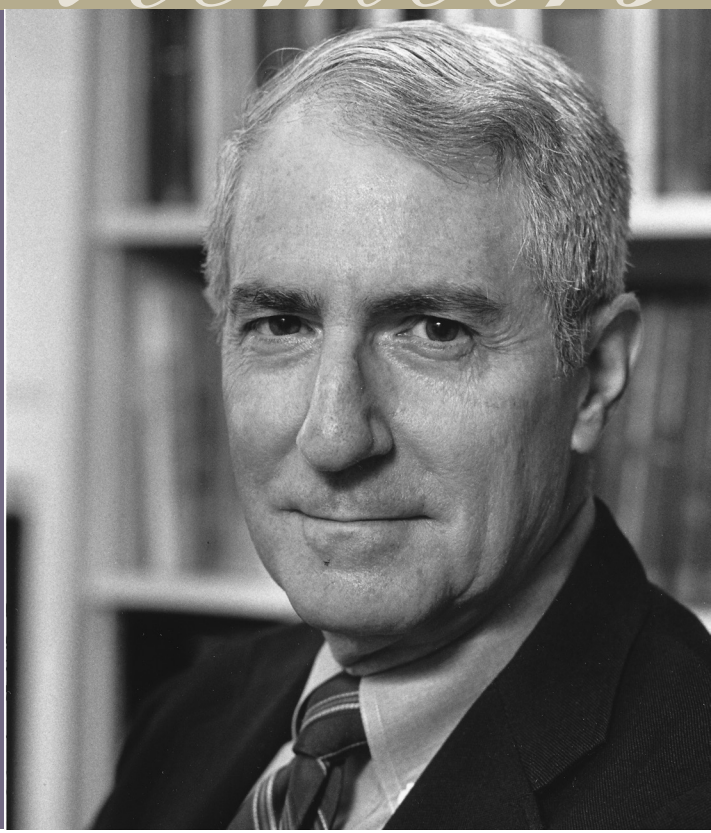
Jerome A. Berson

1924–2017

BIOGRAPHICAL *Memoirs*



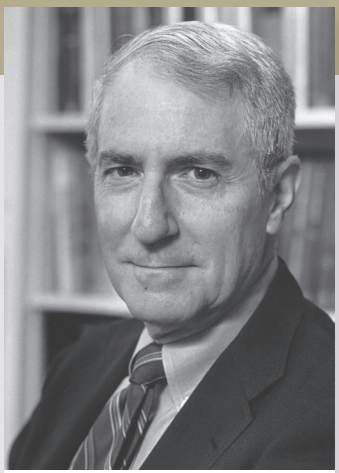
A Biographical Memoir by
Robert Bergman
and Marc Greenberg

NATIONAL ACADEMY OF SCIENCES

JEROME A. **BERSON**

May 10, 1924–January 13, 2017

Elected to the NAS, 1970



By Robert Bergman and Marc Greenberg

Jerome Berson was a leader among a cadre of brilliant investigators who initiated the explosive expansion of research into organic reactions starting in the late 1940s. Berson's thorough, creative, and highly quantitative approach made him a singular contributor to the field. His early work led to important advances in carbocation chemistry, but his career came into full blossom with the arrival of Woodward and Hoffman's orbital symmetry approach to what came to be known as pericyclic reactions. This led to intensive studies of very short-lived species such as biradicals and tetraradicals and factors such as spin that controlled their stereochemical and kinetic behavior. His later work on reactive species, often involving collaborators in physical chemistry, broadened out to incorporate theory, low-temperature EPR and NMR spectroscopy, matrix isolation, and fast and ultrafast kinetics. Berson received his B.S. from City College of New York (CCNY), did his graduate work at Columbia University with William Doering, and carried out his postdoctoral studies at Harvard University with R. B. Woodward. He began his independent career at the University of Southern California (USC) in 1950, moved to the University of Wisconsin–Madison in 1963, and then moved to Yale University in 1969. He was elected to the National Academy of Sciences in 1970. Jerry's additional honors include the ACS Roger Adams Award, the ACS Award in Physical Organic Chemistry and an Arthur C. Cope Scholar award.

