

## Klaus Fischer (PSNA Phytochemistry Pioneer) ☆



Klaus Fischer was recognized by the PSNA in 2006 as a Phytochemistry Pioneer. Having retired from academic life in 2003, we were delighted to recognize him with this award. Below is a description of Klaus' scientific life, courtesy of PSNA, written by Klaus himself.

### “Ein Wanderer” and “Einwanderer” in Science

At the PSNA meeting in Merida, Mexico, I was asked by Peter Facchini to write an article for the PSNA Newsletter Series *Phytochemistry Pioneers*. After the very interesting readings of Neil Towers' “Memories of a Budding Scientist” and Ragai Ibrahim's “Journey in Plant Biochemistry”, I felt very honored to be in the good company of two phytochemists that I respect and admire. I have decided to write about individuals, that are my “Pioneers”, but not only in Phytochemistry. I wish to add individuals that have had significant influences on my career and my life in general from my childhood to the present.

At the Merida meeting, I showed a slide of Jeffrey Harborne, that I had taken in the fall of 1986 during the Phytochemical Society of Europe meeting in Lausanne, Switzerland. At the time of my presentation in Merida, I did not know that Jeffrey had died just one day before, on July 21, 2002. The photo resembles the way I wish to remember Jeffrey Harborne, a quiet, somewhat shy person. He made immense contributions to phytochemistry and chemical ecology as a scientist, an editor and as a prolific writer. As a writer, he was a critical analyst with a quick pen and a great gift for detecting and summarizing new

and significant contribution to our field of science. Jeffrey was never my mentor, but he has had a positive influence on my career and my life and has given me guidance in my budding years as a scientist. It is about individuals like Jeffrey that I wish to write about in this newsletter.

A brief comment on the above title. In the German language “Ein Wanderer” translates into “A Wanderer” on a journey. However, the English translation for “Einwanderer” is “Immigrant”. Both terms apply to my life's journey.

### My life's journey and scientific odyssey

I had no choice! I was born into Hitler's Third Reich three years before Second World War started. My family lived in a small farming community named Kunzendorf on the river Biele in the then German Province of Silesia, which is now a part of Poland. My father Ernst was a mechanic with a little repair shop for motor cycles and my mother Luzia took care of the Shell gas station. She very much enjoyed serving the customers, that were traveling to the popular health spa Bad Landeck; for my mother this represented a window to the world. My older brother Siegfried and I grew up in a caring, large family of farmers. Even the war years had little negative impact on our life, except that our father had been drafted in 1939, serving in the German Army from day one of the war. I wish to mention one little story from the war period. In 1943, a family from Bremen had been evacuated due to heavy bombardments of their hometown; “Oma Rabe”, “Mama Fifi” and her children Helga and Heiner lived next door in the house of my grandparents. During their short stay, I

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enjoyed the company of Helga, the girl from the big city. This girl is now my wife for over 30 years.

At the end of the Second World War, our carefree small-village life changed dramatically. My father did not return from the war; he was missing in action since 1944. Over 50 years later, in 1996, my mother was informed by the Red Cross, that father had died in a Russian prison camp near Wolgograd one month before the end of the war. Our mother was a widow at age 33 and never remarried until her death at age 90.

In April 1946, my mother, my brother and I had to leave Selesia just with our possessions that each of us could carry. After a long odyssey on railroad cattle cars, we were transported west and were resettled in a small village in Westfalia in the British Zone of Germany.

