

In Memory of Sir Jack Baldwin

August 8, 1938 to January 4, 2020

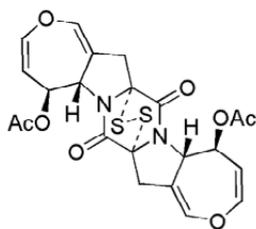
By Michael P. Filosa



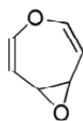
As an MIT freshman in 1970-71, I took first year organic chemistry, 5.41 and 5.42. We used notes written by Professor Dan Kemp¹ as well as the text book written by Hendrickson, Cram and Hammond. Through rowing, I became acquainted with William Rastetter who was a senior chemistry major and crew jock and he became somewhat of a role model for me. Bill taught a very popular recitation section for 5.42 in the spring of 1971 which I attended. Bill also did an undergraduate project with Jack Baldwin as an MIT senior before he attended Harvard to be a graduate student of R. B. Woodward.²

Woodward's graduate students were expected to develop their own projects. He became interested in the total synthesis of acetylaranotin and a subunit, symoxepine oxide which provided a possible pathway to the natural product.^{3,4} After an associate professorship at MIT and a successful career at Genentech, Bill became renowned later for founding IDEC Pharmaceuticals in 1986 and was co-inventor of Rituxan, the first monoclonal antibody approved by the FDA for cancer therapy. IDEC merged with Biogen in 2003 and Bill was the Executive Chair of the merged company from 2003-2005.

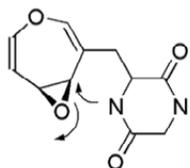
Like Bill, I majored in Chemistry and spent four years on the lightweight crew team. By the time I was a senior I was attending the very intense problem-solving seminar held by Professor Kemp for a small group of the entering first year graduate students. I had learned about them my sophomore year from my classmate, Virginia Lightner, who was already attending Kemp's seminar while doing undergraduate research in Sid Hecht's laboratory. I was intrigued by the problems she was working on for the seminar. Many of the problems had a great personal history with Professor Kemp going back to his days as a Woodward graduate student and his time at Harvard. I recall one problem in which he said it helped him get his job at MIT because he managed to impress Professor Büchi with his answer.



acetylaranotin



oxepin oxide



Proposed Rastetter
Approach to
Acetylaranotin ring
system

Remembering Bill Rastetter's teaching of recitation sections when he was a senior, I asked Professor Kemp and my senior advisor, Professor Fred Greene, if I could teach a recitation section. Professor Baldwin was teaching 5.42 that semester and they sent me to see him. He didn't interview me at all, just welcomed me aboard. Prof. Kemp and Prof. Greene's recommendation was good enough for him.

Attending Kemp's problem-solving seminar and teaching a 5.42 recitation section were two of the best decisions I ever made. However, unlike Bill I did not do undergraduate research with Jack Baldwin. I sought out Barry Sharpless at the beginning of my senior year, but he said he was writing grants and to come back in a month. I should have waited him out but, in my impatience, I instead went to Prof. Greene and did research that year in his laboratory.

I still recall the first class in 5.42 with Prof. Baldwin as the lecturer. He instructed the class, "This class is organized like the Catholic Church. If you have a problem, you first see your clergyman, aka your recitation section leader. If your needs are greater you go to your Bishop, Dr. Viavattene.⁵ However, like the Church you never, ever expect an audience with the Pope." Another time he got a laugh from the class when he said, "Emil Fischer and Sir Robert Robinson are two of the three greatest organic chemists of all time." He intentionally did not name who in his mind was the third greatest organic chemist and left that to our imagination.

That year I also visited grad schools with visits to Columbia and Harvard. My other choice was Stanford, but I did not venture to the West Coast for a visit and their acceptance came in late. I also thought in the spring of 1974 that there was not a compelling reason to go to Stanford as a synthetic chemist in comparison to Harvard and Columbia. Professor Kemp's stories about Woodward and Harvard, and Stork and Columbia were enough for me.

That was quite the experience having audiences with Prof. Stork, Breslow, Lippard, and Katz at Columbia and Prof. Woodward, Corey, Doering and James Wuest at Harvard. When I visited, Bill Rastetter took me out to lunch in Harvard Square, and showed me

around and described his approach to acetylaranotin and Professor Kishi's shared interest in that molecule. We also talked about his undergraduate project with Jack Baldwin.

I chose Harvard over Columbia and my teaching of 5.42, as well as taking Prof. Kemp's graduate level synthesis course, and Prof. Whiteside's graduate course in Physical Organic chemistry, prepared me exceptionally well as I prepared for my first year as a graduate student. I still take a lot of pride in the fact that Bill Roush and I were the only two first year graduate students who got A's on the organic qualifying exam. I used to tease him that I was sure I got the higher grade. Of course, he was equally certain he got the highest grade.

