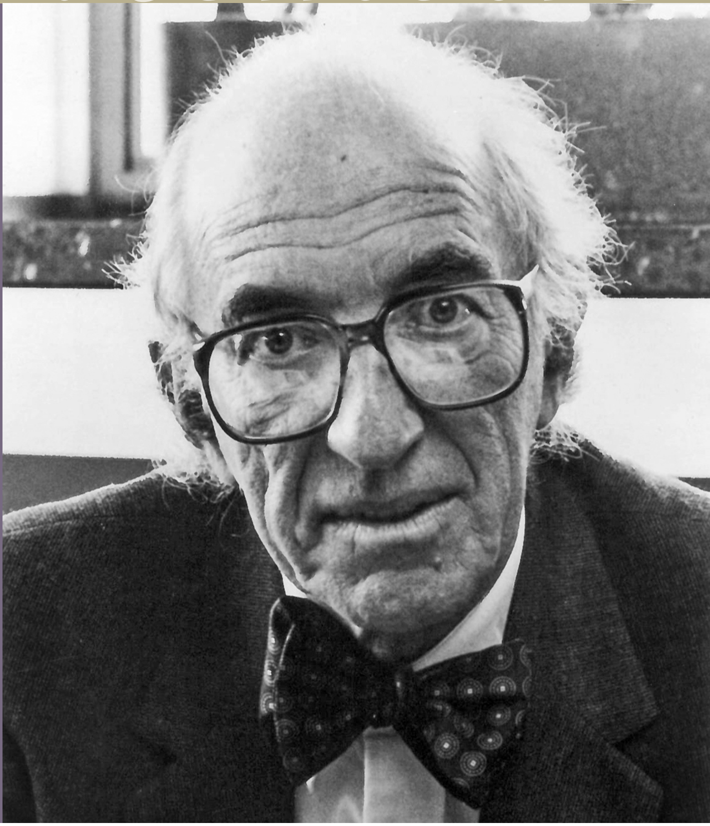
Stanley J. Cristol

1926–2008

BIOGRAPHICAL *Memoirs*



A Biographical Memoir by
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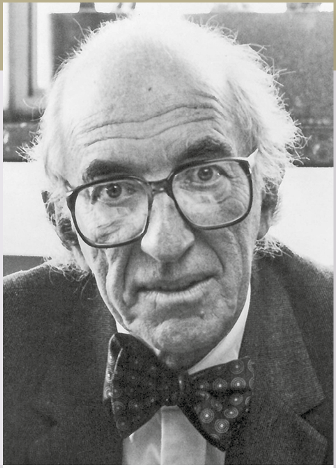
STANLEY J. **CRISTOL**

June 14, 1916–January 23, 2008

Elected to the NAS, 1972



By Charles H. DePuy

Stanley J. Cristol was one of the pioneers of physical-organic chemistry, a field that flowered in the United States during the years following World War II. He was born in Chicago, Illinois, of immigrant parents; his father, Myer J. Cristol, came from Cork, Ireland, where he had served as mayor, and Stan's mother, Lillian B. Young Cristol, hailed from Lithuania. Both of them came to the United States as young adults, his mother after a significant stay in England. Stan attended the Chicago public schools, and his interest in chemistry, as with so many of his generation, grew out of his fascination with a Chemcraft set and was reinforced by interaction with an excellent high-school teacher.

Stan received a B.S. degree with highest distinction from Northwestern University in 1937, having been elected to the Marcy Scholarship in his senior year. As a junior he worked in the laboratory of Charles D. Hurd and as a senior in the lab of Malcolm Dole. At Hurd's suggestion, Stan applied for graduate work at UCLA, which was then in the process of expanding course offerings and building a new campus. After a year, in which he later reported that he spent as much time as possible at the nearby beaches, he decided to take a break from school and accept a position in the research department of the Standard Oil Company of California. There Stan studied the catalytic aromatization of hydrocarbons, a process that became a very important source of high-octane fuel and a critical step for producing the high explosive TNT—both of which were required by the Allies during World War II.

