn't think science was a worthy thing to be in. He thought you should be a GM executive. So between all the circumstances, I say, I went to Berkeley over their

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objections. Bert and I drove across country. My father had given me a graduation present of a new car from the farm in Idaho.

SM: This was 1950?

NT: 1950, yes. The car cost \$2,000 —a nice, new, red Chevy. And Bert came back by train and we drove it across country and had a wonderful time.

VM: But when you decided you wanted to go to Berkeley, was it your decision that you wanted to go?

NT: It was strictly my decision.

VM: And what did you do — you wrote Calvin or what? How did you decide to do it?

NT: Oh, gosh, I don't remember. I guess I may have, must have written and he said "Yes, come ahead." At the same time, Bert was already in charge of Calvin's administration in Donner and I don't remember who pulled strings but anyway they just said "Come."

VM: And they gave you a post-doc.

NT: They gave me a post-doc, the reason being that in January of 1950 phosphoglycerate was still not identified for sure. I think Bassham was on the verge of identifying that, and they had to do kinetic experiments to see whether the first product was phosphoglycerate or something else. I came from the Midwest where Gaffron was the big power at Chicago and we were just miles away from Chicago, and so we were really of the Gaffron camp. As you recall from those days, Gaffron thought it was some large molecular weight compound that would not move much from the origin of his paper chromatograms. From running chromatograms you also know that if you overload or have salts or anything in there the compounds don't move away from the origins, so that's where he went wrong.

VM: And you knew Gaffron personally?

NT: I knew Gaffron pretty well, yes. And Marty Gibbs knows him very well. You will find out that Marty Gibbs took care of, godfathered, Gaffron after retirement. And we also knew the Illinois group — Emerson and Rabinowitz. So that glycollate, then, was just one of the products being formed from CO₂ and we had no idea how fast or anything kinetic. Actually, Calvin was so interested in this that he had brought in six months earlier, before I got there, a post-doc. from Sweden by the name of Schou, Lisa Schou.

VM: She is now Lisa Wilkinson — she married Geoff Wilkinson who is a professor, retired now, a professor of organic chemistry who was at the Imperial College in London. We have already been in touch and had dinner with her last year and we're going to talk to her when we get back.

NT: Calvin had already taken her in just for glycollic acid and she published a paper with several of the people — Bassham and Benson and Calvin and herself and maybe Stepka or somebody else — as I was getting there or just shortly after I got there.

VM: So when you arrived in Berkeley you had not previously met Calvin?

NT: I can't answer that for sure. I may have met him when I went through Berkeley during the war. No, I did not know Calvin before then.

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VM: Was this after he'd had his heart attack, after he had his big heart attack? I think that was '49.

NT: I think it probably was after. He must have had that heart attack before I got there because when I was there in the '50s all he did was come into the office and then every afternoon around one or so he would lay on his couch and we would go in and talk to him.

VM: While he was laying on his couch?

NT: While he was laying on his couch. He was told to lie down and rest, and of course he didn't consider mental thinking as resting. So he would talk to us. However, I clearly remember him coming into the lab., and bouncing up and down and saying, "Let me see that chromatogram." And Al Bassham and Andy would get the chromatograms out and he would say, "Oh look, there's that spot!" — his typical enthusiasm and then he would go back to his office and think.

VM: So when you got there, you were assigned space in ORL which was where the photosynthesis group was?

NT: Yes, in the old building.

VM: Had you had experience at that time of running chromatograms?

NT: I had run chromatograms because in Burris's lab. we ran chromatograms, yes, but nothing at the intensity numbers that they did in the old Rad. Lab. — what did you call it, ORL?

VM: It was called ORL, the Old Radiation Lab.

NT: The Old Radiation Lab., yes, where they had a whole room full of chromatogram boxes. When I got to Michigan, here, the first thing I did was build a room like that.

VM: I think all ex-Calvinists did that sort of thing.

NT: And we just tore it out about two years ago, two or three years ago, and as soon as they tore it out I wanted to use it and I hadn't used it for ten years before.

VM: When you got to there can you remember who were the other people at that time present in the lab.?

NT: Well, let's say that in the lab. the people that I associated with the most was built around who went skiing and who went hiking and this were Al Bassham who would lead the trail singing "Come follow, follow me through the green woods, through the green woods", and Andy Benson, who loved to go rock climbing, and my brother and myself, that's four; we would generally go up in two cars and there would generally be eight of us. Clint Fuller came in about that time but he went some of the time but he wasn't so much an outdoor person. Bill Stepka — I don't remember him going with us on our mountain trips but he was also very energetic and, I think, a person that didn't accept anything unless he understood it. He was always critical of the thought processes; he would make you think. Dick Lemmon to some extent, but Dick was over in Donner making compounds but he also was an outdoors man.

