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A Biographical Memoir by

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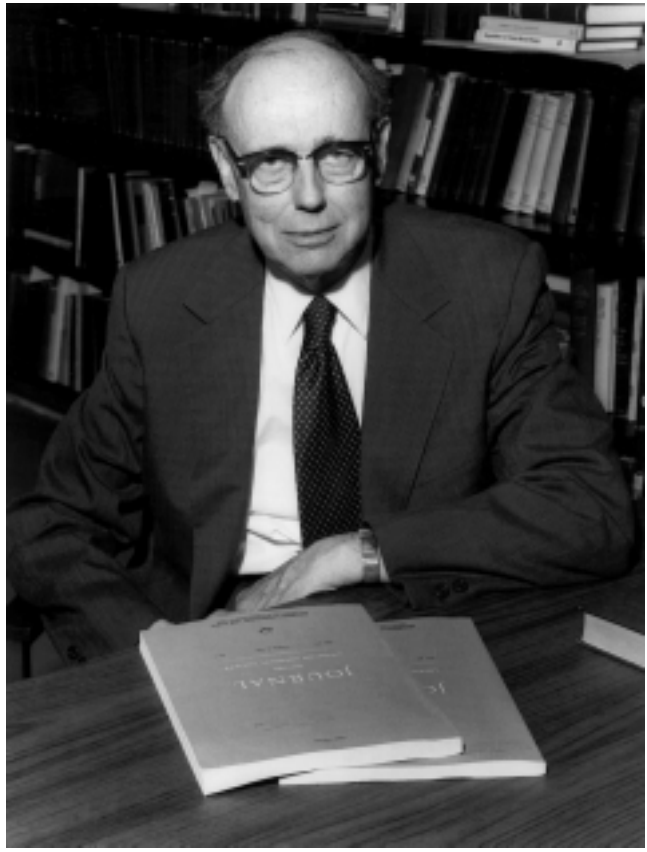

Courtesy of William Tarbell, Bolingbrook, Illinois

Dear Stanley Tarbell

DEAN STANLEY TARBELL

October 19, 1913–May 26, 1999

BY NELSON J. LEONARD

DEAN STANLEY TARBELL had a distinguished career in research and teaching in organic chemistry. His contributions to physical organic chemistry included elucidation of addition reactions to olefins, determination of intermediates in the Claisen rearrangement of allyl aryl ethers, and quantitative comparison of the behavior of organo sulfur versus organo oxygen compounds. He discovered new categories of organic compounds, including mixed carboxylic-carbonic anhydrides, and delineated their chemistry. He established the structures of important natural products, notably those of colchicine, which arrests the process of cell division in plants and animals, and the antibiotic fumagillin, which has emerged as an inhibitor of angiogenesis.

In the course of his research, Tarbell also contributed substantially to the methodology of organic synthesis. The University of Rochester and Vanderbilt University, in turn, benefited greatly from his presence on their faculties, and he was most effective in his role as a teacher and a director of research for many, many students. He also established himself, along with his wife, Ann, as a biographer of chemists and historian of science. A true scholar of language as well as history, he could read Latin, French, German, Classical

Greek, and Arabic, and he enjoyed such reading, especially in his retirement.

Stanley Tarbell was born on October 19, 1913, in Hancock, New Hampshire, on a farm that had been in the family since the settlement of the village. His older sister Irene and he constituted the seventh generation of the family to have lived there. The earliest Tarbell in the colonies was one Thomas Tarbell, who lived near Boston around 1650. When Stan was studying Caesar's Commentaries in high school, he was amused to read of an obscure tribe called the Tarbelli who lived in the Pyrenees, but the potential link to the forebears' name in England was not established! The descendants of Thomas Tarbell moved to Groton, Massachusetts, and worked their way westward along the New Hampshire-Massachusetts border. Stan's grandfather, Joseph A. Tarbell, married Amaret Lakin of the ancestral farm in Hancock. Stan's father, Sanford McClellan Tarbell, remained on the farm and raised hay, apples, hens, and Morgan horses, while establishing himself as a harness maker and forger. Stan's mother, Ethel Milliken Tarbell, was born in Alstead, New Hampshire, the daughter of Charles A. and Eva Strickland Milliken. The Milliken family could also be traced to pre-revolutionary times, and ancestors on both sides of Stan's family fought in the Revolutionary and Civil Wars.

