



An Interview with Prof. Wolfgang Kroutil

Conducted by Robin Padilla (26.06.2013)



Prof. Wolfgang Kroutil
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RP: Can you briefly describe your research interests?

WK: I'm using enzymes, or as we call them biocatalysts, for organic synthesis. We try to shorten synthetic routes to natural products and pharmaceuticals by using enzymes and exploiting their high regio- and stereoselectivity. I'm also interested in identifying new enzymes with respect to organic chemistry; systems which are known for biochemists but have not yet been shown to be usable in organic synthesis. We also come across enzymes where the mechanism is not known and we study this more deeply. The main topics are redox reactions and C—C bond formation.

RP: What would you say is the biggest scientific challenge of today? Of tomorrow?

WK: It's definitely the raw materials, asking where does the carbon come from. You need efficient reactions to have a low carbon footprint and to produce less waste in the reactions. In society, I think chemists also need to work on the reputation of chemistry, because everything which is "bio" is considered fine but chemistry is...

RP: It's considered "dirty" by many people?

WK: Yes, exactly. I think there is also a duty to the society to show that life is chemistry! It's a big challenge.

RP: For synthetic organic chemists, there's this view that biocatalysis is a strange, exotic topic. What are some of the key points from biocatalysis that are relevant for organic chemists? What lessons from biocatalysis would you say are useful for the average synthetic organic chemist?

WK: The important thing is that the catalyst must be easy to obtain, that one doesn't need many synthetic steps. The catalyst should, of course, be used only in low amounts. Enzyme catalysis uses a lot of acid-base catalysts, it's mostly acid-base chemistry. Here you can avoid more complex intermediates. Nature uses some tricks but at the end, it is self-sufficient and rather simple.

There's the impression that one needs water and the aqueous phase to use [bio]catalysts. In most cases, it's done like that but there's definitely the chance to have the [bio]catalysts in the organic phase. It's standard for lipases, for example, and other enzymes. I think there are more chances to use other catalysts in organic solvents. Of course, in some cases, you desire to be in the aqueous phase, so it depends on each case.

If you want a biocatalyst, you can think of it as a big organocatalyst or if the catalyst has a metal, you can think of it as just a big ligand. I think the wording and language of organocatalysis and metal-based catalysis meet at some point. I'm also fascinated by organocatalysis, in particular, how to handle, use, and design the catalysts. Here biocatalysis is still far off because it aims for the specific reactions that nature provides. The way nature has designed enzymes, in terms of the size or rigidity, makes them more difficult to design in the way you would design a small organocatalyst. I think each area can definitely learn from the other. There are many opportunities to make fruitful interactions.

RP: That's a good point, because the language may be very different but the basic concepts are usually the same.

WK: Yes, that's right!

RP: What methods or what reactions from biocatalysis do you see as becoming as useful or becoming standard for organic chemists? What particular systems or reactions do you think will become popular?

WK: <laughs> This is always a little bit hard to say! I think the reduction of ketones was first the domain of organometallic catalysis and enzymes have stepped in and taken over a major part, especially on an industrial scale. Something similar just happened for the amination of ketones. Here, the organocatalytic methods were good but not excellent, and the enzymes quickly took over. I think the next step is extending [biocatalytic] methods to include C—C bond formation and I hope for Friedel–Crafts acylations or alkylations. This is probably going to take some time but there is a lot of potential. I would expect the Pictet–Spengler reactions to be one of the next big areas.

There is definitely another area which is coming up fast and that is taking enzymes and using them in cascades to do several steps simultaneously in one pot. I think this is another topic which is advancing fast. It would avoid many separation and purification steps, which is better for the environment and also relevant for biotechnology.

RP: What kind of interests and hobbies do you have outside of the lab?

WK: I have a ten-year old daughter, so I'm rather occupied with family. We like to do some sports together. I also like gardening. Currently, I don't have much time to go up into the mountains but I do enjoy climbing. I also enjoy swimming too!

RP: Is there anything else you'd like to add?

WK: I think we have to cross barriers between the different catalysis fields. There are some "catalysis" conferences where the topics are almost all heterogeneous catalysis and there's little knowledge of biocatalysis, for example. It's a problem of language but sometimes it goes back even to teaching. We need to incorporate the different types of catalysis to show the connections. It's important to show in the teaching lectures what they have in common.

Some of Prof. Kroutil's own favorite, recent publications:

Voss, C. V.; Gruber, C. C.; Faber, K.; Knaus, T.; Macheroux, P.; Kroutil, W., Orchestration of Concurrent Oxidation and Reduction Cycles for Stereo-inversion and Deracemisation of *sec*-Alcohols. *J. Am. Chem. Soc.*, (2008) **130**, 13969.

Lara, M.; Mutti, F. G.; Glueck, S. M.; Kroutil, W., Oxidative Enzymatic Alkene Cleavage: Indications for a Nonclassical Enzyme Mechanism. *J. Am. Chem. Soc.*, (2009) **131**, 5368.

Schrittwieser, J. H.; Resch, V.; Sattler, J. H.; Lienhart, W.-D.; Durchschein, K.; Winkler, A.; Gruber, K.; Macheroux, P.; Kroutil, W., Biocatalytic Enantioselective Oxidative C—C Coupling by Aerobic C—H Activation. *Angew. Chem. Int. Ed.*, (2011) **50**, 1068.

Simon, R. C.; Grischek, B.; Zepeck, F.; Steinreiber, A.; Belaj, F.; Kroutil, W., Regio- and Stereoselective Monoamination of Diketones without Protecting Groups. *Angew. Chem. Int. Ed.*, (2012) **51**, 6713.

Sattler, J. H.; Fuchs, M.; Tauber, K.; Mutti, F. G.; Faber, K.; Pfeffer, J.; Haas, T.; Kroutil, W., Redox Self-Sufficient Biocatalyst Network for the Amination of Primary Alcohols. *Angew. Chem. Int. Ed.*, (2012) **51**, 9156.

[1] Professor Kroutil's contributions will appear in the upcoming *Science of Synthesis: Biocatalysis*.