VM: Was Lisa Schou still there when you were there?

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NT: She was there when I arrived; I don't remember too much more about that. It caused Calvin to, before they had done kinetics of labelling, the rate of labelling, to feel that glycollate was not a first product. They published her paper actually a year or so after she left. I think she left about as I was coming there. But I remember her as a lovely-looking blond woman. Because they had already done the labelling and monitoring of this one spot on their chromatograms, that was glycollic acid, Calvin urged me to start on something else.

VM: He did urge you to start on something else?

NT: Yes, he said there wasn't anything more to do on glycollate. And I still have, but I couldn't find my file on all the projects he wanted me to work on, but I remember one of them — he was very interested in cyanide, why cyanide inhibited CO₂ fixation, because we knew that cyanide inhibited the cytochrome oxidase system and he was wondering whether it was cytochrome oxidase (*indecipherable*) cytochrome-C was involved in the electron transport so he was terribly interested in cyanide in addition. So I really did probably the first experiments — did almost 6 months on a whole stack of chromatograms with different algae, different cyanide levels and so forth and there was nothing to show from that. Nothing was done with the data because it didn't tell anything — it just inhibited CO₂ fixation — but that later developed into big stuff. Clint Fuller picked it up when I left and showed that the cyanide (he used radioactive cyanide), and showed that the cyanide was forming a compound which was a cyanhydrin complex with ribulose *bis*phosphate. So here was a new spot on the chromatogram labelled by cyanide which he knew was a cyanide complex with something and it turned out to be ribulose *bis*phosphate. And that led to the concept that the ribulose *bis*phosphate had a reactive carbon to activation that would bind CO₂, oxygen or cyanide and some other compounds. I picked that up in a Ph.D. thesis by the future director of Dow Chemical, sorry Dupont (he is now in charge of the Dupont European Programme). His name is John Pierce and John Pierce, for his thesis with me, reacted the ribulose *bis*phosphate with cyanide and then hydrolysed it to the acid CO₂ (COO) to form carboxyarabinitol *bis*phosphate and that compound binds to the enzyme (Rubisco) with a dissociation constant of 10⁻¹² — in other words it does not dissociate on the enzyme — and then we had the answer to why cyanide inhibited.

VM: Pierce was your student?

NT: Yes. So that the cyanide was inhibiting Rubisco by binding to the ribulose *bis*phosphate forming and being hydrolysed to this acid, carboxyarabinitol *bis*phosphate...

VM: Which just stayed there.

NT: ...then it could not dissociate on the enzyme. That probably was the compound that Fuller was working on; it was the reason we originally said cyanide was inhibiting and that compound was used all the '70s to study the enzyme. That compound would totally take Rubisco out of the picture and then you could isolate the enzyme and say how much there was and study its properties and most of the x-ray crystallography was done with the carboxyarabinitol bound into the enzyme because you could stabilise the enzyme.

VM: So when you were in Calvin's lab. you actually never worked on glycollic acid at all?

NT: No, I did not really work but I did work on it. We talked a lot about it, we followed it. Calvin, at that time, published a series of papers with chromatographic maps and on respiration (he called them "respiration") and on the products with different algae and

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glycollic was one of those and my name was on all of those papers because he put everybody's name on the papers.

VM: But you contributed to the work that was done.

NT: They used everybody's chromatograms. So I contributed chromatograms to those general papers at the beginning, that came out for the next year, actually, in '51 and '52.

VM: Did you also participate in the writing of the papers or the discussion that went on in the...?

NT: Certainly we discussed the papers and made the first drafts. Generally speaking the papers were published about a year later after he worked them over.

VM: I was making the point, asking about the point: was it usually the case that all the authors actually contributed to the discussion or did some of them just contribute experimental data for others to interpret?

NT: Well, that's a very big question and I would like to address it. First of all, the direct answer to that question: I have both in my CV. I may have my name on four of the papers, four of the *Paths*. I have both examples. Maybe a chromatogram or two from my file was used in the paper and we all discussed the stuff and you know Calvin had his research group meetings and seminar presentations so that certainly we all discussed them. And I think frankly — my impression is that Andy wrote the first drafts of those — that's my impression, and then Calvin polished them particularly to fit a scheme. And I don't know what the others will say about that but that's my feeling. Because I remember Andy working on papers because Calvin had to give a speech at the ACS meetings or some place and we worked up the first draft of the report which he then gave at the meetings and then those became a paper later. There was quite a long drag there.