Neither parent had received much formal education, but they sacrificed in order to provide it for Irene, Stan, and his younger sister, Elva. The family moved to Antrim, New Hampshire, and into a house near the school in that village. After two years there was another move, this time to Winchester, New Hampshire, to a large house that remained in the family until 1995. Stan went through Winchester schools until he started college. He recalled for us in his self-published 1966 *Autobiography* the many seasonal family chores for which he was responsible. He was paid for help-

ing the neighbors, pumping the bellows for the pipe organ in the Universalist Church, and also loading and aiming the trap for clay pigeon shooting at the local gun club. His childhood fascination with baseball and books grew into major hobbies in later life. In the case of baseball, that meant attendance at the games of the professional team located wherever he lived.

Thayer High School in Winchester had excellent teachers. The college preparatory course consisted of four years of Latin, French, English, and mathematics, along with courses in history and physics. Stan learned some German by studying informally with the Reverend Mr. Houghton of the Universalist Church, who, along with Stan's mother, father, and sister Irene, encouraged him to apply to Harvard College and to take the College Boards, which qualified him for admission. A tuition scholarship of $400 from the New Hampshire Harvard Club and $750 in savings supported Stan's freshman year. He was sustained in subsequent years by scholarships, savings from summer work at a YMCA camp and in a tannery, and by a loan from Irene (which he repaid within the family by a loan to Elva when she attended Middlebury College).

At Harvard, a course in organic chemistry taught by Louis Fieser led Stan to consider specializing in that subject, but he was proudest of his performance in a German course devoted to the reading of Goethe, which he took in his junior year. He felt fortunate also to have taken a course in advanced organic chemistry with E. P. Kohler in his senior year, which reaffirmed his previously aroused interest. Any real pleasure as an undergraduate seemed to be derived mainly from Stan's friendships at Lowell House and its excellent library and record collection. His acquaintance with symphonic music was enhanced by regular appearances of Serge Koussevitzky and the Boston Symphony in Sanders

Theatre. As Stan approached graduation, he did not receive any guidance in applying for a job or for a graduate assistantship at Harvard or elsewhere. However, through a series of fortunate coincidences (his words), he was provided with a tuition fellowship for one year of graduate work at Harvard. Stan earned or borrowed money necessary for living expenses. He elected to do research with Paul Bartlett, with whom he received training in physical organic chemistry and chemical kinetics. Employed by Bartlett during the summer after his first graduate year, Stan worked on a project that indicated the addition of halogens to a carbon-carbon double bond was a two-stage process; the first stage was an electrophilic attack by halogen. During his second year, Stan obtained results on the halogenation of dimethylmaleic anhydride that reinforced the earlier findings. The papers, published in the *Journal of the American Chemical Society*, that described the halogenation work were cited in 1938 when Bartlett received the Langmuir Prize of the American Chemical Society.

During Stan's third graduate year at Harvard, he obtained an assistantship at Radcliffe College, where he taught laboratory courses in organic chemistry. There he met his future wife, Ann Tracy, who graduated from Radcliffe that year and subsequently qualified for a Ph.D. degree with Robert C. Elderfield at Columbia University. Stan spoke warmly of the friends he had during the graduate years, including Charles Stauffer, Charles C. Price III, and Charles K. Bradsher, with whom he shared the interests of tennis, squash, and, in the case of the third Charlie, travel by bicycle through Germany in the summer of 1937. This Charlie and Stan had actually completed their Ph.D. theses and examinations half way through their third year. In September they set out together for the University of Illinois and postdoctoral positions, Charles with Reynold C. Fuson and Stan with

Roger Adams. After a year at Illinois, Stan felt more attached to that university than he did to Harvard (his words). He found that the organic chemistry faculty members consisting of Adams, Marvel, Fuson, and Shriner were notable for the harmonious way they worked together and for their scientific performance. Also striking was the size of the Illinois group of graduate students, their very high morale, and their devotion to the school and its faculty (again, his words).