Early Life

Jerome Abraham Berson was born on May 10, 1924, in Sanford, Florida, to Joseph and Rebecca Berson, Jewish immigrants who had met in the New York City area. Jerry's childhood was marked by the Great Depression. The financial struggles that his family experienced shaped his unrelenting work ethic and passion for social and economic justice. His mother, Rebecca, was born in Warsaw, Poland. She had little formal education but enjoyed reading and music, especially opera. She worked as a milliner and later in her short life devoted herself to raising Jerry and his younger sister, Phyllis (whom

he called "Foof"). Jerry's father was born in 1905 in Vilna (now Vilnius), Lithuania, during Russian control. He came to the United States with his older brother around 1920, motivated in part by the danger of being drafted in the Czar's army as cannon fodder. They settled in Pensacola, Florida, where their sister had put down roots some years earlier.

Berson as a young boy with his parents and sister. Ca. 1928.

Jerry's father also had little formal education. His Yeshiva studies had been interrupted by about the ninth grade. Still, education was his father's main source of income. He worked as a Hebrew teacher in various synagogues and also did freelance teaching as well. Years later, Jerry got a chance to read some of his father's sermons, which had appeared in local newspapers. He was stunned by their eloquence, even though English was his father's third language. Indeed, his father later taught himself Esperanto, a language invented to facilitate communication between people around the world. Many of Jerry's scholarly, artistic, and political passions can be traced to these family roots.

As the Depression wore on, it seemed that for Jerry's family, fortune was always hiding. His father's unstable employment required the family to move frequently between New York and Florida, and this also forced Jerry to change schools often. Despite these disruptions, Jerry excelled academically, skipping grades more than once (which he later said was a bad idea). He was not quite fifteen years old when he graduated high school.

When Jerry was about ten years old, his mother was diagnosed with cancer. Her family insisted that she come to New York for the surgery and post-operative care. There was not much to detain them in Daytona, Florida, so they relocated to the Bronx, where his father obtained employment in a synagogue.

As a pre-teen, Jerry began to develop a strong interest in chemistry for reasons he could never really reconstruct. He became fascinated by the properties, odors, and colors of chemicals that he was exposed to in a biology course. His move to New York was a turning point in his development because the teachers at his junior high school there encouraged him to apply to Stuyvesant High School, a selective public school emphasizing science. He was admitted, and his time at Stuyvesant was challenging and exhilarating. Unfortunately, Jerry had to transfer after less than two years when the family's

financial situation forced yet another move, this time to Long Beach, a suburb of New York City on Long Island. In his new high school, Jerry took what may have been his first formal chemistry course, but it lacked a laboratory component. Attempts to set up his own lab at home were impractical.

Jerry and Bella Berson, October 1990.

This period was followed by what we now call a "gap year," during which his family reestablished New York City residency so that he could attend tuition-free CCNY. Jerry filled that year by taking additional high school courses in the fall and working fifteen hours per day, seven days a week. He sold Good Humor ice cream from a tricycle during the spring and summer. It was during this period that he met Bella Zevitovsky. An academically gifted Brooklyn native, Bella shared Jerry's Eastern European Jewish roots, his passion for learning including chemistry, and his progressive political outlook. It was a love affair that would last more than seven decades.

At CCNY, Jerry was surrounded by other highly motivated students grateful to have the opportunity of a college education. There, he earned a bachelor's degree in chemistry. Although it was the experimental aspects of chemistry that attracted Jerry most, his undergraduate studies continued to be largely limited to the classroom. He was exposed to the concepts of resonance theory, which (perhaps unfathomably to current undergraduates) was in development at that time. Following his graduation in 1944, Jerry gained his first serious laboratory experience at Hoffmann-LaRoche, a Swiss pharmaceutical company with facilities in New Jersey. His work on the structure of penicillin lasted only five months, but it solidified his interest in the chemistry of natural products.

World War II cut short this first stint in the lab. Though the conflict was in its late stages, the Army still needed educated people to serve as medics. Jerry was drafted in 1944 and shipped to the China-Burma-India Theater as a combat medic. Hostilities in Burma had all but ended at that time, and Jerry spent most of his time in military service in Calcutta as a medical technician in the base hospital. Thankfully, he never had to fire a shot in anger, but Bengal province had its own special hazards—not bullets or bombs but a rich selection of tropical diseases, a few of which Jerry contracted during his time there.

