ADHOC 2005 in Cologne: The Latest in Dioxygen Activation and Homogeneous Catalytic Oxidation[**]

Christian Limberg*

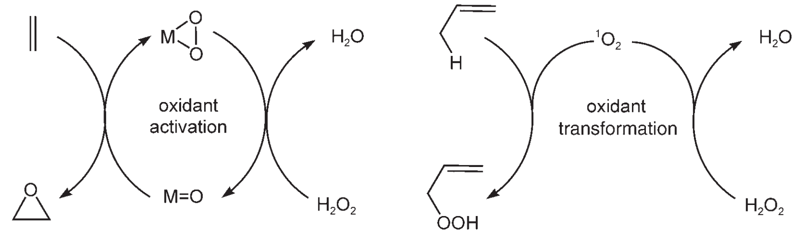
The selective functionalization of hydrocarbons is one of the most important challenges of chemistry and is of great interest for the purposes of basic research and technology. Homogeneous, heterogeneous, and enzymatic processes are being pursued worldwide as potential solutions to this problem. The mechanisms of oxidation reactions remain among the most puzzling issues in chemistry. To gain better insight, model systems with well-defined active sites are being developed, while with the aid of kinetic measurements, sophisticated isotope-labeling experiments, molecular probes, and especially computational chemistry, structure–activity relationships can be discussed and current proposed mechanisms can be either supported or rejected. Naturally, there is an intense interest in new oxidation reactions and catalysts as well as in novel applications of oxidation chemistry. All of this was the subject of the 9th International Symposium of Activation of Dioxygen and Homogeneous Catalytic Oxidation (ADHOC) in Cologne, Germany, which was organized for over 200 participants from industry and academia by Albrecht Berkessel (University of Cologne) and Henrique Teles (BASF, Germany).

The opening lecture was given by R. Diercks (BASF, Germany) in which he introduced industrially relevant oxidation processes for the production of base chemicals, explained some problems therein, and addressed the importance of catalyst and reactor design. It was clearly pointed out that the use of HNO_3 as an oxidizing agent is frowned upon, as the nitrogen oxide byproducts are frequently cited in the literature as environmental hazards. However, the coupling of industrial oxidations to other processes (NO_x recovery, N_2O decomposition) can effectively turn HNO_3 into a "green" reagent. Remaining N_2O can also be an attractive source of oxygen, as outlined in the talk given by G. I. Panov (Boreskov Institute, Novosibirsk, Russia). With this reagent it is possible to oxidize benzene to phenol and its derivatives, as well as various olefins to carbonyl compounds, and to carry out the chemical modification of polymers such as polybutadiene.

New perspectives in the use of singlet oxygen were also highlighted. It has been known for some time that Na_2MoO_4 at appropriate pH values can catalyze the disproportion of H_2O_2 to give $^1O_2$. J.-M. Aubry (ENSCL, Lille, France) reported that $[Mo(O_2)_3O]^{2-}$ represents the catalytically active species. He introduced a method with which the $^1O_2$ produced can be used for "dark" oxygenations of hydrocarbons. A problem with this is the short lifetime of $^1O_2$ in aqueous medium, which opposes the oxidation of hydrophobic compounds. It is possible, however, to carry out peroxidations as a continuous process by using specially designed multiphase microemulsions. P. Alsters (DSM, The Netherlands) discussed the applications of this procedure and simultaneously presented a way to solve the problem of parallel concurrent activation of H_2O_2 for epoxidations (Scheme 1): the use of pure inorganic compounds in heterogeneous phases. Elsewhere, A. Griesbeck (University of Cologne, Germany) described how $^1O_2$, with the aid of tetraarylporphyrin-loaded polystyrene, can be used for ene reactions, [4+2] cycloadditions, and can make ordinary organocatalytic reactions "chiral".

Many contributions this year also focused on natural approaches toward oxygen activation. These include direct investigations of metalloenzymes and studies concerning for the use of biocatalysts, as well as the development of biomimetic and bioinspired systems. J. D. Lipscomb (University of Minnesota, USA) was able to show that in soluble methane monooxygenase, the formation of a complex between the regulatory protein MMOB and the active component MMOH creates a very narrow pore, through which only methane has access to the active site (Scheme 2). This was proposed as one reason for this enzyme's high substrate selectivity for methane. This understanding should facilitate mutagenesis experiments designed to expand the oxidation capacity of this enzyme. Furthermore, this represents the first time that the dioxygenase mechanism could be followed spectroscopically through systematic substrate variation.

Such non-heme-containing enzymes were also the basis for the talk given by L. Que, Jr. (University of Minnesota, USA). He reported molecular models that catalyze the H_2O_2-mediated oxidation of olefins through a nonradical mechanism. The results of isotope-labeling experiments with these systems have led him to conclude that the active species bears an $O{=}Fe^{V}{-}OH$ unit (Scheme 3).



Scheme 1.

