Ronald Breslow

1931–2017

Ronald Breslow, one of the most influential chemists of the past 60 years, passed away on October 25, 2017, in New York City at the age of 86.

Breslow was born March 14, 1931, in Rahway, New Jersey, the son of Gladyz and Alexander Breslow. His interest in chemistry was whetted in part by interactions with Max Tischler, a family friend and the director of chemistry at Merck & Co. at the time. At the age of 17 he was a finalist in the prestigious Westinghouse Science Talent Search, and later that year entered Harvard, graduating with an A.B. in chemistry in 1952. At Harvard, Breslow worked in Gilbert Stork's laboratory, coauthoring two papers that described the structure elucidation of the tricyclic sesquiterpene cedrene. Breslow initially began graduate studies in Harvard's program in medical sciences in 1952, which he left a year later with a master's degree to focus on graduate studies in chemistry. He completed his Ph.D. in 1955, working with R. B. Woodward on early studies directed at the structure of the macrolide antibiotic magnamycin. Breslow then spent one year in Cambridge University working with Alexander Todd on early efforts to develop chemistry for synthesizing deoxyribonucleotides and at the same time initiating his independent studies on thiamine (vitamin B1). In 1956, at the age of 25, he joined Columbia University as an instructor in the Department of Chemistry.

Breslow's remarkable insight and broad vision of chemistry became immediately apparent when over a 10-month period in 1957–58 he authored two landmark publications in the *Journal of the American Chemical Society*. In the first, he reported the synthesis of triphenylcyclopropenyl cation, the earliest example of the simplest aromatic ring. In the second, after showing that thiazolium salts readily form zwitterions by loss of the C-2 hydrogen of the heterocyclic ring, he proposed the mechanism by which the coenzyme thiamine pyrophosphate functions in important biochemical reactions. Thiazolium zwitterions were the first examples of *N*-heterocyclic carbenes, whose chemistry—often involving Breslow intermediates—remains an active area of research today. Following up on his cyclopropenyl cation work, Breslow went on to show that cyclic conjugated ring systems having 4n electrons were not only not stabilized by delocalization, but also destabilized—molecules he termed anti-aromatic.

Ron Breslow was one of the founders of the field of bioorganic chemistry. Inspired by nature's ability to selectively functionalize molecules not at their intrinsically most reactive position, but rather by steric approximation within an enzyme-substrate complex, Breslow began in the mid 1960s systematic investigations to mimic enzymatic selectivity by the positioning of reagents and substrates. In initial investigations, an oxidant was tethered to a substrate to functionalize remote C—H bonds. Later studies exploited several types of non-covalent molecular recognitions, with this approach to achieving high selectivity in chemical reaction being pursued by many researchers worldwide. He also pioneered in developing simple chemical systems that mimicked both the binding and active-site turnover steps of enzyme action. In collaboration with Paul A. Marks, at the time president and CEO of Memorial Sloan-Kettering Cancer Center, Breslow developed the first cancer therapeutics that worked by inhibiting members of the zinc-binding class of histone deacetylases. This discovery was commercialized by Merck, with Zolinda® (suberoylanilide hydroxamic acid, vorinostat) being approved by the FDA in 2006 for treating cutaneous T-cell lymphoma.

Ron Breslow's impact on the chemical enterprise extended far beyond his research accomplishments. He had leadership roles in the chemical section of the National Academy of Sciences and served as president of the American Chemical Society in 1996. In this latter role, he was unusually active in articulating the accomplishments and promise of chemistry to a wide audience in part through the book *Chemistry Today and Tomorrow: The Central, Useful, and Creative Science*, which was authored by Breslow and published by ACS in 1996. Ron was a member of the editorial board of *Organic Syntheses* during the 1960s and edited Volume 50, which appeared in 1970. In addition, Ron was a long-time member of the *Organic Syntheses* board of directors.

Ron Breslow's many honors and awards include the National Medal of Science, the Welch Award, the NAS Award in the Chemical Sciences, the American Institute of Chemists Gold Medal, the Swiss Chemical Society's Paracelsus Prize, and American Chemical Society Awards in Pure Chemistry, Arthur C. Cope Award, and Priestley Medal. He was a member of the National Academy of Sciences, the American Academy of Arts and Sciences, and the American Philosophical Society. Breslow was also a foreign member of the Royal Society and an honorary member of many other scientific bodies around the world. In recognition of his classroom teaching skills, Columbia awarded him both its Mark Van Doren Award and its Great Teacher Award.

More than 250 Ph.D. students and postdocs trained in the Breslow research group. The fundamental nature of the training one gained working with Ron is apparent in the diverse fields his former coworkers have pursued, which include polymer chemistry, organometallic chemistry, chemical biology, organic synthesis, and drug discovery. Like many former coworkers, the author considers the time he spent in the Breslow group as indispensable to his academic endeavors. Ron coupled his love of chemistry and intensity for research with enormous personal warmth. His quick mind and intellect is legend yet was projected in a way that inspired rather than intimidated. Ron was immensely loyal and supportive of his former coworkers.

Ronald Breslow is survived by his wife Esther, professor emerita of biochemistry at Weill Cornell Medical College; their daughters, Stephanie and Karen; and

grandchildren. Ron's friendship and wise council will be deeply missed by all who knew him.

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