VM: When Calvin went to these sorts of meetings, which he presumably did more than anyone else in the lab...

NT: He was the only one.

VM: ...did he consult you before? Did he keep you informed about his doings at meetings? Did he come back with information and things like that?

NT: I really think that Al and Fuller and Benson, who were there longer than I, could answer that better. But my impression is that he simply came into the lab. and said he had been invited to give a paper at a symposium at the next ACS meeting and didn't say it this way, but get to work and let's get a summary out on where we stand right now.

VM: And when he came back did he tell you what had happened or what else he heard?

NT: Yes, he came in, well the few times I was there, he would come to the group meeting and summarised what happened.

VM: So he was a window for you on what was going on, at least in some sorts of areas?

NT: As far as I was concerned. I never went to a meeting or anything while I was there although I had from Wisconsin because I was close to Chicago where many of the Chem. meetings were held. Now the other answer to this question — one is

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authorship which others may address — one of the standing thoughts were that he often listed the authors alphabetically. Because his name was ‘C’ and he only had to fight it out with Bassham and Benson and then Calvin, and Bill Stepka would be ticked off because he was clear down with me at the end of the alphabet! At this stage in life that didn’t concern me at all, didn’t care, but when you look back on it, and I don’t mean to be negative on this, but because how else do you determine authorship? As far as I am concerned, when I later had my own groups, the guy who did the Ph.D. thesis, he was always senior author. But then you had the problem of how to throw in a lot of other people so I always took the position for myself, I was the last author and that is how most professors have done it; they become the last author. Because there are two places on a paper, the first author and the last author and all the rest are chickenfeed in between.

VM: That was actually the case on many of the Calvin papers by the time I got there.

NT: Later, that was true. He adapted that system and became the last author. So you should ask Stepka and Fuller about that.

VM: Yes, well I will, next week.

NT: You know, I don’t know how to answer these questions because fifty years have gone by and your perspectives have changed. At that time there were just several things that counted. One was the weekend trips to the mountains; and your research. I didn’t have any axe to grind or any thoughts about the future or anything.

VM: Well, you were a young man at the time, weren’t you, making your way.

NT: Let me think, what...But at the same time we were a group of people who had had no previous contact so everything turned around the research. Your social life, what you thought about, what you did all week was strictly related to the research.

VM: Everybody in the group, not just your own bit.

NT: Not just your own although your own was what you knew best — it was the general problem of how was this thing worked out.

One other contribution, which isn’t in my preparatory chapter, when I went to Oak Ridge, which wasn’t until the last of ’52, one of the things that Benson needed, because they still didn’t know for sure how you got from the sugars over to ribulose *bis*phosphate on the cycle, so we made carbon-14-labelled sedoheptulose, and large amounts of sedoheptulose as well, and sent them out to Berkeley and then they used that to work on the transketolase reactions.

VM: But you’ve moved ahead a bit, you’re now in Oak Ridge.

NT: Yes, I’ve jumped ahead.

VM: What was the transition from Berkeley to Oak Ridge, your transition?

NT: My transition? Well, first of all, it’s in the preparatory chapter which you may have read.

VM: Well, I read it very quickly but we would like to hear it from you.

NT: Basically, my career at Berkeley was cut short after only half a year because the Atomic Energy Commission at that time had only one man in charge of the biology

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NT: Yes, that's right. Now you could say, "Oh boy, he's pretty smart isn't he?"

VM: Yes!

NT: But that idea wasn't even discussed at the time." As it turned out we developed or had big plant science programmes at Brookhaven, which was a big photosynthesis group, at Oak Ridge where Arnold and other photosynthesizers worked, Argonne and Berkeley. And of course I got to go to all of those and talk to them about the research so it was quite a broadening experience.

VM: Don't give me any secrets or break confidentiality that even now you shouldn't talk about, but when the grant applications came in — I seem to remember them as being a very formalistic sort of thing that they turned in every year, a progress report and said what they were going to do next year and the money seemed to come.

NT: The money came.

VM: Was there much of a scrutiny in the office?