Marriage and Post-Baccalaureate Training

With war over, Jerry was able to come home. His troopship landed in New York in early June of 1946. Within the month, he and Bella were married. Jerry soon started graduate work in chemistry at Columbia. Bella, who had graduated Phi Beta Kappa from New York University, was interested in biochemistry. She had contemplated attending graduate school along with Jerry, but there were few if any female role models in academic science in those days. Instead, she took a position as a technician in Robert Elderfield's laboratory in Columbia's Chemistry Department.

Many of the chemistry graduate students there at the time had backgrounds similar to Jerry's and Bella's. They had all been branded by the upheavals of the Great Depression and Second World War and were all driven to get on with their lives. Jerry's short stint at Hoffmann-La Roche led him to abandon an early interest in biochemistry and focus on the structure and synthesis of organic compounds. He was especially curious about naturally occurring substances, such as steroids and alkaloids, with powerful pharmacological applications. Jerry was fascinated by the intricate connectivity of the bonds holding these structures together. He wanted to learn how to unravel such molecules and, especially, how to build them from simpler starting materials.

Jerry chose to do his doctoral studies with William von Eggers Doering, then a thirty-year-old associate professor at Columbia. Just two years earlier, Doering and his postdoctoral mentor at Harvard, Robert Burns Woodward, had made a big splash with a total synthesis of the alkaloid quinine. By 1946, however, Doering's interests had shifted to the elucidation of the mechanisms of organic reactions, but he agreed to mentor Jerry on a structural problem. Jerry was the only natural-products chemist in Doering's lab at that time, but he was surrounded by contemporaries who would go on to illustrious careers in physical organic chemistry, including Ken Wiberg (Jerry's future colleague at Yale), Andrew Streitweiser (University of California, Berkeley), and Chuck DePuy (University of Colorado Boulder).

After five months of work on an intractable structural problem, Jerry switched to a project involving the combination of two molecules of a naturally occurring ethereal oil, isohomogenol. It took him only eleven months to complete this work. His thesis research at Columbia also broke new ground with the first use of IR spectroscopy at Columbia to solve an organic structure.[1] Molecular orbital theory, which would become such a crucial foundation for Jerry's future research, was not a part of his graduate organic chemistry training, even in a research group as cutting-edge as Doering's. It was not until 1951

as a young independent scientist that Jerry learned of his former mentor's embrace of molecular orbital theory in Doering's paper on the synthesis of tropone. That was also how Jerry came to know the work of Erich Hückel, which would play such a large role in his later research.

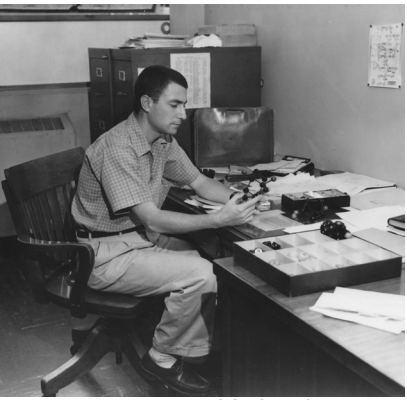
Jerry spent less than two-and-a-half years in graduate school. Toward the end of that time, as he later recounted, Doering approached him and asked, "Have you given any thought to what you are going to do with the rest of your life?" The question was completely unexpected. Jerry had to admit that he had no clear idea, just some vague notions about getting a job as an industrial chemist. Doering responded, "I think you should consider academic work. But first you will need some post-doctoral experience. There is only one person you should go to for that: Bob Woodward at Harvard."

Of course, Jerry was aware of Woodward's already towering reputation. Also, his thesis project had amplified his interest in natural-products chemistry, a good fit for Woodward's lab. With the help of a postdoctoral fellowship from the National Research Council, Jerry spent a year (1949-1950) at Harvard with Woodward working on a problem in alkaloid synthesis. During their time in Cambridge, Bella worked in a micro-analytical laboratory at the Massachusetts Institute of Technology under the supervision of Steven Nagy.