While I was in grad school, Baldwin published his "Baldwin's Rules" for ring formation which were a huge subject of discussion. His "Rules for Ring Closure" published in Chemical Communications in 1976 is by far his most cited paper with 1509 citations according to a recent search in Chemical Abstracts.⁶ Prof. Baldwin left MIT for Oxford in 1978 but his influence on my chemistry career did not end there.

In October 1979 I started at Polaroid where I would work for the next 26 years, which was followed by 8 years at ZINK Imaging. ZINK was a spinoff of Polaroid's R&D in 2005 after Tom Petters purchased Polaroid from One Equity Partners. One Equity Partners acquired Polaroid in 2002 after the initial bankruptcy, reorganized under Chapter 11 and sold for a nifty profit in 2005 to Petters. For all of those 34 years, one of Jack Baldwin's first Ph.D. students at MIT, Stephen Herchen, was both my esteemed colleague and future supervisor, corporate VP and eventually CTO of ZINK Imaging.

Steve had many hilarious stories about his time in Professor Baldwin's laboratory. In one of the stories Jack was taking the group out to a famous restaurant of the day, Maison Robert. Jack managed to get himself thrown out of the establishment before dinner was over. His group was left thinking, "How are we going to pay for this? Are we going to need to wash dishes or something?" The manager basically said, "We've thrown him out before. Enjoy your dinner and we'll settle with him."

In another story, Jack purchased a really hot sports car. His group had a pool as to how fast it would take him to wreck the car. The shortest time anyone chose was 24 hours. Jack wrecked the car that same night on a sharp curve in Memorial Drive where it passes under the Massachusetts Ave. Bridge.

On a more serious scientific note, Jack came back to Boston and delivered a major talk at Harvard around 1995 in one of the big lecture halls in the Science Center. It was a tour de force about his work on penicillin biosynthesis. He gave a spectacular talk about the

enzymes that create penicillins and cephalosporins. Jack and his students were able to take many tripeptides, both natural and unnatural, and cyclize them in vitro using enzymes like isopenicillin N-synthase (his second most cited work) into a large number of penicillins and cephalosporins.⁷ When Jack finished his talk he listed the 70+ students who worked on the project in chronological order. One of the first one or two students on the project was Steve Herchen.⁸

Jack had his usual colorful commentary in his incredibly distinctive and much imitated English accent during his presentation. One line I recall with great amusement: “Those of the more hostile persuasion will say this synthesis is backwards! The tripeptide starting material is many dollars per gram and the resulting penicillin is pennies per gram!”

Jack Baldwin blessed the world with much incredible science and a powerful and colorful personality. He directly or indirectly had a great influence on me with his science, his teaching and through his students. The world of science has lost an iconic figure.

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1. Professor Kemp was early in the process of writing his textbook with Frank Vellacio. He thought enolate chemistry was a perfect tool for teaching organic chemistry and the Kemp Notes reflected his pedagogical thinking. In 1970-71 we used Kemp's Notes far more than any organic chemistry textbook of the day, such as Hendrickson, Cram and Hammond's textbook.
 2. *Use of chiral isopropyl groups in biosynthesis. Synthesis of (2RS, 3S) - (4-13C) val*; Baldwin J E; Loliger J; Rastetter W; Neuss N; Huckstep L L; De la Higuera, N.; JACS (1973), **95**(11), 3796-7.
 3. *sym-oxepin oxide*; Rastetter W. H.; JACS (1976), **98**(20), 6350-3.
 4. Proton magnetic resonance studies of sym-oxepin oxide, Haas Daniel D; Rastetter W. H.; JACS (1976), **98**(20), 6353-9.
 5. Ron Viavattene was a Ph.D. student of Fred Greene who was a head teaching assistant that spring for 5.42. He later went to Polaroid and ZINK Imaging where his physical organic skills were extremely valuable. He also became an exceptional process analytical chemist. Like Steve Herchen, Ron, has been a valued colleague and friend for my entire professional career.
 6. *Rules for ring closure*; Baldwin, J.E.; Chemical Communications (1976), 18, 734-736.
 7. *Structure of isopenicillin N synthase complexed with substrate and the mechanism of penicillin formation*; Roach, Peter L; Clifton, Ian J.; Hensgens, Charles M. H.; Shibta, Norio; Schofield, Christopher J.; Hajdu, Janos; Baldwin, Jack E.; Nature (London) (1997), **387**, 827-830.
 8. *Recent biosynthetic studies on betalactam antibiotics*; Baldwin, J.E.; Jung, M.; Singh, P.; Wan, T.; Haber, S.; Herchen, S.; Kitchin, J.; Demain, A.L.; Hunt, N.A.; et. al.; Philosophical Transactions of the Royal Society of London, Series B: Biological Sciences (1980), **289**, 169-172.