

# A Feast and a Reflection on Organocatalysis – Notes from the ISO $\mu$ in Mülheim<sup>[‡]</sup>

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The past ten years have witnessed the rediscovery and rise to prominence of organocatalysis as a so-called “third pillar of asymmetric catalysis” in organic synthesis.<sup>[1]</sup> This field has experienced a truly explosive growth to which few in the community have been indifferent. From July 14 to 17, 2010, the International Symposium on Organocatalysis, Mülheim (ISO $\mu$ ),<sup>[2]</sup> chaired by Benjamin List, one of the pioneers of this emerging area, took place at the new lecture hall of the Max-Planck-Institut für Kohlenforschung in Mülheim an der Ruhr (Germany). This particular conference was organised under the auspices of the Deutsche Forschungsgemeinschaft's (DFG, the German Science Foundation) “Schwerpunktprogramm Organokatalyse”, a Priority Programme funding research in this competitive area from 2005 to 2010, and served as its closing event. In effect, it was a unique gathering of an overwhelming majority of leading researchers in the field, providing a singular meeting point for many of them. For instance, Karl Anker Jørgensen (Denmark) and Yujiro Hayashi (Japan), whose names are inextricably connected by virtue of their simultaneous development of a well-known, highly versatile secondary amine catalyst (compound **3**, Figure 1), had actually never met in person prior to this conference!

The ISO $\mu$  opened with a Reporting Colloquium on the very first day, featuring short presentations by all the DFG-funded researchers. This particular setting allowed a unique exposure of the leading advances in organocatalysis made by German researchers to an audience itself containing many of the leaders in this domain. The conference proper

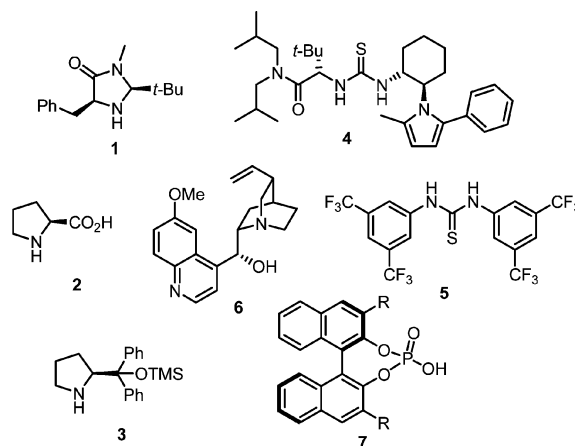


Figure 1. Structures of some of the most well-known organocatalysts.

featured contributions from 36 distinguished speakers,<sup>[2]</sup> in addition to the 20 German researchers who reported their most recent findings in the aforementioned colloquium. I will therefore refrain from a tedious description of each lecture; it is my belief that this symposium represented an invaluable opportunity to gauge the current state of organocatalysis as a field, to acknowledge the actual trends and to attempt to gaze into what the future may hold.

Among the interesting features of this symposium was the very high collegiality shown between participants and speakers. Fast-paced, “crowded” and competitive areas of research in synthetic chemistry have a tradition of generating rivalries that, not infrequently, degenerate into unnecessary bickering. Whilst organocatalysis certainly has not escaped the development of such rivalries, they stand in contrast to the positive atmosphere experienced by participants

[‡] International Symposium on Organocatalysis in Mülheim an der Ruhr, Germany, July 14–17, 2010.

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throughout the event, as well as to the respectful and friendly tone of all lectures, considering that almost all the lecturers are in direct competition for specific niches of the organocatalytic realm.

The main focus of the lectures reflected well the current trends in the field. Organocatalytic methodological development is very much oriented towards the establishment of new catalytic transformations that proceed with high efficiency and very high enantioselectivities. Figure 1 portrays some of the most familiar organocatalysts, typically divided between secondary amines (**1–3**, employed in the now “standard” enamine/iminium activation modes), hydrogen-bonding catalysts (thioureas such as **4** and **5** being among the most popular) and Brønsted acids (generically represented by binaphthylphosphoric acids **7**, also capable of relaying chiral information through ion-pairing). Although the true measure of “catalytic efficiency” may be difficult to standardise, an underlying concern of many presentations was in reducing the traditionally “high” catalyst loadings associated with organocatalytic transformations (e.g. Helma Wennemers, who reported catalyst loadings of 0.1 mol-% in the Michael addition to nitro olefins). A relatively smaller number of presentations sought direct applications of organocatalytic key-steps to total synthesis (of which we could highlight Matthew Gaunt or Yujiro Hayashi), a tendency which appears to be growing in recent years, as well as mechanism-oriented, physical organic chemistry approaches towards a qualitative and quantitative understanding of reactions catalysed by small organic molecules (as exemplified by Herbert Mayr’s development of quantitative descriptors for nucleophilic organocatalysts).