Stan obtained a teaching position in 1938 at the University of Rochester, where W. Albert Noyes, Jr., head of the Department of Chemistry, also presented him with the challenge of building an outstanding program in organic chemistry. This he did in the course of his almost 30 years on the Rochester faculty. During his first year at the university, Stan had one graduate student, Clay Weaver, and worked diligently in the laboratory himself. He collaborated with John F. Kincaid, a new instructor in physical chemistry, with whom Stan shared an office, in a kinetic study of the Claisen rearrangement of allyl aryl ethers in solution. They applied transition-state theory to the reaction and obtained its entropy of activation, which was apparently the first time this had been done for an organic reaction. They learned that the reaction was first-order and unimolecular for migration of the allyl group to both the ortho and para positions. The results indicated a highly ordered transition state, which they suggested to be the same for both ortho and para migrations. This conclusion was shown subsequently to be correct by an accumulation of evidence from other laboratories.

Stan trained new graduate students on problems concerned with novel aspects of the Claisen rearrangement, while emphasis on the kinetic aspects became secondary to the synthesis and determination of the scope of the reaction. Other investigations included the finding that the reaction

of phenyl isocyanate with phenols was catalyzed by Lewis acids and bases. The observation of catalysis was important in the later development of polyurethane polymers from diisocyanates and polyhydroxy compounds. Stan and his students discovered a new method for the synthesis of sulfilimines, R_2SNSO_2R', and determined the products of the rearrangement of benzyl ethers of representative salicylic acids. With the entrance of the United States in the Second World War, Stan became involved in defense contract research that included methods for the detection of toxic agents, in particular arsenical compounds, and synthesis and testing of compounds for antimalarial activity.

Beyond the 1942-45 responsibilities remained the obligations of building the Rochester faculty in organic chemistry, helping to raise a family, and continuing a program of outstanding research and teaching.

BUILDING THE ROCHESTER FACULTY

Theodore Cairns, with a Ph.D. from the University of Illinois, was added to the faculty in 1939, but he left in 1941 for the beginning of a distinguished career at DuPont. Warren McPhee, with a Northwestern Ph.D. followed by a postdoctoral year with Roger Adams, was his replacement, and Marshall Gates, who received his Harvard Ph.D. with Louis Fieser, was added in that same year. True to Fieser's expectation, Marshall would become a leader in American chemistry. Robert Carlin, another University of Illinois postdoctorate who followed McPhee as an instructor in organic chemistry, left to take a position at Carnegie Institute of Technology. His position was then filled by Virgil Boekelheide, a Minnesota Ph.D. with C. F. Koelsch, who was in 1946 an instructor at the University of Illinois. Virgil had the added responsibility of looking after Stan's research program while Stan activated a war-delayed Guggenheim

Fellowship of a year at the University of Oxford. Stan regarded this a "superb appointment," and here is a quotation from Virgil Boekelheide, reprinted with his permission.

> After I moved to Rochester, Stan and I worked together extremely well. Our ideas of how things should be done were in complete agreement. So he went off to Oxford on his Guggenheim Fellowship, and I took over the supervision of his graduate students as well as my own. The excellent relationship between Stan and me continued in the following years. . . . In 1960 the University of Oregon offered me an appointment of a Professorship. . . If I moved to Oregon my long-standing relationship with Stan Tarbell would be broken and this would be a considerable loss. . . . Eventually, I chose the challenge (1960) of Oregon even at the cost of weakening my close relationship with Stan Tarbell.

The triumvirate of Tarbell, Gates, and Boekelheide guaranteed a Rochester tradition for organic chemistry and for further outstanding faculty appointments.