NT: Pearson and I read them and we were the sole decision makers and my recommendation Dr. Pearson could override it if he didn't want to, but basically the Director of the Biology and Medicine Division of the Atomic Energy Commission at that time was in Boston at the Children's Hospital. His name was Shields Warren. I used to drive him back and forth from the AEC Building downtown Washington out to the airport and had nice discussions with him and his attitude was that we will put all the money we can into biological research. Don't worry about overhead, don't worry about anything, just worry about getting more money because the biology programmes need to be supported. That attitude led in, while I was still there before I left Washington, to the beginning of the National Science Foundation.

VM: Incidentally, was the name of that man Shields Warren or Warren Shields; which way round?

NT: Shields Warren, Warren was his last name. He was a big power, along with the guy who founded the NSF. I used to complain, "Oh, look, these places are getting a big overhead," and he said, "Well, they need it. Universities have to build up their programmes. Don't you worry about the overhead". And that has been a good attitude that was followed in the States until recently. The last 20 years the overhead has become a debatable situation with Congress but in the beginning, even for NSF, the idea had been to get money into the universities to build up their research programmes. That was true in physics, chemistry and biochemistry.

VM: How long did you spend in Washington?

NT: I was there from the last of '50 to the last of '52 — two years.

VM: And earlier, before we started this conversation, you mentioned you were also responsible for funding Arnon's work in Berkeley? Or was that at a later stage?

NT: You know, I suspect Arnon had a grant. Yes, I think he had a grant from us then. I don't remember that detail.

VM: But you knew Arnon at the time or was it later that you got to know him.

NT: Let's say I don't know for sure. If you had a way to confirm it I would guess that when I went to Berkeley I went down to see Arnon.

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VM: When you went as a post-doc.?

NT: No, as an administrator.

VM: I see; yes.

NT: When I went as an administrator I also would look at all the AEC grants at Berkeley and Arnon had one probably by that time.

VM: That means that you were presumably aware of the lack of collaboration between the two big photosynthesis groups on the Berkeley campus.

NT: Oh, yes, yes. We all, in the lab. in the '50s, were well aware of that. As far as I am concerned, from the very beginning of the time when Arnon started. And, I don't know, Bob Buchanan might tell you when Arnon became really active. Probably in his Ph.D. thesis (Buchanan's).

The Gatlinburg Photosynthesis Symposia in the '50s were the only photosynthesis symposia and I ran those through Alexander Hollander, the Director of the Oak Ridge National Lab. Those were in '55, '56 and '58 — 3 Gatlinburg Photosynthesis Symposia — of which I was sort of in charge of and even then they were writing the song I gave you last night to the tune of "Davey Crockett" about Arnon.

VM: Was the AEC concerned that two of its grant holders on the Berkeley campus were not communicating very well — or did they not regard it as their problem?

NT: No, they never were concerned. When I was there, there was no great concern, at least. We were just supporting (*both*). This was a wonderful time for science. When we got a good research programme in we either said, "Hey, this is great. This is from a top man. Support it." Or, if we had doubts we would send it to somebody that we knew knew the topic and ask them for their comments. But we made the decisions. We were basically supporting most things in photosynthesis. That was then radiation, light radiation.

To just finish up on this administrative...there's a lot of things involved...but historically my post-doc. in Oak Ridge was Bob Rabson.

VM: Yes. He was your post-doc.?

NT: He was my post-doc., period. He came from F.C. Steward, who was a friend of Fowden (*Editor: Leslie Fowden, a British plant biochemist, later Director of the Rothamsted Experimental Station*) — Fowden and F.C. Steward. This was an amino acid metabolism guy. He (*Rabson, presumably*) got his Ph.D. at Cornell with him (*Steward*) and came directly down and spent several years with me worrying about the glycine/serine story, where we worked it into the C₂ cycle, and then he took over the same programme for 30 years.

VM: Where is he now?

NT: He just retired and is still living in Washington, DC.

VM: You have...?

NT: I guess you don't want too far beyond this era, you would like to stay with...

VM: We would like to stay within the period roughly up to about 1960.

