Role Models in Chemistry

This new feature column, edited by Balazs Hargittai and István Hargittai, will cover acclaimed persons in the international chemistry community.

Nelson Leonard
by Balazs Hargittai and István Hargittai

N elson J. Leonard is a world-renowned organic chemist acclaimed for his skill in organic synthesis. His work has answered questions of fundamental importance to biochemistry and life processes. Leonard invented fluorescent probes and dimensional probes of enzyme-coenzyme binding sites and DNA double-helical cross sections. Leonard has been very active in IUPAC. He served on the Editorial Advisory Board of IUPAC from 1984–1991 and he was President of the Organic Chemistry Division of IUPAC from 1991–1993.

Leonard (born in 1916 in Newark, New Jersey) is the Reynold C. Fuson professor of chemistry emeritus of the University of Illinois, Urbana-Champaign, and faculty associate at the California Institute of Technology in Pasadena. He received his B.S. degree from Lehigh University in 1937; a B.Sc. Degree from the University of Oxford in 1940, following his Rhodes Scholarship there; and his Ph.D. from Columbia University in 1942. Leonard retired from the University of Illinois in 1986 after 44 years. He served as scientific consultant and special investigator, Field Intelligence Technical Agency, U.S. Army and U.S. Department of Commerce, European Theater, during 1945–1946. He was elected a member of the National Academy of Sciences of the USA in 1955. Leonard’s distinctions include the Roger Adams Award in Organic Chemistry (1981) and the Arthur C. Cope Scholar Award (1995).

Leonard’s father was a salesman in New York and his mother was a housewife. As a child, he had his own chemistry set and in high school he had a good chemistry teacher. Following his career at Urbana-Champaign, he started a second career at Cal Tech where he first went as a Sherman Fairchild Distinguished Scholar in the fall of 1991.

While at Cal Tech he has written review articles based upon some of his earlier discoveries, such as fluorescent derivations of ATP and related compounds. According to Dr. Leonard, it is a good though passive way to keep up with the field. One of his projects, upon invitation from Tetrahedron, was to write a “Perspectives” article about his career. He decided to write about what was different about his scientific life. He enjoyed collaboration with other scientists in other places and in other disciplines, so he titled the piece “The ‘Chemistry’ of Research Collaboration.”

When WWII broke out in Europe, Leonard was in Oxford and had to return to the USA. Back in the states, he pursued a Ph.D. at Columbia University, where he worked on alkaloid chemistry. He soon determined that the fun part for him was synthetic organic chemistry and working with natural products. After receiving his Ph.D. in 1942, he headed to the University of Illinois, where his research was concentrated on antimalarials. As a confirmed New Yorker, he thought he would give the Midwest a year and then return to New York. However, he found the Illinois campus a fascinating place, with excellent people at the time: Roger Adams, Carl S. (“Speed”) Marvel, Harold Snyder, and Charles C. Price III were his colleagues.

When the war ended, Dr. Leonard got a temporary job with the U.S. Army overseas as part of an industrial intelligence unit (F.I.A.T.). Stationed in Höechst, Germany, the unit was charged with examining the research publications and research reports of the I. G. Farbenindustrie. Before the war had ended, the intelligence unit had started interviewing directors of research and others from German industry. Eventually, the unit was instructed to obtain details from research reports and manufacturing procedures. They found a number of things that could be applied in American industry. For example, the production of good synthetic rubbers in the USA was aided by information about a particular long-chain mercaptan that had been used in Germany as a modifier in rubber manufacture.

However, they did not see any reports from the infamous I. G. Farben Auschwitz, the Buna and synthetic fuel works. This was not surprising because, according to Joseph Borkin of the Antitrust Division of the Department of Justice, writing in his book The Crime and Punishment of I. G. Farben, most of its records were destroyed so that the slave workers in concentration camps could be obscured. When the Cold War started, the idea of taking technical information from Germany ceased to be popular. It was
considered important that German industry should be given an opportunity for revival. The decision was political and military, but this change happened after Dr. Leonard’s time in Germany.

Being stationed in Germany allowed Leonard to be reunited with a Dutch woman, Louise Vermeij, to whom he had become engaged just before he returned to the USA in 1939. His fiancée spent all of the war years in the Netherlands. They met again in 1945 and married in 1947. In 1987, Louise died of cancer. In 1992, Leonard married Peggy Phelps.

Dr. Leonard’s research interests kept shifting during his career. In the first decade, he and his students worked on reductive cyclizations, electrolytic reductions, molecular rearrangements, and the stereochemistry of 1,2-dicarbonyl compounds. After his first sabbatical leave, he worked on medium-ring compounds, discovering some transannular interactions and reactions, and on small charged rings, discovering some ring-enlargement reactions of aziridine and azezidine salts.

During a sabbatical leave in Switzerland in 1960, he started reading biochemistry, but the initiative for research came from one of his students back home, Jim Deyrup, who was working on a natural product, triacanthine, that turned out to have a 3-substituted adenine structure, 3-(1,3-isopentenyl) adenine. Most of the adenines known up to that time were substituted at the 9-position. The 3-substitution was a nice surprise and served as a channel into biochemistry through 3-isoadenosine and its mono-, di-, tri-, and cyclic phosphates. For example, 3-iso-ATP turned out to have many coenzyme activities similar to those of natural ATP, adenosine triphosphate. An isomer of triacanthine, namely N6-isopentenyladenine, because of its cytokinin activity (plant-cell growth, division, and differentiation) was a channel into plant physiology. Leonard started collaboration with Folke Skoog, professor of Plant Physiology at the University of Wisconsin. They worked together for 20 years and published more than 40 papers together.

Another scientist with whom he had a fruitful collaboration was Professor Gregorio Weber (1916–1997), a great man in fluorescence. Weber went to the University of Illinois from Argentina by way of England, and he excited everybody about fluorescence. In the early 1970s, Leonard’s group made fluorescent derivatives of the nucleic acid bases so that they could be detected and would indicate, by fluorescence lifetime, yield, and polarization, and how they were attached to an enzyme or structural protein. The fluorescent derivative of ATP, namely 1,N6-etheno-ATP, became the most popular in numerous applications thereafter.

Leonard and his group continued with many different research projects based upon fluorescence. They constructed a compound that was a fluorescent dimensional probe of ATP (i.e., linear-benzo-ATP, with the same terminal rings as in ATP but with a central benzene ring built in, thus making it 2.4 angstroms wider than the natural coenzyme). One of Leonard’s final projects, conducted with Dr. Balkrishen Bhat, involved a fluorescent, covalently linked cross section of DNA consisting of five fused rings and having the same or very similar geometry to a hydrogen-bonded pair of DNA bases. It just wouldn’t come apart. The final goal, which is still unobtained, was to incorporate the covalent cross section to see, in a replicating cell system, whether there was something inserted that prevents the two DNA strands from coming apart, thus inhibiting replication, especially as in fast-growing cancer cells.

Leonard has directed over 120 Ph.D. students and 91 post doctorates and published over 400 papers. His legacy is honored by the annual Nelson J. Leonard Lectureship at the University of Illinois, which is sponsored by his students and former colleagues. Before joining Cal Tech in 1992, Leonard held visiting appointments at the National Institutes of Health in Bethesda, Maryland, and at the University of California, San Diego.

Leonard’s heroes include Roger Adams, who was still fully active when he got to Illinois, although he was tied up with the war. In turn, he was to become General Clay’s science advisor in Germany and General MacArthur’s science advisor in Japan. At Oxford, Leonard appreciated Robert Robinson and at Columbia, Harold Urey was his hero.

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