Woodward and Doering strongly influenced Jerry's scientific values. They generated an atmosphere of intense devotion to science that resonated with Jerry's own passion. With this training, one might think it was all clear sailing for Jerry to launch an academic career in natural-products research and teaching. In truth, though, he struggled to land his first academic job. Having just about given up on securing an academic position, he applied for an industrial job at Merck and Company. Fortunately, when Doering got wind of this, he called Jerry at Harvard to question his sanity and to give him a stern scolding for even considering such a step. Eventually, after much searching, Jerry received and accepted an offer of an assistant professorship at USC.

California: The Metamorphosis from Natural-Products to Physical Organic Chemistry

Jerry and Bella arrived in Los Angeles in 1950 and started a family. Ruth was the first to arrive, in 1951. Two sons David (1954) and Jon (1956) following shortly thereafter. Bella suspended her professional efforts until all three were young adults, volunteering in addition to holding down the fort at home while Jerry spent long hours launching his own lab. He tried to get a research program going in natural-product structure and



Berson at USC, Ca. 1957.

synthesis, but it was tough sledding. USC's chemistry department had strong competition in the Los Angeles area from both the University of California, Los Angeles (UCLA) and the California Institute of Technology (Caltech). Natural-products work, especially synthesis, was a labor-intensive enterprise. Scientists heading major synthesis groups routinely supervised fifteen to twenty students and postdocs at a time. This was out of reach for Jerry at the time, but he was determined to make his mark just the same.

The synthesis of emetine had captured Jerry's interest since his time in Woodward's group. Ted Cohen, who went on to a long career at the University of Pittsburgh, was the first student to work on emetine in Jerry's lab, and they published several papers on the topic, including mechanistic work.[2] However, as the project passed on to other students, multiple groups scooped them on the total synthesis.

It didn't take long for Jerry to understand that his small research group could not compete in natural-products synthesis and that he needed to find a new direction. Doering himself had transitioned to physical organic chemistry during Berson's time in his lab. Also, Louis Hammett and Paul Bartlett, two physical organic chemists he greatly respected, had been active in the departments in which he had trained. Though physical organic chemistry had not previously evoked his passion, he realized that the natural-products chemists that he admired, including Woodward, Stork and Barton, were also skilled physical organic chemists.

Jerry began to work on reaction mechanisms, probing the detailed pathways by which chemical transformations take place. He knew that he had much to learn and needed to find an environment that would familiarize him with the methods and goals of the field. Fortunately, this subject was being intensely pursued nearby at UCLA and Caltech. Jerry began to attend the famous Thursday night seminars hosted by Saul Winstein at UCLA. Other attendees included such luminaries as Donald Cram, who would later win a Nobel prize, George Hammond, and Jack Roberts. Winstein was a powerful scientific personality, and Jerry later described his interaction with him as like a decade-long postdoc with one of the most demanding intellects in chemistry. Tragically, Winstein died in 1969 at the age of 57.

Wisconsin: Thermal Rearrangements

A major turning point in Jerry's career came in 1963, when he accepted an offer to join the chemistry faculty at the University of Wisconsin–Madison. It was also an important opportunity for Bella. With their three children now older, Bella returned to her own professional aspirations, but with a new focus. She obtained her Master's in Library Science from Wisconsin in 1969. Jerry described his time at Wisconsin as six of the happiest years of his life. But it was also a time of great political strife in the country, and Madison was very much in the middle of it. Like many of their colleagues and friends, Jerry and Bella strongly opposed the war in Vietnam. Jerry had been funded to do basic research by the Defense Department but gave this up, as he felt it was inconsistent with his opposition to the war. Foregoing Defense funding did not hinder his research, however. On the contrary, the group increased in size at Madison, and Jerry's research blossomed dramatically. His group made important contributions to carbocation chemistry[3] and pericyclic reactions, facetiously named "no-mechanism" reactions at the time. Jerry was full of enthusiasm, frequently coming into the lab with new ideas to bounce off his coworkers and running group meetings on the Winstein model (long hours and intense discussions, followed by "après-seminar" hours at Paisan's restaurant near the university).

Jerry seldom presented at group meetings, preferring to hone his coworkers' presentations and understanding with insightful comments and questions. He made a notable exception, however, when Woodward and Hoffmann published their first communications on orbital-symmetry analysis of pericyclic reactions. Jerry took over the meeting with a stunning explication of the meaning and impact of those papers. That seminar impressed all of Jerry's coworkers not only with his scientific brilliance, but also with his incredible skill as a teacher.