NT: In the chloroplast the same enzymes. They occupy the Rubisco and the regeneration of the ribulose biphosphate. You see, each cycle has to regenerate the ribulose biphosphate every time it wants to turn around. Now, the C_2 cycle was grossly underestimated. You can talk to your friends in Britain and they know that we began to say, “looky, half the photorespiration is half the rate of photosynthesis”. Because all the work that we did in Calvin’s era was done with carbon-14 which labelled the C_3 cycle but not the C_2 cycle until it went around the C_3 cycle and then billowed. But if you started with oxygen-18, and I have a whole section in here — you may have read it — if you start with oxygen-18, you label the C_2 cycle and you never would see the C_3 cycle so we have grossly underestimated the C_2 cycle and, when you really look at the kinetics of the whole thing, you find out they are about equal because that is the equilibrium level. It takes the same amount of oxygen that you get from 21% oxygen, water saturated with 21% oxygen, gives you K_M values for the oxygenase activity and it takes 1,500 ppm of CO_2 to saturate the carboxylase. So the two cycles are running in very major amounts, and balancing the oxygen and CO_2 . That’s the new concept that I’m peddling and I think you will find that it will slowly take over but everybody — particularly all of my competitors: Zelitch, Olgren (*spelling?*), Butts in England, the Canadians — they all have been — and Marty Gibbs — they have all lived in the era of photorespiration, like me, and they all are retired so there is nobody but me who doesn’t have the sense to quit and I want to get the record set straight.

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VM: OK.

NT: We were talking about the chromatograms. One of the biggest things is the identification of the radioactive spots on the chromatograms and how that was done (and you are an expert on that). You not only had to get it to co-chromatograph, you first of all had to co-chromatograph with two solvents, that was the main thing. And then you had to do some chemistry on it, convert it into another product or something to be sure that it was as predicted.

VM: Well, you had to have a certain amount of inspiration to decide what the likely candidates might be for the compounds you were interested in.

NT: That's right. You had to know the chromatogram. This was the amazing thing that all of us who worked in it, including you, we could...I've seen my graduate students' mouths drop open when showing me a chromatogram and I say, "Oh, there's malic, there's glycollate, there's serine and here's..." "How do you know that?" Well, I just know it.

VM: You live it!

NT: You live it. But you know it because you have identified it. And later when you come to identify a compound you have to do very rigorous chemistry on it. And that was developed by Benson. You must give Benson credit for that. Primarily I would say Benson was a chemist also and his biology came later, and he and Bassham really were the original people in developing that. And then you followed.

VM: Well, they were the backbone, Benson and Bassham were the backbone who kept the thing running. People like me came in but we came in and learned from them. True enough, we contributed our own bit but they were the ongoing things (*!people*) for a long period.

You said two years in Washington and then did you go to Oak Ridge after that?

NT: I went to Oak Ridge. It is all in this preparatory chapter but basically I could see right away where I wasn't going to get into a university from an administrative position without any teaching experience and not much research experience. So I had to wiggle out. I had two cards in my hand. One was that I was going to work with a guy named Sterling Hendricks, which was phytochrome, and I had a programme there. And the other one was the Director of the Biology Division at Oak Ridge, which was Alexander Hollander, and he had said, "Come on down and I'll let you be in charge of my plant biochemistry group". So I moved to Oak Ridge.

VM: And you were there for several years, weren't you?

NT: Yes. I was there from the last of '52; I was there six years to '58.

VM: Until you came up here to Michigan State.

NT: Until I came here.

VM: And you have been here, then, since '58?

NT: Since '58.

VM: That's a long time.

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NT: That's a long time. I came here with two other people as professors of biochemistry. One of them you should know — W.A. Wood, Willis Wood, the famous microbiologist.

VM: Of the Wood-Workman reaction?

NT: No. That Wood was Harland Wood from Ohio but he and Willis Wood are very good friends and I also was a good friend of Harland Wood (he died).

VM: I should know who Willis Wood is.

NT: Well, he was the Editor of *Methods of Enzymology* and he did some work with Nate Kaplan and...

VM: I don't think I have ever met him but I vaguely remember the...

NT: He is at the Salk Institute. Anyway, the three of us came here to begin a Biochemistry Department. I had to get out of Oak Ridge because I developed an extreme allergy to the pollens. Oak Ridge is a beautiful, beautiful place, covered with rhododendrons and redbud trees — it looks just like England in the spring — but they have an awful lot of pollen and it is more humid — much more humid than in England — in those Smoky Mountains and I developed such a severe pollen (*allergy*) there but I found if I went to a coastal region or came up this far north, I got away from whatever was bothering me.

VM: But you enjoyed your stay in Oak Ridge.

NT: Yes. That era in the '50s the national labs. were well supported and you could do full-time research, you could have post-docs., and you could teach if you wanted to and go into the university level. It was a good research environment but essentially since the '60s those places have gone down hill and the research programmes have been transferred to the universities — university research build-up — which is probably good.

VM: So by the time you came up here Bert had already left Berkeley.

