



Q&A Robert Grubbs

The bond shifter

Rebecca Melen talks to the joint winner of the 2005 Nobel Prize in Chemistry about how his research is being applied to many different processes.

What was your introduction to organometallic chemistry?

Early in my undergraduate organic chemistry course, at the University of Florida, I heard a talk by a professor from the University of Texas about cyclobutadiene. On its own, cyclobutadiene is extremely reactive and can't be isolated, but you can isolate the metal complex. It struck me as very interesting that metals could stabilize such reactive species.

Later, I moved to Columbia University in New York and trained as a physical organic chemist. But there were many great physical organic chemists doing remarkable things. I recalled that lecture from the Texas professor and found that the organometallic field was still very small: you could read four or five papers and call yourself an organometallic chemist, and stabilizing reactive organic species such as cyclobutadiene was still really exciting. So during my post-doc I decided to switch to organometallics.

In fact, there are a group of us, all about the same age, who trained as physical organic chemists and ended up in organometallic chemistry. We're good friends — and sometimes competitors.

With so many metals to choose from, why did you select ruthenium for your catalyst?

Millions of tonnes of polymers such as Teflon, polythene and polystyrene are produced each year, and catalysts that improve polymer synthesis are crucial. I started my independent research looking at alkene polymerization; in particular, the polymerization of norbornene into poly-norbornene, which is often used as a test substrate for catalysis.

Several reactions produce poly-norbornene from a solution of norbornene and metal salts. The metal salt ruthenium chloride was thought to be a lousy catalyst because it produced polymer so slowly, but one of my students was attracted to it because, unusually, the reaction

worked in the presence of ethanol. The hydroxyl group in ethanol (and also in water) is one of the most difficult functional groups for catalysts to deal with, and the reason why adding water often kills catalyst activity.

It was exciting that ruthenium could potentially tolerate the presence of water. Organometallics typically work best without water, so we dried everything out and tried it again but then it didn't work at all! Clearly water was important, and it turned out that using pure water as the solvent was best.

Next, we identified the pre-catalyst (the compound we put into the reaction) and the active catalyst (formed from the pre-catalyst). The active catalyst turned out to be ruthenium carbene complex. Knowing this, we changed the other groups bound to the ruthenium and created catalysts that worked faster and could polymerize other things too. Since then it's just been tinkering and having fun.

Do you see a future for non-precious metals in metathesis?

We've been working on other metal carbenes, including metals with similar electronic properties such as iron, which is cheap, and osmium, which is expensive. You can also use titanium. Richard Schrock has been investigating molybdenum and tungsten. Many of these metal carbenes undergo metathesis. However, the metal is really just a small part of the overall cost. A lot of the expense is in making the ligands and the organometallic catalysts themselves.

Robert Grubbs, a chemist at the California Institute of Technology in Pasadena, was awarded the 2005 Nobel Prize in Chemistry, along with Yves Chauvin and Richard Schrock (see page S59), for the development of olefin metathesis and associated catalysts (primarily ruthenium). Olefin metathesis involves rearranging carbon-carbon double bonds and has widespread applications in fields such as drug synthesis and petroleum reforming.

Rebecca L. Melen completed her PhD in chemistry at the University of Cambridge, UK, and subsequently moved to Toronto, Canada as a postdoctoral fellow. She was recently awarded a Humboldt Fellowship to study at the University of Heidelberg, Germany. Her research focuses on the development of main group metal catalysts for chemical transformations important to both industry and academia.



REBECCA MELEN

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Even if we found an iron catalyst for metathesis, I am not sure it would be any better because it would probably have other drawbacks — for example, it would be less stable or active than ruthenium.

What applications and developments do you foresee for olefin metathesis?

I'm particularly happy about a drug that is currently in phase III testing called vaniprevir (from Merck), which is targeted against the hepatitis C virus. Our olefin metathesis catalyst is really important for the formation of this drug. Another application that I am excited about, and that I spoke about at the Lindau meeting, is the use of metathesis in pheromone synthesis. This might allow toxic and unselective pesticides to be replaced by naturally occurring pheromones that can, for example, disrupt mating patterns in selected insects. My intuition tells me that this is going to be big — but most of it is out of my hands.

Olefin metathesis is an important part of undergraduate chemistry. Do you enjoy lecturing on a topic in which your contribution has been so important?

It's fun to talk about because you can provide a lot of background. I'm not sure the students appreciate it, but that's okay. They don't seem overwhelmed at being taught by a Nobel laureate. At Caltech we have five Nobel laureates on campus — three in chemistry — so it's not a big deal for them.

Is academic science research becoming dependent on industry funding?

Yes, but industry is having similar financial problems to academia and has also cut back on its funding of basic research. Big companies used to help the transition from research in the laboratory to commercialization. When I started doing the early metathesis work, people from big companies would show up and want to test the catalysts. Now, most of the commercialization is done by small companies who are bridging the gap between the laboratory and industry.

What advice do you have for young researchers who wish to pursue a career in academia?

It is a great career if you can get in, but it is tough right now because of funding cuts. It will require particularly dedicated young researchers. Ten years ago, when a researcher entered academia there were good start-up packages, with lots of graduate students and funding. We will probably have to reduce some of that support and make tenure decisions earlier. The day of the really big research group is over. I must admit that I am sort of glad I'm old! ■

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Q&A Richard R. Ernst

A man of many dimensions

A pioneer of one- and two-dimensional nuclear magnetic resonance (NMR), Ernst talks to Stephanie Harris about why dimensions are important in life as well as in science.

How would you explain NMR to someone without a scientific background?

First, NMR allows you to determine the structure and connectivity of molecules or even to image the human body. NMR works by probing the responses of atomic nuclei in a magnetic field. These nuclei act like spies who give you coded messages that you record with electronic equipment. Once you've recorded these messages, you can try to analyse and understand them.

The nuclei have a magnetic moment, which means they react to an applied magnetic field. When you apply an external magnetic field the nuclei start to precess, or change the orientation of their rotational axis, with a frequency that is proportional to the field strength. If you measure the precessional frequency you can determine the local magnetic field,

which differs from the applied magnetic field because of shielding from the electrons that surround the nuclei. The difference between the two fields provides important information about the chemical environment around the nuclei within the molecule — whether it is electron-rich or -poor.

NMR can also tell us about the structure of a molecule: how the nuclei are spatially arranged. This is because the magnetic moments of nearby nuclei perturb the local magnetic field of the nucleus under study, introducing fine structure or splitting of the observed resonance. The precise nature of this splitting — whether it is split into two, three, four or a more complex pattern — tells us how many nuclei surround the one of interest. And the spacing of the lines in the pattern allows us to determine the distance between the nuclei.