The Woodward-Hoffmann papers accelerated Jerry's work on thermal rearrangements and cycloadditions. These studies were designed to test the limits of what became known as the Woodward-Hoffmann rules. Jerry's elegantly designed experiments required the challenging synthesis of stereochemically labeled probes and products. The publications also featured rigorous product and kinetic analysis. This line of inquiry led to the discovery of the oxy-Cope rearrangement, which set the stage for the synthetically useful anion-accelerated Cope reaction.[4] In one of his most famous papers, Jerry designed an experiment that he described as a particularly "risky test" of the Woodward-Hoffmann rules. He and his coworkers demonstrated that the stereochemistry of a [1,3]-rearrangement proceeded through a sterically very demanding transition state.[5]

Despite requiring inversion of stereochemical configuration at the migrating group, the reaction proceeded as predicted by the Woodward-Hoffmann theory. This body of work brought Jerry international recognition and, in 1970, his election to the National Academy of Sciences.

Yale: Studies of Long-Lived High-Spin Molecules

After spending nearly half of his academic career in the West and Midwest, Jerry relocated to Yale in 1969. The move offered him opportunities to interact with a larger pool of physical chemists, not only at Yale but elsewhere in the Northeast too. Such collaborations were increasingly important to Jerry's evolving research on thermal reactions.[6] But part of the motivation was clearly cultural as well. Having both grown up in New York, Jerry and Bella missed the intensity, cultural stimulation, and ethnic diversity of East Coast life. The move also brought them closer to family in and near New York. Well into their later years, they held season tickets at the Metropolitan Opera and made countless trips to Manhattan to take in museums and performances and visit family. Yale also offered Bella an opportunity to pursue her budding career in library science, which she did with aplomb. She rose through the ranks, starting as a cataloguer, later serving as Associate University Librarian, and ultimately assuming directorship of the Yale Medical Library. In that role, she oversaw a major expansion of the facility in the 1980s.

The move to New Haven did not diminish Jerry's social and political activism, as was evident during the effort by an international group of prominent scientists to help Dr. Yelena Bonner temporarily leave the Soviet Union (circa 1984) to receive medical care. Bonner, the wife of famous dissident Andrei Sakharov, was in need of open-heart surgery. Jerry and 54 other Western scientists offered to each trade places with Dr. Bonner for a week as "good faith witnesses" in the Soviet Union. Dr. Bonner ultimately underwent a successful sextuple bypass in the United States in 1985, but Jerry did not have to travel to the Soviet Union.

At Yale, Jerry further pushed the limits of thermal reactions controlled by orbital symmetry. His efforts in this area continued into the 1990s with work on sigmatropic rearrangements. This line of work included tests of the intermediacy of 1,4-biradicals in [3,3]-rearrangements and the stereoelectronic control imparted by 3- and 4-membered rings on homodienyl hydrogen shift reactions.[7,8] This triggered his growing interest in the behavior of short-lived diradical and tetraradical intermediates. His studies of concerted versus biradical pathways in thermal rearrangements led Jerry to question whether triplet states could play a role in these processes. Indeed, he wondered how one would even

recognize the involvement of a higher spin species. This led to the study of substituted trimethylenemethanes, which had greater lifetimes than the parent ground-state triplet biradical and exhibited rich, complicated spin-state dependency.[9]

Trimethylenemethanes also brought Jerry back to the seminal work of Erich Hückel on the origin of the separation of energy between spin states of a given species and whether Hund's rule was applicable to biradicals. These intellectual questions provided Jerry with a new frontier to explore with his broad experimental prowess, one that would endure until he closed his laboratory in 1994.[10] Jerry's accomplishments in this area included the first synthesis and characterization (spectroscopic and reactivity) of *m*-quinodimethane, accomplished contemporaneously by his former student Matt Platz at The Ohio State University.[11] Jerry also created the first observable ground-state singlet biradicals, which (with Kurt Zilm) resulted in the first characterization of a captive intermediate by low-temperature, solid-state NMR.[12] The creation of biradicals with tunable singlet-triplet energy gaps and tetraradicals contributed to the fundamental understanding required for the creation of high spin organic materials, an application that grew in popularity in parallel with Jerry's hypothesis-driven research.[13-15]

