Robert E. Ireland

Robert E. Ireland (1929–2012)

Robert Ellsworth Ireland passed away on February 4, 2012 after a prolonged bout with emphysema.

Professor Ireland received an A.B. from Amherst in 1951, a Ph.D. under William S. Johnson from the University of Wisconsin in 1954, and studied as a NSF postdoctoral fellow with William G. Young at the University of California, Los Angeles, from 1954–56. He joined the University of Michigan faculty in 1956, became Professor of Organic Chemistry at the Caltech in 1965, and took leave in 1985 to become Director of the Merrell-Dow Research Institute in Strasbourg, France. He left France for the University of Virginia in 1986, where he served as Chairman and was the first Thomas Jefferson Professor of Chemistry. He assumed Emeritus status in 1995.

Bob Ireland had a major impact on the field of organic synthesis. One of his colleagues noted: "*Ireland is one of the few who has been successful in designing novel synthetic methodologies that are generally useful.*" An outstanding example is his development of the Ireland–Claisen rearrangement. This reaction was shown to have significant utility in the synthesis of prostaglandins and ionophore antibiotics, for example, lasalocid A and numerous other natural products, by him and other leading research groups. The method is based on the finding that the enolate of an allylic ester undergoes a Claisen-like rearrangement under very mild conditions, resulting in a carbon–carbon bond-forming process with a high degree of tunable stereocontrol. This methodology and its variations have been widely used by both academic and industrial chemists worldwide.

The Ireland–Claisen rearrangement is a discovery that alone would be considered an enviable lifetime achievement. But there are many more which bear strongly on synthetic methodology and strategy. Ireland's early work on the synthesis of tricyclic diterpenes, which included means for the construction of abietic acid, the pimaric acids, and several biogenetically significant precursor hydrocarbons, is noteworthy. He used similar themes in his investigations on the synthesis of even more complex triterpenoids, which led to the first synthesis of an unsymmetrical pentacyclic triterpene, germanicol. Further work yielded a general convergent synthesis of a pentacyclic precursor that was used to make a number of natural triterpenes, especially alnusenone and friedelin. The convergency of the route to this precursor and its general application to specific triterpene systems makes Ireland's strategy exceptionally efficient. Completely different conceptual patterns were employed in syntheses of two terpenoid antibiotics: fusidic acid and aphidicolin. Ireland's routes are wonderfully efficient and flexible, enabling analogues of the latter to be prepared by total synthesis in sufficient quantity for biological evaluation.

Ireland also developed convergent syntheses of polyether antibiotics; methodologies quite different from those used earlier were formulated and deployed. Simple sugars served as chiral building blocks to synthesize tirandamycin, streptolydigin, and lasalocid A. Each of these substances showed promising therapeutic and biomedical interest. Among other milestones, Ireland's syntheses of chlorothricolide, monensin, and FK-506, three totally different complex natural products should be mentioned, in which he demonstrated the power of the Ireland–Claisen rearrangement. The success of these major synthetic undertakings depended on the development of new synthetic methodology as well as logical convergent synthetic strategy.

Ireland and his co-workers also devised other valuable synthetic processes. One is the butylthiomethylene blocking group used extensively by them, and others as well, in steroid and terpenoid synthesis. He also demonstrated the utility of magnesium chelates in the biosynthetically patterned (biomimetic) monoacylation of malonic half esters and discovered a novel conversion of enol-phosphoramidates to olefins.

Ireland's significant impact on synthetic organic chemistry was the result not only of his scientific achievements, but also his style of presentation. His publications are a model of clarity and thoroughness. Early in his career, he wrote *Organic Synthesis* (Prentice Hall, 1969), the first textbook on synthetic strategy. In it, the oft-quoted passage "Stereochemistry Raises its Ugly Head" can be found as the title of Chapter 5. The final chapter, "Multistage Synthesis: Logistics and Stereochemistry Combine to Produce Nightmares," presages the present era of complex molecule construction. Though over 40 years old, the book could well serve as a text for a modern mid-level course in organic chemistry.

It is worth noting that many of Ireland's former co-workers have become successful chemists themselves and now hold leadership positions in industry, government, and academic organizations both in the U.S. and abroad. As one of his very first graduate students, I can attest to his inspirational leadership and high standards of scientific and professional discipline. He will long be remembered as an outstanding organic chemist and a colorful and fun loving human being.

James A. Marshall
Charlottesville, Virginia (USA)

DOI: 10.1002/anie.201203366