Stan returned to UCLA in the fall of 1941, where the Department of Chemistry had started to blossom under the leadership of William G. Young, who had brought in three outstanding young organic chemists—Theodore A. Geissman, Thomas L. Jacobs, and Saul Winstein—and was assembling an excellent group of graduate students, including Lawrence J. Andrews and John D. Roberts. Stan did his doctoral research under Young, a pioneer in the study of allylic rearrangements, by investigating the stereochemistry of iodideion-promoted eliminations from isomeric dibromides; he also did preliminary work related to the synthesis of Vitamin A. After being awarded his Ph.D. degree in 1943 (the fifth awarded in organic chemistry at UCLA) he spent a postdoctoral year at the University of Illinois with Roger Adams.

Stan then left Urbana to take up war work with H. L. Haller at the Beltsville, Maryland, laboratory of the U.S. Department of Agriculture's Bureau of Entomology and Plant Quarantine. Haller was responsible for coordinating the research on insecticides and insect repellents being done in his laboratory and in those of Paul D. Bartlett (Harvard), Nathan L. Drake (Maryland), and Melvin S. Newman (Ohio State)—all of which was supported by the federal Office of Scientific Research and Development. As Stan told the story, there was a cage containing mosquitoes at one end of a long lab, and a second cage of mosquitoes at the other as a control. They knew they had a breakthrough when they sprayed the test mosquitoes with a trace of a compound that came to be called DDT and the mosquitoes at *both* ends of the lab died!

Because Haller was so busy as the bureau's senior operating chemist, he gave Stan freedom to develop his own program once the original problem of isolation and identification of impurities in technical DDT had been resolved. In all, 14 impurities were discovered in the four samples studied by the four research groups. Of these, none was as toxic to insects as p,p'-DDT, which by the standards of the time was judged to be innocuous to humans. Hence DDT was used on a large scale during the war against malaria-carrying mosquitoes, typhus-carrying lice, and other vectors of insect-borne diseases. The compound played an especially key role in preventing outbreaks of such diseases during the Pacific war.

While at Beltsville, Stan initiated his work on reaction mechanisms involved in dehydrohalogenations with DDT analogs and with benzene hexachloride isomers (the gamma isomer of this compound is also a potent insecticide). This research arose from a theory that insecticidal activity might somehow be related to the ability of these chlorinated chemicals to poison their insect hosts by elimination of hydrochloric acid under alkaline conditions within the hosts' bodies. Stan began measuring rates of base-promoted dehydrohalogenations of a variety of DDT analogs, as well as of five isomeric benzene hexachlorides. No correlation between elimination rates and insecticidal activity was found, but he noted that while four of the five hexachlorobenzenes readily eliminated HCl to form halobenzenes, the fifth—the so-called beta isomer, whose structure was known to have all six chlorine atoms trans (on the opposite side of the six-membered

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ring) to adjacent chlorines—was extremely resistant to elimination (10^5 times slower than the others). He proposed that easy base-promoted elimination requires that the hydrogen atom and the leaving group (here a chlorine atom) must be trans to one another. In the beta isomer, each chlorine is trans only to another chlorine atom and never to a hydrogen atom, while for each of the other isomers there is at least one chlorine with a trans hydrogen. While trans elimination had been postulated earlier, this work remains a classic for its clarity and rigor.

Stan left Beltsville in 1946 to begin a career at the University of Colorado in Boulder, where he was appointed assistant professor in the Department of Chemistry—a department that had been relatively undistinguished in research but that had just received encouragement from the university administration to improve. Stan and Colorado proved to be an ideal match, and despite offers to move elsewhere he remained devoted to the university and the department. By the time he retired, 40 years later, the Department of Chemistry was recognized as among the best in the country. During this time he was honored by the university as the department's first Distinguished Professor. Eight years after his retirement, during which he spent nearly every working day in his office or lab, the university named the department's main building the Cristol Chemistry and Biochemistry Building. He had directed the research of 90 graduate students and postdoctoral fellows and the chemistry education of thousands of undergraduates. He received the James Flack Norris Award in Physical-Organic Chemistry from the American Chemical Society in 1972 and the Distinguished Alumnus Award from Northwestern University in 1975.

Stan's life was greatly enriched by his marriage in 1957 to Barbara Wright Swingle, who brought three children—Larry, Kurt and Sharon—to the marriage. To these three were added Marjorie Jo and Jeffrey Tod Cristol. The whole family took advantage of the riches of the Colorado outdoors. In the early days, Stan enjoyed fishing during the lunch hour in Boulder Creek, which runs through the city. When that was no longer allowed, he pursued fly-fishing together with his children, whom he taught to make their own flies. Camping and hiking, if a stream or lake was on a trail, made for many family outings.