NT: Yes. That is a very interesting and important topic for Calvin's group. All of those people in Berkeley, and you lived this too, the original group before you got there, Benson, Bert, Fuller, Stepka and so forth all wanted university positions. So did I. And we all had to leave because the Chemistry Department wasn't going to allow Calvin to give them faculty appointments. Naturally, first, most of them weren't top-notch chemists, they were biologists and secondly they didn't want Calvin to empire-build so they simply blocked anything and all he could do was keep them as post-docs. And just for the record, you know the only person who stayed there was Al Bassham. The group of biochemists who came in to start the Biochemistry Department brought in other people. They did give Al Bassham a joint appointment.

VM: Yes, much later.

NT: Much later. And that didn't pan out very well. And that again is just history.

VM: But Bert had left by the time you came here so what were your links with the Calvin group after you took up your appointment in Michigan?

NT: None. I had no links with the Calvin group except through personal research discussions. I would see Al at meetings.

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VM: You would do that?

NT: Oh yes.

VM: You would be in touch in that sort of way?

NT: We would be in touch in correspondence with Al. He, too, became primarily interested in stuff related to the C_2 cycle. Essentially the C_3 cycle was finished by the time you were through. The C_3 cycle was accepted, was called the “Calvin Cycle” and that was photosynthesis and that fitted in with 150 years of thinking that photosynthesis is CO_2 fixation and oxygen evolution. But actually the point that we are making now is that photosynthesis is also oxygen fixation and CO_2 evolution and that the two processes give you the net and give you the atmospheric bound so that the C_3 cycle *a la* Calvin was finished with your generation and then Al started really working on photorespiration. He had a very important and famous paper that said there are two pools of glycine. One was labelled quickly and one was labelled slowly, and nobody could understand it. We didn’t doubt Al but we couldn’t understand why should there be one pool of glycine that quickly labelled and one pool that very slowly labelled? The big pool is the slow label.

VM: That’s the protein synthesis pool ultimately.

NT: No, that’s the C_2 pool.

VM: Oh, is that the C_2 pool?

NT: That’s the C_2 pool because it goes from the chloroplast to the peroxisomes to the mitochondria where the glycine is converted to serine. That was so discouraging to Al not to be able to understand that and nobody would believe him. You get discouraged after ten years and nobody would invite you to a meeting or anything. But actually the quick-labelled pool has not been ever figured out until...I think I know what it is. I just published a paper this year on a chloroplast pathway, which is in this paper. In the chloroplast there is another pathway for glycollate metabolism which makes the extra ATP. It becomes the photosystem-1 cyclic phosphorylation that oxidises glycollate to glyoxylate and on to glycine and that is very quick — very quick, instantaneous — you don’t have to move to the other compartments. And that’s probably...one of my ex-post-docs, who is a botany professor, is also looking at some of the other enzymes, and they are in the chloroplast, that would make the glycine. I just wish I had a lab. and could jump on this. I could solve it in two years.

VM: You have to leave something for the next generation.

NT: Yes, but you know there is nobody left. This is another Calvin story, really. Calvin created all these people that went out and kept the photosynthetic carbon metabolism going — people that associated with him, from Marty Gibbs to Clint Fuller — and those people from the ’50s to 1990 who were photosynthetic carbon men. There is nobody now left. There is no Warburg, there is no chromatography room, there is nobody getting grants on photosynthetic carbon metabolism.

VM: No. Fashions have changed completely.

NT: You gotta work on molecular biology.

VM: You certainly have.

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NT: This is a big bitch and I think you should put it in your book; I have it in my (*indecipherable*). To do research you've got to do molecular biology, you've got to do mutant work, you've got to do the biochemistry and enzymology and you've got to do the carbon metabolism. And you've got to do all four and integrate them. Otherwise, the guy just looking at his DNA maps, he doesn't know what he is looking at.

VM: One last question I would like to ask you. It's about the building. People who worked in ORL appear to have a strong emotional and favourable memory of the place.

NT: They sure do.

VM: You do as well?

NT: Sure.

VM: What do you think was so good about it?

NT: That was, I think, was strictly comradeship. It was a crummy lab.; it was a dangerous lab. Let me stop on that one. It was so dangerous, it was radioactive, it was hot. It had phenol all over everywhere. We bathed in phenol and we always had a bottle of methanol around to wipe the phenol off our hands before we got burned. Today phenol is a toxic compound. You can't even have it in your lab.

VM: We used to smell it by the bucketful.

NT: We used to smell it and we used to take our chromatograms — we'd get phenol burns on our hands rather than lose a chromatogram. All of those things were overridden by the comradeship of the people who were there. They were tied together by a desire to solve this problem, this big, hot problem, in just one little group. You take research on the HIV virus. It is a big field but those people are spread all over the world. But this was one little group tied together.