HELPING TO RAISE A FAMILY

In 1942 Stan married Ann Tracy, whom he had met when he was lecturing at Radcliffe, as mentioned earlier. The Tracy forebears were numerous, far flung, and distinguished. Her parents were William and Edith Jackson Tracy, and Ann was born in Helena, Montana. Following her undergraduate and graduate work, Ann had returned to Radcliffe for two years of postdoctorate research in biochemistry prior to her marriage. With the move to Rochester, she was recruited to teach a laboratory course in biochemistry in the medical school of the university and, further, to set up an analytical laboratory (for a division of the Manhattan Project) that had been organized to study the toxicity and pharmacology of substances involved in the atomic bomb program. She ran the laboratory successfully for nearly two years, until the end of the Second World War and the beginning

of the family: William in October 1945, Linda in July 1948, and Theodore in November 1950. The usual domestic, school, and community activities were supplemented by hikes, baseball, and sailing on Lake Ontario, a family displacement to Stanford University during Stan's second Guggenheim Fellowship, 1961-62, and later travel through Europe. The family's move to Nashville, Tennessee, proceeded smoothly with Stan's appointment as a distinguished professor at Vanderbilt.

CONTINUING A PROGRAM OF RESEARCH AND TEACHING

Stan was a splendid teacher, whether assisting in the organic chemistry laboratory at Rochester (his first assignment), giving advanced lectures for graduate students (his second assignment), or instituting departmental and research group seminars (including self-assigned presentations). He had a remarkable memory and an enthusiasm tinged with the appropriate amount of scientific skepticism. His droll sense of humor stimulated the more perceptive students. He believed that self-education was the best education, and he inspired, occasionally goaded, students to think for themselves. In pursuing his goal of developing a recognized center for training and research in organic chemistry at both undergraduate and graduate levels, Stan concentrated on supplying the necessary physical resources, such as library, stockroom, research equipment, and advanced instrumentation. He introduced undergraduates to research and found appointments for them in other graduate schools while recruiting the best possible graduate students for Rochester. The roster of Stan's coauthors is replete with the names of presently well-known professors and industrial, especially pharmaceutical, researchers of established reputation. I rely on the words of Sidney M. Hecht, presently John W. Mallet professor of chemistry and professor of biology at the University of Virginia,

for providing a sense of the research training environment at Rochester:

I had the good fortune to be able to join Stan Tarbell's research group following my second year in college at the University of Rochester. Stan was deeply involved in the chemistry of fumagillin and I was given a project exploring some of the transformations envisioned as part of an eventual total synthesis, as well as a graduate student mentor in the laboratory (David Brust) to guide my initial day-to-day efforts. The choice of projects reflected Stan's thorough, scholarly style. Although less obvious at the time, it also reflected his ability to identify important problems; fumagillin has emerged as an intensively studied inhibitor of angiogenesis, apparently operating by inhibition of one isozyme of methionine aminopeptidase.

Stan was an excellent mentor, always willing to listen to new research results and provide advice, always supportive of his students. He previewed my first public research presentation personally and made several suggestions about the timing and style of my talk, a couple of which I sometimes quote to my own students. Along with his wife, Ann, and whichever of his children were at home, he also hosted a number of social events for his group, including picnics in the summer and dinners at his home during the December holidays.

Throughout my time in the Tarbell laboratory, there was a steady stream of visits from his former students. Stan's determination to stay in touch with his former coworkers was reflected in his policy of encouraging his coworkers to take their notebooks with them when they left; if there was any need for clarification of experiments that had been run, or access to data or procedures, Stan knew how to get in touch with each former student. Therefore, it was a constant source of pleasure but no surprise that Stan and I kept in touch, through correspondence and visits, for more than 25 years after my graduation from Rochester. Ambitious undergraduate researchers have always been welcome in my laboratory, as a reflection of my gratitude to Stan for the opportunity I was given.

Let me return to the research highlights that marked Stan's Rochester years. He became interested in colchicine, a compound that is isolated from the bulbs of the autumn crocus. It arrests the process of division in plant and animal cells and is used medically in the treatment of gout. The