They all loved skiing as well, and Stan was always ready for a few more runs down the mountain. He enjoyed days on Aspen or Vail slopes well into his 80s, and ski days or other shared adventures with colleagues were especially welcome.

In addition to his extensive research, Stan was the guiding hand in the chemistry department's development. When he arrived, the university was still on a system in which the dean, with little or no input from faculty, appointed department heads. According to Stan, it was not unusual for a new chair to meet his (in those days, never a her) colleagues for the first time upon arrival on campus in the fall. Not long afterward, a new president revolutionized the university organization, with department chairs elected by the departmental faculty. Stan was elected chair in 1960 and the department (at his urging) decided on two-year nonrenewable terms for chairs (later extended to three years). In addition, short weekly department meetings would help keep members of the faculty involved.

At Stan's urging, the administration gave the department permission to recruit a senior member to each of its divisions from outside the university, and this policy helped to enhance intellectual depth and diversity. He was also a strong advocate for forging alliances with the Joint Institute for Laboratory Astrophysics—a partnership between the University of Colorado and the National Institute of Standards and Technology —and the National Oceanic and Atmospheric Administration. Both of these organizations are nearby in Boulder, and their members have contributed immensely not only to the department but the university at large.

Stan was very active in faculty governance at all levels, serving for a time as acting dean of the graduate school and also as vice chancellor for academic affairs. He was awarded two Guggenheim fellowships, which he spent abroad at University College, London and at the University of Lausanne.

He served the Colorado section of the American Chemical Society (ACS) as chairman from 1952 to 1953 and as the section's national councilor from 1953 to 1959. He was a member of the executive committee of the ACS Organic Division from 1957 to 1959, chairman of that division from 1960 to 1962, and its section councilor from 1953 to 1959. Stan was elected to the national ACS Council Policy Committee for the term 1968 to 1973, and he served as an associate editor of *Chemical Reviews* from 1957 to 1959 and on the board of editors of the *Journal of Organic Chemistry* from 1964 to 1968.

At the national level Stan was greatly in demand not only by the ACS. For the National Science Foundation he was a member of the advisory panel of the Chemistry Program from 1957 to 1960, of the Graduate Research Facilities Program from 1957 to 1960, and of the Assistant Director for Institutional Programs from 1969 to 1972. He was a member of the Medicinal Chemistry Study Section B of the National Institutes of Health from 1969 to 1972. Stan was a consultant to Julian Hyman and Co. and its purchaser Shell Development Co. from 1947 to 1959, to the U.S. Naval Ordinance Test Station from 1951 to 1952, to a number of departments of E. I. du Pont de Nemours and Co. from 1960 to 1970, to Esso Research and Engineering Co. from 1960 to 1970, and to the Arapahoe Chemical Co. and its purchaser Syntex Chemical from 1977 to 1983.

Stan held memberships in Phi Beta Kappa, Phi Lambda Upsilon (elected honorary member in 1977), Sigma Xi, the American Association for the Advancement of Science (fellow), the American Association of University Professors, the Chemical Society of London, and the Royal Society of Chemistry. He was elected to the U.S. National Academy of Sciences in 1972.

Stan especially enjoyed visiting foreign countries, and he and his family spent several sabbaticals and fellowships abroad. Among such stays were especially well-remembered ones at University College, London, and the University of Geneva. Adventures to the Society Islands and Fiji brought new pleasures and challenges. (An excuse for bone fishing there wasn't hard to find either.) But one meeting, held in his ancestral town of Cork, Ireland, brought him special joy. There he was able to visit the very house in which his father was born, still as it was in the 1890s! He fished nearby with an Irish guide who told wonderful stories, and Stan made an impression with his Irish brogue and his singing of Irish melodies. When he entered the field of photochemistry, he and his colleague Tad Koch, and their wives Barbara and Carol, regularly attended photochemistry meetings in Europe followed by excursions to nearby regions of interest. The first of these trips was to Aix-en-Provence in the summer of 1976, and subsequent ones were to Budapest, Interlaken, Helsinki, and a half-dozen other locales.