VM: Have you ever come across anything like it?

NT: No, not really. In fact I have just the opposite experience. On developing the C₂ cycle over the last 40/45 years, we've all become... everybody in the field doesn't speak to anybody else. We became enemies; we became disrespectful. We just didn't have any comradeship. The C₃ cycle was developed by one group, one person, headed by Calvin, whereas the C₂ cycle has been developed by literally fifty scientists in all the countries, all disbelieving the other person. So, no.

VM: You are right about the comradeship and, of course, it extends to this day that the people now in their mature years in their 70s, many of them, retain this friendly feeling towards one another, very much so.

You agree, then, that the building had its merits. In time, as you know, it was pulled down and another one was built, and you have probably heard the stories about the philosophy that went into the round building that replaced it and you have been in that building. What do you think of that building? Or at least: I don't know whether you were in it at the time it was still a unitary building, when it was Calvin's.

NT: Yes, I was.

VM: What did you think of it as a modern version of something like that?

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NT: Well, I guess you can quote me on that. Basically, at the time it sounded like a pretty darned good idea but I don't think the people were there — it just didn't click for some reason, I don't know why. Maybe they had it too good. Their labs. were excellent but their research didn't click. There was only Al in photosynthetic carbon metabolism. Dick Lemmon had a different programme; Ed Bennett had a different programme. I think Calvin was still there and all of that but I think it didn't work because they didn't have a scientific mission. You see, the Old Rad. programme was held together because they had a scientific mission, a big...

VM: A target.

NT: A target if you think about it. Al Bassham was the only guy there and he was struggling to understand the C₂ cycle. He didn't know about the oxygenase activity in Rubisco. He just was looking at product. So he was using almost an outdated procedure to try to understand the C₂ cycle where there were twenty of us other guys approaching the C₂ cycle by all of the other techniques. And so they were not a controlling force. To this day I doubt if Al really realises what he was working on. He will when he reads my chapter. He, alone, wasn't able to make it into the comradeship. He had nobody to be a comrade with.

VM: But the building, the problem with the building is an interesting one, nevertheless, and it is related to what happens to groups as they mature and they lose their initial fervour. By the time Calvin had his new building, of course, the group was very different from what it was, as you said, their initial enthusiasm and targeting...

NT: It was different, they didn't have people, Calvin wasn't very active — he was still active but he was such a big wheel he didn't really get into the problem. Calvin, from my day, from 1950, he said "Glycollate is not important". And he thought of photosynthesis only as CO₂ fixation...

VM: That's quite true.

NT: ...and even though he and Bassham went out and lectured and lectured about regulating atmospheric CO₂ and the greenhouse effect, they never saw that it was the CO₂-oxygen ratio that counted.

VM: Well, it provided an opportunity to you to spot what it was.

NT: That's what I say in my chapter. "Thanks, Calvin, you gave up half the photosynthetic carbon metabolism for me to play with for the next fifty years."

VM: Well, I think that's a very nice place to leave the story.

NT: I am thinking...you know I didn't prepare for this at all. I do think you are asking about why did Calvin's group succeed so well? And besides, when I used the term "comradeship", I think it was also they played together, they went skiing together, at least when I was there they skied together, they hiked together.

VM: It was a community.

NT: It was a community. We would leave the lab. at 5:00 o'clock in the afternoon and be up to Donner Summit to throw, to pitch our sleeping bags down. And that also promoted comradeship and that ties in with previous remarks. There was also always a certain amount of the people in the lab. against Calvin. Not against Calvin but the people in the lab. hanging together and here's Calvin over here. Now I have experienced that so many times as a professor later on. The professor sits in his office

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and the poor slaves are out here in the lab. working away and they think everything they are doing is their work. It is their hands, their work and their ideas and if the professor gets an idea and says something to them they forget that and it is their idea. So that it is the traditional tug between the graduate students and post-docs. versus the professor and myself and, I think, for Fuller and Stepka and the rest of it, we had no concept of this. Basically we didn't dislike Calvin at all but we would say, "Oh, he's the king, he's the boss, he asks the only questions in the seminars and nobody else opened their mouth until after he emptied his mind of questions"; that kind of stuff. Well, that tradition is actually in the Herr Professor tradition of Germany and Europe, in the European labs. It is a slightly different form but it's still there, even in the American environment where you are supposed to be...everybody is an individual and everybody is free there still has to be a leader that ties things together.

