Angewandte 50 YEARS International Edition Chemie

Dudley Williams

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Professor Dudley Williams died in Cambridge on November 3, 2010 at the age of 73. His early papers and books on NMR spectroscopy and mass spectrometry helped transform the practice of organic chemistry, while his later contributions to chemical biology included elucidating vitamin D metabolism and the mode of action of the vancomycin family of antibiotics.

Dudley was born and grew up in Yorkshire. After a PhD in Leeds working on vitamin D chemistry, Dudley moved to Stanford in California to work with Carl Djerassi. In three stunningly productive years he showed how mass spectrometry and NMR spectroscopy could transform the way that organic chemists worked. Using a large set of related steroids effectively as a database, he explored fragmentation pathways in mass spectrometry, relating them to fundamental organic mechanisms, and he connected NMR coupling constants and chemical shifts to molecular geometry and substituent effects. His early studies of solvent effects on chemical shifts initiated a career-long interest in intermolecular interactions and molecular recognition.

In 1964 he was appointed by Lord Todd to a junior position in Chemistry at Cambridge, where he remained until his retirement in 2004. He made it a condition of his appointment that the Department became competitive by purchasing a Varian 100 MHz NMR spectrometer and an AEI MS9 mass spectrometer. His papers and textbooks from the early Stanford and Cambridge days, including *Spectroscopic Methods in Organic Chemistry*[1] (together with I. Fleming) simply revolutionized organic chemistry over the following ten years. Throughout his career he continued his flow of influential papers across a huge range of topics in chemistry and biology, always insisting on simple physical pictures and utmost clarity of thought from his co-authors. He was one of the most cited chemists in the UK, and was elected a Fellow of the Royal Society in 1983.

Dudley was always keen that his expertise be used for practical benefit: in the early 1970s, with Howard Morris and others, he showed how the inactive form of vitamin D that we eat is hydroxylated first in the liver and then in the kidney to the active 1,25-dihydroxy form; that work led to life-saving therapies for patients with kidney failure.[2] In late 1969 he was very excited about a new problem: a powerful antibiotic of unknown structure. He told his research group—of which I was lucky to be a PhD student at the time—that using mass spectroscopy we would be able to solve this structure in six months. Those six months turned into almost four decades of science: difficult and frustrating for several years—with some very thin PhD theses—but ultimately successful. NMR, mass spectrometry, thermodynamics, synthesis, and molecular biology were all brought to bear by the group on the problem of understanding not only the structures of these molecules, but also the intermolecular interactions leading to molecular recognition and their antibiotic activity.[3] His contribution was enormous: vancomycin and its analogues have become key weapons in the fight against MRSA "superbugs", with sales in 2007 of circa US$1 billion, and have saved tens of thousands of lives. But throughout that time, he also used vancomycin antibiotics and other systems as a testbed for fundamental thinking about molecular shape and flexibility, or about the thermodynamics of solvation, binding, and cooperativity. These are profound questions we still cannot fully answer.

Dudley was never afraid to challenge conventional wisdom and to think the unthinkable. Some of his potential achievements were thwarted by others: he submitted to SERC many years ago a proposal on what we would now call combinatorial chemistry, but it was years ahead of its time and was not funded. He was a compulsive scholar: no conversation with him, whether in a research group meeting, the local pub, or a dull departmental committee, would be complete without him taking a philosophical diversion into Boltzmann distributions, entropy, or the evolutionary origins of the behavior of colleagues. That severely reduced his value on a practical committee—conveniently optimizing the time he had for research—but as a colleague and mentor he was wonderful. When I was Head of the Cambridge Chemistry Department I could always turn to him for wise and unselfish advice, and for his deep insights into our colleagues' characters.

Of course, most of Dudley's results were actually obtained by his students and postdocs. The relationship between supervisor and research group is perhaps one of the greatest pleasures of academic life, and Dudley showed us that we are privileged to have an academic family as well as a biological family. The influence, teaching, and learning flow in both directions in a way that is infinitely enriching and rewarding. Dudley gave his students scientific freedom while also ensuring that everything we did was worth doing. He challenged our sloppy thinking and lazy responses. He encouraged us to think laterally and imaginatively, to challenge orthodox thinking, and to have the courage to work in new areas. He insisted that having provocative and testable ideas that might turn out to be wrong was more important than pursuing boring details. He was hugely proud of his students and postdocs, and he took great pleasure in our successful careers.

Music was a life-long passion, and he was an excellent pianist and singer, exploring across the spectrum from Schubert to jazz. Together with Pat, whom he married in 1963, he was also a great host.

The response of the research community to Dudley's death has been sad and shocked, but it has also celebrated his role in inspiring so many of us to become research scientists in his image. His legacy lives on, not only in his science, but also in his students and postdocs, and then through the generations of their own academic families.

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[1] D. H. Williams, I. Fleming, *Spectroscopic Methods in Organic Chemistry*, 6th edition, McGraw-Hill, London, **2007**.
[2] D. E. M. Lawson, D. R. Fraser, E. Kodicek, H. R. Morris, D. H. Williams, *Nature*, **1971**, *230*, 228.
[3] D. H. Williams, B. Bardsley, *Angew. Chem.* **1999**, *111*, 1264; *Angew. Chem. Int. Ed.* **1999**, *38*, 1173.

DOI: 10.1002/anie.201100049

