E. N. Jacobsen

The author presented on this page has recently published his ***25th article*** *since 2000 in Angewandte Chemie:* "Activation of Electron-Deficient Quinones through Hydrogen-Bond-Donor-Coupled Electron Transfer": A. K. Turek, D. J. Hardee, A. M. Ullman, D. G. Nocera, E. N. Jacobsen, *Angew. Chem. Int. Ed.* **2016**, *55*, 539; *Angew. Chem.* **2016**, *128*, 549.

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Education: 1982 Undergraduate degree, New York University
1986 PhD supervised by Prof. Robert Bergman, University of California, Berkeley
1986–1988 Postdoctoral work with Prof. Barry Sharpless, Massachusetts Institute of Technology

Awards: **2001** ACS Award for Creativity in Synthetic Organic Chemistry; **2002** NIH Merit Award; **2004** election to the American Academy of Arts & Sciences; **2005** Mitsui Catalysis Science Award; **2008** ACS H. C. Brown Award for Synthetic Methods; **2008** election to the National Academy of Sciences; **2011** Janssen Prize; **2011** Noyori Prize; **2011** Nagoya Gold Medal Prize; **2012** Chirality Medal; **2013** Remsen Award; **2015** Esselen Prize; **2016** ACS Arthur C. Cope Award

Current research interests: Our program is dedicated to the discovery of practical catalytic reactions, and to the application of state-of-the art mechanistic and computational techniques to the analysis of those reactions. Our early work focused on the design of chiral complexes for asymmetric epoxidations, conjugate additions, and hydrolytic kinetic resolutions of epoxides; copper diimine complexes for asymmetric aziridination; chromium Schiff base complexes for enantioselective pericyclic reactions. Over the past several years, we have focused much of our group's efforts on the discovery of organic hydrogen-bond-donor catalysts for activation of neutral and cationic electrophiles. Our mechanistic analyses of these catalytic systems have helped uncover general principles for catalyst design, including electronic tuning of enantioselectivity, cooperative homo- and hetero-bimetallic catalysis, hydrogen-bond-donor asymmetric catalysis, and anion-binding catalysis.

Hobbies: Exercise, reading

What I appreciate most about my friends is their not taking themselves too seriously.

My motto is don't complain about things you can't change.

If I had one year of paid leave I would … as luck would have it, I do (having just completed a 5-year term as department chair). I am using it to catch up on writing papers, and on creating a new course I call "Practical Kinetics".

The most important thing I learned from my students is that it is great to be good at what you do, but it is extraordinary if you make everyone around you better as well.

The principal aspect of my personality is that I am pretty disciplined. I try very hard to find balance between my work and my family, and to pay enough attention to my physical fitness.

My favorite painter is Picasso. When he died I was assigned to do a school report on him (I was 13). I have been a student and ardent admirer of his work ever since. I am in awe of his creativity.

My favorite musician is hard to say, but I wish I sang like Eddie Vedder (and so does my wife).

The greatest scientific advance of the last decade was from my perspective, continued improvements in computational methods. I think the ability for synthetic chemists to correlate experimental data with high-level calculations is having a transformative effect on the study of reaction mechanisms, and it will ultimately give us insight into how to design new catalysts.

When I was eighteen I wanted to be the shortstop for the New York Yankees. That continued well into my 50's.

If I could be described as an animal it would be … Moose are simultaneously majestic and ridiculous. I'm far from majestic, but I have had a very serious job for most of my life. But I still feel I look ridiculous most of the time.

I am waiting for the day when someone will discover a "perfect" synthetic catalyst, following Jeremy Knowles' definition of perfect enzymes.

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The biggest challenge facing scientists is communicating effectively with broader society. As science advances, the average person's understanding of science has become thinner. This is very dangerous on many levels. We know that large fractions of the general public do not "believe" in evolution, human-induced climate change, or the benefits of vaccines, despite incontrovertible evidence to the contrary. Chemistry is especially vulnerable, because understanding the world at a molecular level is so important, but so completely alien to almost everyone.

Chemistry is fun because it is both intellectually interesting and potentially useful.

Young people should study chemistry because so many crucially important fields, including human health, environmental science, energy, and materials science, either require or benefit from a molecular perspective. Only chemists think about structure and function at a molecular level, and the value of this skill will only increase in the future.

Looking back over my career, I feel extremely fortunate.

The most significant historic event of the past 100 years was not a single event, but to me it is the gradual process of our society becoming more inclusive. Perhaps for the first time in human history, we are genuinely aiming for men and women, people of different races and religions, and LGBT and straight people to live and work together as equals. We obviously have a very long way to go, and not everyone is yet on board with it, but I am thrilled to witness the progress.

If I could be anyone for a day, I would be a youthful Michael Jordan. I have had to come to terms with the notion that I will never dunk a basketball, but I still dream about it.

The most important future applications of my research are almost certainly the people who have trained in my lab.

In a spare hour, I exercise.

My favorite saying is "If I had more time, I would have written less" (Blaise Pascal).

I admire people who do difficult things while making them look easy.

I advise my students to find balance in their lives, enjoy what they are doing, and become world experts in whatever it is they are working on.