Rochester team provided independent evidence for the presence of the seven-membered B ring and experimental evidence to support Dewar's postulate that ring C was a seven-membered ring of the tropolone type, which was of special interest. Stan followed the structural work with a study of the reactions of colchicine and with syntheses directed toward colchicine and its derivatives. Over a 10-year period, Stan and his students determined the contrasting behavior between series of organic sulfur compounds and the corresponding organic oxygen compounds, including the discovery of the generality of isomerization by base of alkyl allyl sulfides to alkyl propenyl sulfides and elucidation of the mechanism. Another ongoing investigation was concentrated on the synthesis, isolation, thermal decomposition, and reactions of mixed anhydrides: carboxylic carbonic anhydrides, carboxylic dithiocarbamic anhydrides, formic carbonic anhydride, carboxylic thiocarbonic anhydride, dicarbonates, and tricarbonates. This investigation added another dimension for understanding the differences in behavior of sulfur- versus oxygen-containing compounds. A major contribution was Stan's demonstrated use of di-t-butyl dicarbonate (di-t-butyl pyrocarbonate) for 1°-amino protection. His reagent now finds universal use for amino acid protection in automated peptide synthesis.

In 1950 Stan started to work on the structure of the antibiotic fumagillin, which had anti-parasitic and anti-tumor activity and which had been given to him by Abbott Laboratories. Only near the end of the problem could conventional structure establishment by degradation, analysis, partial synthesis, and direct comparison of the separate moieties be augmented by nuclear magnetic resonance spectroscopy. The compound and most of its derivatives had no characteristic ultraviolet or infrared spectra, many were noncrystalline, separable only by chromatography, and detectable

by optical rotation. Nevertheless, the combined efforts of graduate and undergraduate students and postdoctorates explored the novel chemistry thoroughly and accumulated sufficient evidence for the assignment of the complete structure and absolute stereochemistry. A massive paper combined all of the chemical conversions and intermediate structures in a magnificent analysis of the chemistry of fumagillin. Examination of other natural products included the erythrina alkaloids that had muscle-relaxing activity. An initial cooperative study with Virgil Boekelheide was continued in depth by Virgil while Stan maintained an observant interest.

It was about this time, in 1964, that Stan acquiesced to become chairman of the Department of Chemistry and to plan to meet the needs of space and money. The administration of the university responded positively to a 50-page report, prepared by a faculty committee under Stan's chairmanship, that made recommendations for the future direction of the chemistry department. A visiting committee, of which I happened to be a member, helped to convince President Allen Wallis that the funds allocated for a new building for chemistry and related sciences should be augmented by a reasonable percentage to provide necessary new equipment. The report, without much change, was also used in an application to the National Science Foundation for a Center of Excellence grant that was successful during Stan's chairmanship and was fully implemented under his successor, William H. Saunders, Jr.

Another university, however, namely Vanderbilt, had also received Center of Excellence grant that contained provision for making a senior appointment in chemistry at the newly created grade of distinguished professor, which was offered to Stan. Although he did not particularly care for the title, he and Ann finally decided to leave Rochester for the challenges of a different university and city, a different

section of the country, new colleagues to work with, and a new community to know. The graduate students and two postdoctorates who accompanied Stan from Rochester soon had a lively research program going and were joined by Vanderbilt undergraduate and graduate students. The Tarbells were received most cordially by the university people. Ann joined the Nashville chapter of the Tennessee Ornithological Society and became an active bird watcher and licensed bird bander. She also did volunteer work for the Vanderbilt Children's Hospital, for example, tutoring a girl patient in chemistry to enable her to obtain her high school diploma. Stan's teaching responsibilities were similar to those he had had at Rochester. Travels out of Nashville were associated mainly with family occasions and visits to see children and grandchildren, in addition to Stan's professional travels to meetings and for lectures at various colleges in Tennessee and adjoining states. His research continued to provide new methodology for synthesis, both general and specific. He developed further the chemistry of organic dicarbonates and tricarbonates. To all this he added fundamental studies on the carbon basicity of nitrogen in organic compounds and on the hydrolysis of ethers and anhydrides, which he followed by ^{18}O-labeling. Stan's interest was aroused by another antibiotic available from Abbott Laboratories, ristocetin. He initiated a study of its structure and chemistry at Rochester and continued the investigation at Vanderbilt, but then turned the problem over to his colleagues Thomas M. Harris and Constance M. Harris, who ably unraveled the complicated structure. This was consistent with Stan's feeling, developed after some years at Vanderbilt, that Ph.D. students would be better off working for his colleagues rather than for him.