I went to Elementary School and then to Middle School in a neighboring town, which was rebuilding from heavy wartime bombardments. Our barrack-style classroom was used as a dancing hall on weekends. Books were uncommon during the first years after the war. Our teachers were strict, competent and very caring. I was an average student and chemistry was a particularly difficult subject for me; it simply did not turn me on. My science teacher, Dr. Ehlers, was not happy with my performance, but there was no laboratory experience. In addition, at that time my greatest interest and main passion was playing my violin, which I had acquired for very little money and had taught myself, playing for two to three hours every day. In school, my performance in chemistry was slowly drifting towards a failing grade. My brother Siegfried, who had been an excellent student at home in Selesia, loved chemistry, but was not able to continue his education due to the post-war turbulent times. He knew how to trigger my interest in chemistry. I received from him a present that gave new directions to my future life and career: a chemistry laboratory kit. My tortured violin had a long rest. Chemical experiments became my obsession; at graduation from Middle School in 1954, I received a B grade in chemistry; I had earned it and was very proud of it! After recognizing my sincere interest in chemistry, my science teacher recommended that I attend a 2-year school for Chemical Technicians (in German: Chemotechniker). One of the best programs was in Isny, a small south German town just north of Lindau on Lake Constance in the State of Wuertemberg–Hohenzollern. This very rigorous program emphasized laboratory techniques to prepare students for careers in industry and governmental laboratories. One of the most memorable events during the time in Isny was a 1955 class trip to Lindau to attend the annual Chemistry Nobel Laureate Meeting. There I was in the same room with the giants in the field. I remember standing near Staudinger, a natural products chemist in his early career; then he expanded his field to mimic the synthesis of natural polymers to become one of the fathers of synthetic polymer chemistry. I was excited but also saddened by the fact, that I could never be part of the academic community, since my middle school background was an academic dead end; a

high school degree was necessary to enter the University. For me a university degree had to remain a dream.

In my final examination in the spring of 1956, one of the outside examiners in organic chemistry was Professor Heinrich Hellmann from the University of Tuebingen, the man I am still very thankful for opening the door for my higher education.

After a very successful oral exam, he asked me about my future plans. I told him about my dilemma, that I had no choice but find a job in industry. To my greatest surprise, he pointed out that the State of Wuertemberg–Hohenzollern had introduced a new law, which allowed qualified student from technical schools in the state to study in their field at the University of Tuebingen. This university is one of the oldest in Germany, founded in 1477. I was the first member of our greater family who had the opportunity to receive a university education.

After Second World War, Tuebingen held a unique position in the German academic world. The city was untouched by the war and many eminent scientists, including a number of Nobel Laureates, were on the faculty at this university. The director of the Chemistry Institute was George Wittig, who was transferring to the University of Heidelberg in 1956, but his Nobel Prize winning research was done in Tuebingen. The Nobel Laureate Adolf Butenandt of adrenal cortical hormone fame (Nobel Prize together with Ruzicka, 1939) was forced by the Nazi regime to decline, but he accepted the Prize after the war. Butenandt was also the discoverer of insect sex pheromones. I vividly remember the weekly seminars, which were impressive “performances” by the faculty and the visiting speakers. From a student’s point of view, these were intimidating gatherings. Attendance was mandatory from the chemistry freshmen to the almighty German Professor. Students rarely asked questions, but in my first year, I asked a visiting speaker about the stability of organic compounds exposed to X-ray irradiation, then a powerful novel area of structure determination. The new director of the Institute of Organic Chemistry (his name will not be mentioned) stood up and shouted into the audience: “What a stupid question!” I was thankful that the speaker cited several examples of instability of compounds during X-ray analysis, but the damage was done. This was my first and last question I asked in my student career and many years thereafter. This man might have been a good scientist, an educator he was not! But I learned a great lesson the hard way with a very positive outcome. I never forgot this incident and it made me a better and more respectful and caring educator and mentor of my students and postdoctorals in my later academic career.

After my undergraduate years from 1957 to 1961, I joined the research group of a young Dozent, a brilliant young chemist and pianist, Guenther Opitz, who came out of Butenandt’s research group and later became Wittig’s successor in Heidelberg.

My dissertation research was a synthetic-mechanistic project directed towards the formation and chemistry of

sulfene, a group of ketene analogs. After major initial difficulties, the research project had a positive ending. This new and novel method for the synthesis of alkenes from aliphatic sulfonic acids is a variation of the Wittig alkene synthesis.

After my graduation in the summer of 1965, I wanted to get the “American experience”, and do a year of postdoctoral work in the United States or Canada. My application had a very fast positive response from Tom Mabry, who at that time was rapidly building a cutting edge natural products research program in the Department of Botany at the University of Texas in Austin. As I learned later, it was pure luck. My letter had arrived on the same day when Jacques Kagan had informed Tom, that he was leaving for a faculty position at the University of Illinois at Chicago. My postdoctoral experience in Tom’s lab was exciting and refreshing after several grinding years in graduate school. His graduate students Al Wohlpert and Gene Miller and the postdoctorals Ken Markham from New Zealand and Mike Thomas from England introduced me to natural products chemistry and NMR spectroscopy. Mike and Ken were working with Tom on the classic book on flavonoids. On a private note, I will always fondly remember Mike and I watching the soccer world championship final between England and Germany; it was a great game, but Mike had the last laugh.