VM: Well, I think one of the points may be for young people, and it was a very young group at the time when you were there, it was an advantage for these young individuals to have their names associated with Calvin in their publications. For awhile, anyway.

NT: For awhile.

VM: Before they wanted to become independent.

NT: Particularly then when he got the Nobel Prize. Yes, that was the tradition.

VM: Yes. And I think Al is a clear example of that. Al, in time, went completely independent and no longer published with Calvin but in the early days he did.

NT: Yeah. But there again, when I talk to Al sometimes about his data on the glycine and the serine and the amino acid stuff which Fowden was also working on, Calvin didn't even want to be associated with it. It wasn't that Al went independent, I think that Calvin said, "that's not important". Calvin said, "I only want to be involved in electron transport in the photochemistry", at least when I talked to him.

VM: As I saw Calvin in the later period that I was there, up to 1971, what tended to happen was that Calvin had a series of enthusiasms: photosynthesis was one of his earliest ones, of course. But there were the moon rocks enthusiasm, the origin of life, the planaria, the finding the (*cure for*) cancer, and I left off the cancer enthusiasm. Each new one of these things, he was always associated intimately with what went on at the beginning and wrote the papers and then, after a while, he would move on to something else and leave people in place so the lab., in a sense, was a compendium of Calvin's ideas, one after the other, each represented by a research leader.

NT: True, true.

VM: And these people, then, became essentially independent of Calvin, as you say partly because Calvin was no longer so interested and partly because they, themselves, had become older and more responsible.

NT: Yeah, I agree completely. I used to see Calvin at meetings and I saw him in Moscow and we had him here for a Dow Symposium and all that kind of stuff, and you are right. He moved on, so to speak. But, at least in the photosynthesis field, he got off into the artificial rubber game, which was just not viable.

VM: And the *Euphorbia* oil...

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NT: That's right.

VM: Sure. He was always a person who came up with lots of ideas. One of the big advantages in the early days in the photosynthesis group was he had plenty of critics because everybody was so intimately involved that if Calvin came up with an idea which was something related to photosynthesis, there were half a dozen other people who were also very clued in on it who could immediately respond and criticise. But when he then began to develop into areas where he didn't have immediate colleagues, then there weren't people to criticise and people weren't so interested in criticising. So I think in that case he had less fine tuning going on.

NT: In the last of the '40s, Benson and Calvin published papers saying that the first product of photosynthesis was malic acid and they called it the "organic acid cycle". Then, with Bassham's thesis, they discovered the phosphate esters and developed the C_3 cycle. Now, what about that malic acid cycle? Was it wrong? How did they screw up? Point 1. Now the second point is that when I was there in the early '50s the group from Hawaii, the sugar cane industry from Hawaii, came to Calvin's lab. and I and Benson and Bassham sat down in that little office of Benson's and listened to them for a full day and they showed us their chromatograms on sugar cane and there was tons of malic and organic acids. We said, you must be wrong; you just can't be right. But it scared the hell out of us and essentially somebody at the time, and I would attribute it to Calvin's thought process, said, "Well, they're wrong and we'll just show them that they are wrong by publishing all of our data and outrunning them". And they did. They showed all of their data. But they were right because they were using a C_4 plant.

VM: The Hawaii people were?

NT: The Hawaii people were using a C_4 plant which was rediscovered again by Hatch and Slack. Now what about the early papers with Benson and Calvin? What I am showing now in Europe, which I hope we are showing (we've done preliminary experiments) is that as soon as you get up above the present level of air, you get up to 23% oxygen, you completely suppress the carboxylase activity and you only have the oxygenase activity of Rubisco, but you are still fixing CO_2 and that's why nobody discovered it. And you are still fixing CO_2 now by PEP-carboxylase into malic. Now Warburg made this mistake, and Benson/Bassham made this mistake, because they were growing algae on the shelf and putting it into a lollipop — a closed system. I have measured oxygen 100 times in these closed systems; the oxygen shoots right up and within minutes turns off the carboxylase and now you are making only malic. So they were seeing the C_2 cycle products. I can even explain their original data

VM: It has come full circle after 50 years.

NT: Full circle. They were right but they didn't tell exactly how they did their experiments.

VM: Very good.

NT: So I don't know...anyway, to me that full circle...

VM: That does it. Very nice, very good.

NT: I think it's too technical for your book.

VM: Well, that we'll have to wait and see but anyway this now really is a good place to leave the story, OK?

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NT: Right. We've full circled it.

VM: Full circled it.