His sustained interest in history in general was behind his decision to write a history of organic chemistry in the

United States from 1875 to 1955. Stan and Ann together approached this task with the knowledge, diligence, and thoroughness that characterized their previous work in science. They examined practically every paper on organic chemistry that had been published by an American in U.S. or foreign publications during the selected 80-year period, starting with the recognition of chemistry as a profession. The product was an eminently readable collection of essays that recounts the genesis and development of important ideas and experiments and takes into account the social milieu in which the science was done in the United States. To cement Stan's purpose to switch to history, he had joined the History of Science Society and the History Division of the American Chemical Society upon their return from a sabbatical leave in 1974. Both Tarbells began giving papers on leading American organic chemists and they published full articles based upon these presentations. They wrote about discoveries and developments that were crucial to the field. Possibly their greatest joint contribution was the definitive biography of Roger Adams, which actually appeared while they were accumulating material for the volume on the history of organic chemistry in the United States. The Dexter Award of the Division of the History of Chemistry of the American Chemical Society was bestowed in 1989.

Stan was of special service to Vanderbilt in chairing a committee to study the Ph.D. programs at the university. The report made specific recommendations to the Vanderbilt administration, many of them requiring additional funds for graduate work. Although the administration received the report with reserve (Stan's words), many of the recommendations were implemented gradually over the years. The report provided a statement of accomplishments in the past, a charter for the present, and some solid goals for the future. In keeping with academic practice, visiting committees

examined the programs of the individual departments, and I again had the opportunity of serving on a visiting committee for chemistry.

June 15, 1981, was "Stan's Day" at Vanderbilt University and consisted of "a modest tribute to a distinguished American chemist, D. Stanley Tarbell, by a few of his friends and colleagues" to mark his retirement. It would also have been appropriate to call it a distinguished tribute to a modest American chemist, for such were the characteristics of the speakers and the honoree. David J. Wilson and Thomas M. Harris have given me permission to quote from their memorial statement to the faculty of the College of Arts and Science on May 26, 1999, after Stan had died following a long illness:

> Stan was a true scholar with wide-ranging interests. At one point in his youth, he learned Arabic so that he could read the *Koran*. Another time he learned classical Italian so that he would be able to read Dante's *Inferno*. He was a music lover and a lifelong baseball fan. He became a loyal supporter of the Sounds upon his move to Nashville. We loved Stan for his dry wit and deeply respected him as a colleague. He was a man of few words but the words he spoke were always important. He could be relied on for his level head and excellent judgment on University affairs. He would go to great lengths to help his students, even many years after they had departed. He was very generous to the younger members of the faculty. An excellent example of this occurred when we were trying to hire him away from Rochester. The Dean asked Stan how much salary it would take to get him to move here. Stan replied he did not need a raise and that he would prefer to have the money given to the assistant professors.

Stan was generous with his time and his wisdom in service on many national boards: National Science Foundation selection committees, pre- and postdoctoral; National Institutes of Health, Medicinal Chemistry Study Section B, of which he was the chair during 1964-68; National Research Council Advisory Committee to the U.S. Quartermaster Corps

Laboratory, Natick; American Chemical Society Committee on Professional Training and chairman of the Division of the History of Chemistry; National Cancer Chemotherapy Committee; a panel of the Walter Reed Army Institute of Research; the Marshall Scholarships Selection Committee, southeast region; and the advisory board of the Beckman Center for the History of Chemistry, University of Pennsylvania. He was elected to the National Academy of Sciences and the American Academy of Arts and Sciences. He was fundamentally a scholar and a teacher, and he brought both personae to every enterprise of which he became a part. In considering his own career, Stan deemed it lucky, varied, absorbing, and productive.

I AM MOST GRATEFUL to Virgil Boekelheide, Sid Hecht, Tom Harris, Dave Wilson, and Bill and Ted Tarbell for the information they provided. I was also guided by the material that Stan himself placed on file in the Office of the Home Secretary of the National Academy of Sciences and, of course, by Stan's lucid *Autobiography*. It was my pleasure to serve under Stan's chairmanship on the NIH Medicinal Chemistry Study Section B, which gave me faith in the peer judgment process, and to see him at innumerable chemistry meetings and symposia during our parallel careers in the profession.

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