Tom, a typical Texan, was contagiously enthusiastic, encouraging and very generous; it was a carefree and enjoyable period and we worked hard and played hard. In Tom’s research program, the application of natural products toward the new field of chemotaxonomy used different chemical markers. I was introduced into the sesquiterpene lactone area by Gene Miller. Tom brought many eminent scientists to the UT campus. Visiting professors during this time were Jacques’ brother, Henry Kagan from France, and “Mr. Chemical Fundamentalist” André Dreiding from the University of Zurich.

During the spring semester 1966, the whole research group was actively involved in the planning of the logistics of the sixth annual meeting of the Plant Phenolics Group of North America. The organizers chose as a Symposium topic “The role of chemistry in modern biology” with emphasis on the use of natural products in systematic botany. Many of the big names in the field attended the meeting: Holger Erdtman from Sweden, Ted Geissman from UCLA, Hans Grisebach from Freiburg, Germany and Werner Herz among others. The meeting was a great success and several months later led to a reorganization of the Phenolics Group into the Phytochemical Society of North America. Our society, the PSNA was born and Tom Mabry was the first president.

In early 1967, we attended the first Mardi Gras Symposium in Organic Chemistry at Louisiana State University (LSU) in Baton Rouge. The chemistry department at LSU was also looking for a natural products chemist. After the obligatory interview process, I joined the LSU faculty in August 1967, in spite of my DSP-66 visa. My

laboratory had no air conditioning and running chromatographic columns was nearly impossible in this tropical summer climate. But I was able to get some research done, usually late at night due to the extreme heat during the day. My first paper at LSU was in collaboration with the NMR specialist, the late Norman Bhacca. We determined the conformation in solution of a germacranolide-type sesquiterpene lactone by the then novel method, the Nuclear Overhauser Effect. *Tetrahedron Letters* turned us down, but the prestigious chemistry journal *Chemical Communications* accepted without changes this frequently referenced paper.

The dean of our college was very optimistic about getting my visa changed, but in the spring of 1968, I was informed that I had to return to Germany for at least 2 years, before I could apply for a green card. Back to Europe! At the time it appeared that my career was put on hold, but looking back, it was a blessing in disguise. I joined Dreiding’s group in Zurich and learned from the master in the fundamentals of organic chemistry, in particular, stereochemistry. Our group meetings were exercises in the logic of approaching chemical problems with stereochemistry representing the foundation of all considerations. My research project contributed to the understanding of the biosynthesis of the betalamic acid portion of betalains from dopa. Contrary to the previous hypothesis, these alkaloidal pigments in cacti and red beet were formed by aromatic cleavage, not between but next to the catechol moiety of dopa. This unexpected pathway is found in one biosynthesis textbook; my only contribution to the teaching literature.

After returning to LSU in the summer of 1970, the days were filled with teaching and the nights with research. In collaboration with Tod Stuessy at Ohio State, whom I knew from his graduate years in Austin, an extensive chemical study of the genus *Melampodium* was initiated. Tod and his students provided us with very valuable plant collections from Texas to Central America. The chemical analyses occupied our efforts for a whole decade with multiple new structures and publications on the isolation, structure elucidation and chemistry of the melampolide-type sesquiterpene lactones. Now my strong stereochemical foundation gained in Zurich paid off in the extensive configurational and conformational analyses of sesquiterpene lactones. *Melampodium* and several hard-working graduate students secured my tenure and promotion to Associate and Full Professor at LSU – many, many thanks!