My science "heroes" are … I had great research mentors in Yorke Rhodes, Bob Bergman, and Barry Sharpless, and they each inspired me in different and fundamental ways. Other than my advisors, my most important role model has been Peter Beak, my former colleague at the University of Illinois. Peter's life and work are a never-ending source of inspiration to me. He showed me that it is possible to be a generous, kind, and balanced person while doing the most interesting science. And he taught me by example to appreciate the amazing profession that I have.

Has your approach to chemistry research changed since the start of your career?

In some ways, certainly. I completed graduate school as an inorganic chemist, and now the main focus of my work involves purely organic compounds. Also, I could never have imagined that computational analysis would become an important part of my program. But on the other hand I think my research philosophy has been consistent. I occasionally run into former students from early in my career, and they will remind me of guidance I gave them when they were in my lab. I find it reassuring that it sounds very similar to what I tell my students today.

What advice would you give to up-and-coming scientists?

The same advice I received from Chuck Casey when I was interviewing for academic jobs back in the 1980's. He told me to pursue what interests me most, no matter how unfashionable that might be. I see some young scientists trying to anticipate what will be a hot area, or what will be "fundable". Not only is that incredibly hard to do while still maintaining originality, but I think it misses the point of doing independent science.

What's the biggest challenge you have faced in your career thus far?

Research is always challenging, by definition. But there have been a couple of times during my career when crises in my family have coincided with particularly challenging periods at work. The biggest challenge for me has been to find a way to maintain the necessary focus on my science when I am concerned about people I love. I do not think there is a simple answer to that.

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How do you know when it's time to continue holding on or time to let go when dealing with a difficult project that doesn't seem to work out?

This is clearly one of the biggest challenges we all face in basic research. We don't know the answer to the questions we seek to answer, and we are failing most of the time. My sense is that no more than half of the projects in the lab should be working to some degree at any given time. Higher than that, and we are probably not aiming high enough. Much lower than that, and things become very discouraging. But there is no simple answer to knowing when to let go of an idea, especially since we all know that the key breakthrough in a project can come in a most unexpected way.

What do you consider to be the most important skill an organic chemist should have?

Organic chemists are master problem-solvers. We have to love the challenge of confronting something that we do not understand, and taking it apart and using our brains and our hands to solve it.

Some interview questions were contributed by Nuno Maulide (University of Vienna) and Meike Niggemann (RWTH Aachen University).

My 5 top papers:

1. "Enantioselective Epoxidation of Unfunctionalized Olefins Catalyzed by (Salen)manganese Complexes": W. Zhang, J. L. Loebach, S. R. Wilson, E. N. Jacobsen, *J. Am. Chem. Soc.* **1990**, *112*, 2801.
   This was my first paper as an independent researcher, and it opened up a very important area for my group. It is also my most cited paper, and I wonder how unusual it is for someone's first paper to have that distinction. I suppose it could be said that it has all been downhill for me since then!
2. "Asymmetric Catalysis with Water: Efficient Kinetic Resolution of Terminal Epoxides by Means of Catalytic Hydrolysis": M. Tokunaga, J. F. Larrow, F. Kakiuchi, E. N. Jacobsen, *Science* **1997**, *277*, 936.
   In its first embodiment described in this paper, the so-called HKR (hydrolytic kinetic resolution) seemed like it would be a valuable transformation. I had the nerve to submit the work to *Science* at a time when *Science* published very few papers focused on synthetic methodology. I sent it in the day before my wedding, and the acceptance letter arrived the day I returned from my honeymoon. That was a very happy period!
3. "The Mechanistic Basis for Electronic Effects on Enantioselectivity in the (salen)Mn(III)-Catalyzed Epoxidation Reaction": M. Palucki, N. S. Finney, P. J. Pospisil, M. L. Güler, T. Ishida, E. N. Jacobsen, *J. Am. Chem. Soc.* **1998**, *120*, 948.
   I think the concept of electronic tuning of enantioselectivity may be my group's most important contribution from the conceptual standpoint. I am very proud of this paper, which provides a detailed analysis of the basis for the effect in the case of the reaction where we first observed it. The paper elicited a wonderful compliment from Peter Beak, who told me that he thought one could teach an entire course in physical-organic chemistry around it. I could never have hoped for a more flattering response!
4. "Asymmetric Catalysis by Chiral Hydrogen-Bond Donors": M. S. Taylor, E. N. Jacobsen, *Angew. Chem. Int. Ed.* **2006**, *45*, 1520; *Angew. Chem.* **2006**, *118*, 1550.
   It is often said that the best way to learn about a field is to teach it or to write a review article about it. That was absolutely the case for me with this review. Working on it with Mark Taylor was one of the most intellectually satisfying experiences of my career, and it had a big impact on my subsequent research.
5. "Asymmetric Cooperative Catalysis of Strong Brønsted Acid-Promoted Reactions Using Chiral Ureas": H. Xu, S. J. Zuend, M. P. Woll, Y. Tao, E. N. Jacobsen, *Science* **2010**, *327*, 986.
   The goal of my research program is to discover new catalytic principles, translate those discoveries into practical and useful new reactions, and understand the catalysts mechanistically to the point that broadly general principles might emerge. This paper is special to me because I think it illustrates each of those objectives in a very satisfying way.

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