Stan's research spanned the full range of physical-organic chemistry, and he made significant contributions to the body of knowledge on the reactive intermediates carbocations, carbanions, and free radicals. In nearly all of his work he paid special attention to the relative positions of the reactive atoms—for example, hydrogen and halogens—that allow reactions to occur most readily. Using deuterium as a tracer he showed that in base-promoted cis eliminations, hydrogen-deuterium exchange usually occurs faster than elimination, thus demonstrating that a carbanion is an intermediate. By contrast, in the much-faster trans elimination no H-D exchange is observed, showing that trans (now called anti) eliminations are concerted—i.e., they occur in a smooth single step—while cis (now called syn) eliminations occur stepwise.

Following up on his work on the hexachlorobenzene eliminations, Stan studied analogous eliminations from noncyclic molecules. He and J. J. Pappas were able to show, using deuterium as a tracer, that even in these noncyclic examples, most trans eliminations occur by a concerted mechanism while cis eliminations occur by way of intermediate carbanions. Stan's studies of reactions that proceed by way of intermediate carbocations also gave striking results. Collaborating with C. H. DePuy and R. M. Sequeira, he investigated the loss of chloride ions from substituted cyclopropyl halides and showed that the reaction rates are sensitive to the nature of the stereochemistry of the substituents attached to the ring. The results could be rationalized easily in terms of the just-developing Woodward-Hoffman Rules, and they furnished strong evidence for the validity of those rules.

In further work involving highly strained and interlocking carbon rings, Stan's group was the first to prepare quadracycloheptanes (molecules with seven carbons incorporated into four rings) by other than photochemical reactions. They took advantage of their extensive knowledge of elimination reactions to devise a precursor carbanion that could displace a bromide ion from the rear (analogous to a trans elimination) to close the final ring. The isomeric bromide, in which front-side displacement would be required, was inert, again showing that stereochemistry controls the ease of organic reactions.

Stan's group also carried out extensive investigations of acid-catalyzed addition reactions to unsaturated organic molecules—the reverse of base-promoted eliminations—and he and his colleagues studied free-radical additions as well. In a series of five papers they described the additions of acetic acid to norbornadiene under a variety of conditions (acid-catalyzed and uncatalyzed) and compared them with solvolysis results within the same system (all with deuterium labeling to observe possible rearrangements of the carbon skeleton).

Toward the end of his career, Stan began a wide-ranging investigation of the influence of light on the mechanisms of organic reactions. In particular, his group studied photo-induced rearrangements, including those in which small-ring compounds such as the cyclopropyl halides are formed from noncyclic halides. In the case of benzyl chloride, wherein ring-closure is not possible, the researchers found that direct irradiation leads to free-radical products while triplet sensitization leads to ionic intermediates. He and his colleagues developed a useful analytical procedure for measuring the rate of energy transfer from a photosensitizer both to a substrate and to a quencher. The lifetime of the quenched substrate can also be determined by this technique.

Boulder is an attractive place to live, and graduates would like to be employed there, but at least in the early days suitable jobs for newly minted Ph.D.s were virtually nonexistent. One of Stan's students took the problem into his own hands by founding the Arapahoe Chemical Co. and began production of a number of chemicals that were useful for synthesis but not, at that time, commercially available. Stan served as a consultant and the company was a success, eventually being bought by Syntex. Now owned by Roche, the much-enlarged facility is still an important factor in Boulder's economy.

Stan's relationships with his Department of Chemistry colleagues were not confined to the scientific. For example, he often served as advocate for their welfare. As an active researcher he often commented on the precarious position of the tenured faculty member whose only grant was suddenly terminated in mid-career. While the department could usually offer the member's research students teaching positions to tide them over, it did not have the money to purchase chemicals and other necessities to keep the research going until a new grant could be obtained. So Stan and Barbara took it upon themselves to make a generous gift to the department to make grants of up to $10,000 to just such faculty members—grants that helped save the careers of several chemists. In addition, the Cristols contributed generously to a fund for the establishment of a Cristol Lectureship in Physical-Organic Chemistry, a fund also supported by his former students and other faculty members. Once, finding himself on the same Aspen ski-lift chair as the university's president, Stan sold him on a crucial remodeling project for the department by the time they reached the top of the mountain!

After his official retirement in 1986, Stan still spent most days in the department—doing research, attending seminars, talking with students and faculty, going to faculty meetings, and lunching with his many friends there. As his health began to deteriorate, he and Barbara moved to Durango, Colorado, to be near a daughter and son. There they continued to enjoy their family, within one of the most beautiful parts of the state, until Stan's death on January 23, 2008.

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