Metals in Synthesis 2008 (MIS-08)

PGM-CATALYSED PROCESSES FOR ORGANIC SYNTHESIS

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On the 15th October 2008, the University of Bath, U.K., hosted a half-day symposium entitled “Metals in Synthesis 2008 (MIS-08)”. The symposium was held in honour of Professor Masakatsu Shibasaki (Graduate School of Pharmaceutical Sciences, The University of Tokyo, Japan) (1), the winner of a prestigious Royal Society of Chemistry (RSC) Centenary Lectureship. Professor Shibasaki won the Lectureship for his numerous seminal contributions to the discovery and development of asymmetric catalysts for organic synthesis. As part of the lectureship tour, Professor Shibasaki visited six U.K. universities: the Universities of Sussex, Bath, Warwick, York, Strathclyde and Southampton, and was presented with the RSC Centenary Lectureship medal at MIS-08 at the University of Bath (2).

The MIS-08 symposium was organised by John S. Fossey (then at the University of Bath, now at the University of Birmingham, U.K., and co-author of this review) and aimed to showcase some of the U.K.’s leading talents in metal-mediated synthesis. As such, three other speakers, Professor Jonathan M. J. Williams (University of Bath, U.K.) (3), Michael Willis (University of Oxford, U.K.) (4) and Paul Davies (University of Birmingham, U.K.) (5), were invited to present their most recent and exciting results. This was followed by a well attended poster session where researchers from all over the U.K. presented highlights of their work.

Conference Highlights

The MIS-08 symposium began in the University of Bath’s main University Hall lecture theatre in front of a packed audience of delegates from all over the U.K. Gareth Price, the head of the University of Bath’s chemistry department (6), welcomed delegates and handed over to the chair of the first session, Christopher Frost (University of Bath, U.K.) (7). Frost has developed his own metal-mediated tandem catalysis strategies for organic synthesis (8, 9). He gave an especially warm welcome to the first speaker, his former Ph.D. supervisor, Professor Jonathan Williams.

Professor Williams’ presentation detailed his methodology of ‘hydrogen borrowing’ for the formation of carbon–carbon and carbon–nitrogen bonds. In this chemistry, ruthenium or iridium catalysts temporarily remove hydrogen (H₂) from an alcohol to give an aldehyde. This aldehyde may then react to give an alkene (in a Wittig-like reaction) or with an amine to give an imine. The earlier ‘borrowed’ hydrogen is returned to the substrate, furnishing products in which the oxygen of the alcohol starting material is replaced with a –CH₂R carbon or an –NHR nitrogen, Figure 1 (10–14). These procedures allow alcohols to be used as alkylating agents in place of more conventional, but often toxic or mutagenic, alkyl halides. The usefulness of this methodology has been demonstrated by application to drug molecule synthesis.

Next, Michael Willis discussed developments surrounding intermolecular hydroacylation...
reactions with respect to reactivity and enantioselectivity. He detailed atom-economical reactions that involved rhodium(I)-catalysed addition of aldehydes across C–C multiple bonds, in conjunction with catalytic C–H activation and C–C bond formation. He elaborated on the impressive scope of intermolecular chelation (β- S- or β- O-substituted aldehyde) controlled alkene and alkyne hydrosylation, Figure 2 (15–17). Willis then showed that this process could be applied to some rather elegant asymmetric examples.

Paul Davies followed up with an impressive story of how his metal-activated reactions encompass activation of alkynes towards nucleophilic attack and the use of alkynes as masked ylides. When activated by gold or platinum catalysts, the alkynes can potentially react as an alkylidene carbeneoid by the pull-push nature of the catalytic activation, Figure 3 (18, 19).

Davies went on to describe a one-pot cascade reaction catalysed by gold, which exploited his masked ylide protocol. The reaction proceeds via rearrangement of propargylic carboxylates in the presence of sulfides, to give 2-substituted 4-allyl-2,3-dihydrothiophenes, Figure 4 (20).

After a short break, John Fossey opened the second session and introduced Professor Masakatsu Shibasaki. At this point Mike Willis took to the floor once again for his second official role of the day: as a member of the Executive Committee of the Organic Division of the RSC, the privilege of presenting Professor Shibasaki with the Centenary Lectureship medal fell to him, Figure 5.