My first sabbatical in the fall of 1977 was spent in Ferdinand Bohlmann’s laboratory in Berlin, Germany. I had first met Bohlmann in Monterrey, Mexico, where I was a regular attendee of Xorge Dominguez’s annual natural products symposia. Bohlmann was hard to approach and the word arrogant came to mind. After knowing him better, I learned that he was a shy person. After extensive investigations of polyacetylenes, Bohlmann had entered the terpenoid field and produced many publications on the chemical constituents of the Compositae. He was one

of the ten most prolific authors worldwide and I often referred to *Phytochemistry* as the “Bohlmann journal”. He had the discipline of a Prussian officer. He arrived early in the morning, taught his organic chemistry class at 7:30 a.m. and then set up a chromatographic column. In a lab saturated with ether/petroleum ether, he generally took care of his correspondence at the lab bench while collecting fractions. Generally, he completed one plant extract per day, ran all necessary spectroscopic data and interpreted them on the spot. At noon he disappeared to his office and wrote the manuscript. His photographic memory was an invaluable plus in structural work! I learned then that some people are more equal than others.

While in Berlin, my wife Helga and I started collecting the literature for a comprehensive review on sesquiterpene lactones in the Zechmeister series, *Progress in the Chemistry of Organic Natural Products*. This review of nearly 350 pages appeared in 1979, covering close to 1000 naturally occurring lactones. During the early 1980s, we investigated the chemistry of several major genera of the Asteraceae, mainly *Calea*. A collecting trip with my friend and LSU taxonomy colleague Lowell Urbatsch to Jamaica and the mountain areas of Venezuela is still a very pleasant memory.

More and more sesquiterpene lactone papers appeared in the literature; this field had become a mature area of research and it was time to move on. At that time, Bruce Williamson, a fire ecologist joined the LSU Botany faculty. He got me excited about his fire hypothesis related to the long-standing question, why the Florida Scrub and the adjacent Sandhill plant communities remained separate entities over time. Our investigations led to a number of significant chemical and ecological findings related to plant-plant interactions (allelopathy) in several dominant species in the Florida Scrub. The most significant and exciting outcome included the first case of a photochemical activation of non-toxic plant constituents into potent phytotoxins in a cascade of chemical events. We had great fun and convincing results, but the contribution of allelopathy in plant-plant interactions seems to be still in the doghouse of chemical ecology. I learned then that scientists can be a highly conservative bunch.

Another collaborative project at that time involved Hector Flores in Plant Pathology and Martin Hjortso in Chemical Engineering at LSU. We studied the biotechnological potential of “hairy root” cultures and learned that “hairy roots” are excellent systems for studying biosynthetic pathways of root constituents, using  $^{13}\text{C}$  labeled precursors.

The 1990s were highly active years of a collaborative bioassay-guided search for anti-tuberculosis agents from

higher plants. Again, our collaboration with Scott Franzblau, then at the Hanson’s Disease Center stationed at LSU, provided no new anti-TB drugs, but we learned about many essential structural features from our structure-activity studies essential for future developments.

After 32 years on the LSU faculty, I retired and moved to the Magnolia State Mississippi. I joined the Department of Pharmacognosy in the School of Pharmacy at the University of Mississippi (Ole Miss) as Professor and Chair and, as a balance to my administrative duties, find enjoyment in the study of the genus *Magnolia* and related taxa, retiring in 2003.

### Epilog

Looking back on a career of over 35 years of research in natural products chemistry, I realize now that we had extensive and highly successful collaborations between our chemistry group and scientists in various areas of biology. This was well before most granting agencies knew how to spell the word “collaborations”. I accept that these areas of science are now “mature”, and have lost the cutting edge status in modern natural products research. But long-lasting friendships grew out of our scientifically rewarding endeavors. These close friendships with colleagues, former students, postdoctorals and visiting scientists still remain when all the scientific accomplishments disappear into the shadows of new findings and developments. My journey as an active researcher is now slowly coming to an end and I am observing with great interest the new developments that advance the field of Phytochemistry to the next level of understanding. The new tools of molecular biology provide insight into the formation, location and ecological function of natural products. Understanding all details of biosynthetic pathways as well as the pharmacological functions of natural products will not only provide new knowledge but lead to new sources for medicinal drugs and agriculturally useful products.

After a long journey, the “wanderer’s cane” in the field of natural products is now in the hands of the next generation of scientists. All my best wishes for the journey. Don’t forget that it is not the destiny but the journey that makes our lives interesting and fulfilling.

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