Another focus of the lectures was on catalyst design. While the dream of identifying “general catalysts” for very broad classes of transformations (be it within aminocatalysis, hydrogen-bonding activation, NHC mediators or Brønsted acid catalysis) is still very much alive, the flurry of new motifs presented and the revival of “older” scaffolds based on catalysts that are well-established in the community (Figure 1) highlight the constant drive for innovation in this young research area.

In a nutshell, this conference served as a very special meeting point and a one-of-a-kind opportunity for almost all the current leaders in the field of organocatalysis. While achieving this, it presented a very accurate portrait of an exciting area, which has travelled great lengths over the past ten years, and which seems to stand at a crossroads. On one hand, it slowly becomes apparent that the deceitful simplicity of many transformations belies fairly complex mechanistic pictures (as beautifully illustrated by Ken Houk or Jeffrey Bode), and a welcome trend of the conference was the growing concern of many researchers in a deeper mechanistic understanding of the chemical reactions involved. On the other hand, the aforementioned drive for innovation also typically underscores the importance of establishing new activation paradigms of small organic molecules (a point driven home by David MacMillan with the development of SOMO catalysis).

The participants were also entertained by a refreshing and enjoyable social program, as all evenings featured festive conference dinners held at the Mülheim campus. In a unique demonstration of the multifaceted talents of chemists, Albrecht Berkessel (Köln) and Peter Schreiner (Giessen, and a member of the *EurJOC* International Advisory Board) presented the audience with a live concert of relaxing music (Figure 2).



Figure 2. Snapshots from the lively social programme. Albrecht Berkessel (right) and Peter Schreiner (left) are featured in the bottom photo, showing off their talents.

What therefore are the future perspectives of organocatalysis that could be inferred from such a meeting? It is my (personal) impression that this is a field where new cutting-edge developments are always around the corner, particularly because organocatalysis appeals irresistibly to the synthetic organic chemist’s heart by virtue of its conceptual elegance and theoretical (apparent) simplicity. How long will it take, then, for organocatalytic reactions to become the “bread and butter” in the general toolbox of synthesis? It is tempting to speculate that the main force of organocatalytic transformations resides perhaps in their ability to quickly and stereoselectively generate relatively small build-

ing blocks with dense functional group arrays. Most known organocatalytic reactions actually achieve conceptually simple transformations but in unprecedented levels of selectivity. As such, the potential of these transformations as opening manoeuvres of synthetic sequences is largely untapped by the broad community. And it may well remain so until more catalysts become commercially available and the sensation of “predictability” (warranted or not) that most chemists experience towards many well-established metal-catalysed transformations settles in. That will, in any event, surely not deter the scientists that were present at the ISO $\mu$  and their colleagues around the world from developing even more spectacular organocatalysed transformations.

- [1] For selected reviews and treatises, see: a) A. Berkessel, H. Gröger, *Asymmetric Organocatalysis*, Wiley-VCH, Weinheim, Germany, **2005**; b) B. List, J. W. Yang *Science* **2006**, *313*, 1584; c) D. W. C. MacMillan *Nature* **2008**, *455*, 304; d) P. I. Dalko (Ed.), *Enantioselective Organocatalysis*, Wiley-VCH, Weinheim, Germany, **2007**; e) P. I. Dalko, L. Moissan *Angew. Chem. Int. Ed.* **2001**, *40*, 3726.
- [2] For detailed information, see the conference website: [http://www.mpi-muelheim.mpg.de/kofo/institut/arbeitsbereiche/list/Organokatalyse\\_30\\_04/index.html](http://www.mpi-muelheim.mpg.de/kofo/institut/arbeitsbereiche/list/Organokatalyse_30_04/index.html)

Received: May 31, 2010  
Published Online: October 25, 2010