As these and other projects illustrated, Jerry was one of the few to recognize that in-depth understanding of dynamics required analysis by theory and new technical innovations such as EPR and solid state NMR spectroscopies, matrix isolation, and fast and ultrafast kinetics. This led to productive collaborations with organic and physical chemists such as Weston Thatcher Borden (Harvard, University of Washington), Michael McBride (Yale), Kevin Peters (Harvard, University of Colorado Boulder), Angelo Rossi (University of Connecticut), J. C. "Tito" Scaiano (National Research Council Canada) and Kurt Zilm (Yale).

Later Years

After closing his lab in 1994, Jerry was, as ever, hungry for new challenges. He had a long-standing interest in the history of chemistry, which overlapped with his fascination with the work of Erich Hückel from the 1930s and his drive to understand the turbulent political events in Europe at that time. Over the course of more than a decade, he published several papers and two books that explored how important discoveries were made (and missed) in the field.[16,17] He also took advantage of his retirement from laboratory research to pursue his interest in music by taking up the piano.

Jerry was greatly admired by his coworkers and colleagues. Many who passed through his research group formed bonds with him that endured long after they moved on to independent careers. Their fondness for Jerry was clearly on display two decades after he closed his research laboratory when more than twenty coworkers gathered from as far away as England to celebrate his 90th birthday. It was held at one of his and Bella's favorite restaurants, Le Petit Café in Branford, Connecticut.

An important hallmark of Jerry's career is the unusually large number of coworkers who went on to become successful academic scientists in their own right. Many of these "Berson persons" went on to work on topics far afield from those they pursued with Jerry. However, the Berson influence—the joy of discovery and the emphasis on rigor and creativity—is plain to see. Jerry was justifiably, though quietly, proud of all he and his group had accomplished. But he was unwilling to take any credit for the broad and deep success of his intellectual progeny as independent scientists. At a Caltech symposium honoring Jack Roberts, someone congratulated Jerry on "having done it again" after a former member of his research group had spoken. Jerry's response was "I don't make them, I just have them." In truth, the successes of his coworkers are testimony to Jerry's winning combination of exacting standards and enthusiastic encouragement for independent thought and experimentation.

Berson family: Jon, Bella, Jerry, David, and Ruth, 1998.

One can see a bit of Jerry and Bella in each of their children as well. They encapsulate their interests in the sciences, arts, and history. An art historian, Ruth worked in museums serving for many years as Deputy Museum Director for Curatorial Affairs at the San Francisco Museum of Modern Art. She was knighted as an Officer in the French Order of Arts and Letters. David, like his father, is a basic scientist. He studies the structure and function of the retina at Brown University. Jon has focused on the live entertainment industry and is currently a pyrotechnic display designer and producer and Chairman for the APA Proximate Pyrotechnics Committee. The seed for that career might have been

planted when Jerry wowed his kids with the fascinating colors he could produce by just sprinkling a little dust he'd brought home from the lab into the flames of the family fireplace in Madison.

Jerry's late years, though full in many ways, were darkened by Bella's long decline into dementia. They had been married sixty-six years when she died in 2012. Jerry knew how lucky he was to hold on to his sharp mind until the very end. He read the New York Times, the Nation, and the New Yorker religiously, kept a deeply skeptical eye on current events, and found ways to stay positive and engaged. In his last year, at 92, he was still taking piano lessons and pushing himself to tackle more ambitious pieces and keeping up his language skills at weekly Yiddish lunches.

Jerry Berson was an amazing scholar and human being; a true "mensch" in the deepest sense of that word. Those who were lucky enough to work with him received a priceless gift—a mentor who recognized and fostered talents they had yet to see in themselves.

ACKNOWLEDGMENTS

This memoir benefited from substantial contributions from Jerome Berson's children Ruth, David, and Jon Berson. The authors are grateful for their assistance.

We are grateful for access to the Jerome A. Berson interview by Leon Gortler at New Haven, Connecticut, 21 March 2001 (Philadelphia: Chemical Heritage Foundation, Oral History Transcript #0196).

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