Professor Shibasaki proceeded to deliver his lecture entitled ‘Recent Progress in Asymmetric Two Centre Catalysis’. He began by revealing the requirement for enhanced activation modes in catalysis, and proposed that dual activation or ‘two centre’ catalysis has the potential to afford new reactivities and higher selectivities, particularly in asymmetric transformations. He provided details of asymmetric two centre catalysis promoted simultaneously by Lewis acid complexes (with metals such as aluminium, titanium, lanthanum, gallium or zinc) and Brønsted bases or by Lewis acids in conjunction with Lewis bases (for example S=O, P=O), Figure 6 (21).

Excellent results were achieved in a wide range of bond-forming transformations, with high enantiomeric excess and high yields possible under dual activation conditions (22–28). Furthermore, the methods have been used in the practical synthesis of a key intermediate for ranirestat, AS-3201, a highly potent aldose reductase inhibitor, Figure 7 (29, 30).
Poster Session and Prizes

Following an invigorating question and answer session, Fossey brought the seminar to a close and invited delegates to the poster session and wine reception held in the University’s Department of Chemistry. The poster session was an opportunity for more than thirty young scientists to present their work and discuss ideas with the other delegates. The Japan Society for the Promotion of Science (JSPS) was the main sponsor of the poster session and wine reception, which allowed it to distribute details of its exchange programmes connecting U.K. and Japanese researchers and facilitating bilateral research projects. Professor Yuko Furukawa, Director of the JSPS's London Office attended the event. Full details of JSPS programmes for pre- and postdoctoral fellows may be obtained from the JSPS London Office’s website (31).

Professor Furukawa drew the event to a close by awarding prizes for the most innovative and exciting posters. The first prize of a signed copy of a book edited by Professor Shibasaki “Multimetallic Catalysts in Organic Synthesis” (32) (donated by Wiley: *Chemistry – An Asian Journal*) and a presentation lacquer-ware clock (from the JSPS) went to Michael Shaw, a Ph.D. student in Professor Varinder K. Aggarwal’s group at the University of Bristol, U.K., for his poster presentation on studies towards the synthesis of natural...
products (33), Figure 8. JSPS runner-up prizes were awarded to five Ph.D. students: Paul Fordred (in Steven Bull’s group, University of Bath), Marta P. Pereira Morais (co-supervised by John Fossey, University of Bath) Simon Pridmore (Professor Williams’ group, University of Bath), Tomoki Nishimura (Royal Society visiting scholar from the University of Kitakyushu, Sakurai Laboratory, Japan) and Hannah Edwards (Christopher Frost’s group, University of Bath).

Conclusions
Platinum group metals (pgms) are playing an increasingly important role in organic synthesis, especially in the asymmetric synthesis field. Synthetic methodologies based on pgm-catalysed reactions that form new chemical bonds under progressively milder conditions, with greater ease and increasing power, will continue to be at the heart of intriguing and useful discoveries.

Acknowledgements
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18 Davies Research Group, University of Birmingham, School of Chemistry: http://www.chem.bham.ac.uk/labs/davies/research/ (Accessed on 30th March 2009)
33 Aggarwal Group, University of Bristol: http://www.chm.bris.ac.uk/org/aggarwal/aggarhp.html (Accessed on 30th March 2009)

The Reviewers

Dr Wenbo Chen is a Leverhulme Trust-funded postdoctoral research fellow working with John S. Fossey at the University of Birmingham, U.K. His work is focused on new asymmetric motifs for C–C bond forming catalysis. Prior to this, Wenbo was a Ph.D. student at the Shanghai Institute of Organic Chemistry, China, where he worked on organosulfur chemistry with Professor Long Lu.

Dr John S. Fossey is a recently appointed lecturer in chemistry at the University of Birmingham, U.K. Prior to this, he spent three years at the University of Bath where he established his research group and published on a range of topics, including nickel- and cobalt-mediated chemistry. Before that, John was JSPS postdoctoral research fellow in the laboratories of Professor Shu Kobayashi (The University of Tokyo, Japan), where he worked on nickel-catalysed reactions of enecarbamates. He obtained his Ph.D. from Queen Mary, University of London, U.K., under Dr Chris J. Richards, working on Group 10 pincer complexes as C–C bond forming catalysts. For more information please visit: http://www.chem.bham.ac.uk/staff/Fossey.shtml