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[*] Prof. Dr. C. Limberg
Humboldt-Universität zu Berlin
Institut für Chemie
Brook-Taylor-Straße 2
12489 Berlin (Germany)
E-mail: Christian.limberg@chemie.hu-berlin.de

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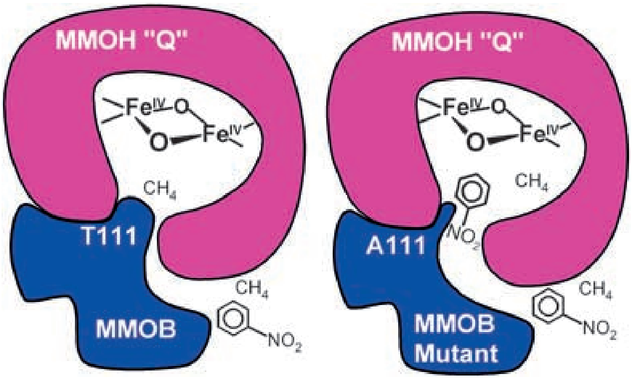
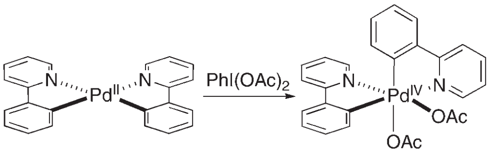


Scheme 2.

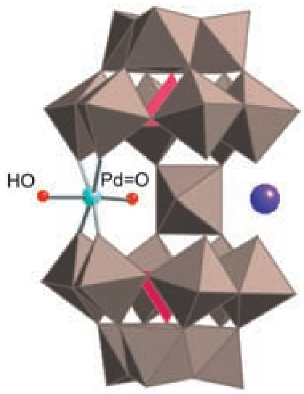


Scheme 4.

A dioxygenase reaction intermediate inspired T. D. P. Stack (Stanford University, USA) to employ single-core Fe and Mn complexes to catalyze the epoxidation of terminal olefins with peracids. A group of Mn complexes has proven itself especially active and selective, and its heterogenization by binding to silica gel adds to its list of advantages. W. Kroutil (University of Graz, Austria) was able to show that a dehydrogenase from *Rhodococcus ruber*, which is stable in organic solvents, can carry out highly stereoselective alcohol oxidations. It differentiates between not only *R* and *S* stereocenters, but also primary and secondary alcohols (intramolecular as well).

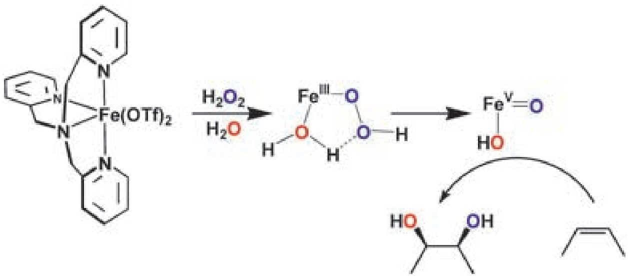
Many newly developed systems use Pd catalysts in combination with O_2. The prime example for such systems, namely the Wacker process, occasionally served as a source of ideas. S. S. Stahl (University of Wisconsin, Madison, USA) discussed an aza-Wacker process, which gives rise to enamines, and M. S. Sigman (University of Utah, USA) reported the dialkoxylation of olefins. Alcohol oxidations can also be carried out in aqueous media with water-soluble catalysts, as described by I. W. C. E. Arends (TU Delft, The Netherlands). D. De Vos (University of Leuven, Belgium) introduced a new procedure for the alkenylation of aromatic compounds, the mechanism of which was also studied in detail. Furthermore, he discussed the application of immobilized tungstate catalysts with haloperoxidase activity: these effect the oxidation of bromide to bromonium ions, which in turn, can be reactive under nonacidic conditions with olefins and aromatic compounds. M. S. Sanford (University of Michigan, USA) dealt with ligand-directed oxidations of C−H bonds, and in the process of investigations with the oxidizing agent $PhI(OAc)_2$ she successfully isolated and characterized a Pd^{IV} intermediate. The relevance of the $+4$ oxidation state in Pd-catalyzed reactions has been the subject of controversy for some time, and here could be some initial evidence that such compounds actually do exist (Scheme 4).

The "slow-burners" of oxidation catalysis are the polyoxometallates (POMs), for instance, as ligands for other transition-metal oxo units, which then become active as the oxidant. M. Bonchio (University of Padova, Italy) reported the synthesis of POM–Ru and POM–Fe complexes, which catalyze reactions with O_2 upon microwave irradiation. POMs can also exhibit interesting chemistry in combination with noble metals. Not long ago, M=O compounds of late transition metals were unknown, as their d electrons occupy the π* orbitals of the M=O bond. The latter, however, are clearly stabilized by POM ligands; their use, as described by C. L. Hill (Emory University, Atlanta, USA), had recently allowed the isolation and characterization of the first Pd=O complex, and now he reported $K_9Na_4[(O{=}Pd^{IV}\text{-}OH)WO(OH_2)L_2]$ ($L = [PW_9O_{34}]^{9-}$). Furthermore, there is evidence for the first O=Au complexes, which can be produced by oxidation in air (Scheme 5).



Scheme 5. Blue circle right: K^+

The talk given by R. Neumann (Weizmann Institute, Israel) made it clear just how broad the range of POM–transition-metal-catalyzed oxidation reactions really is. Interestingly, with substrate-immobilized dipyrimidylplatinum–POM hybrid compounds, even the catalytic oxidation of methane with O_2 in water was achieved, whereby methanol and acetaldehyde are formed, the mechanism of the surprising formation of $CH_3C(O)H$ is currently investigated. Altogether, there is still great interest in the oxidation of methane, the simplest natural yet most resistant source of C_1 hydrocarbons. After a mechanistic discussion of proton-coupled electron transfer, J. M. Mayer (Uni-



Scheme 3. Tf = trifluoromethylsulfonyl.

versity of Washington, Seattle, USA) first introduced results of his investigation of the reaction of OsO_4 with H_2 and subsequently described initial results of the extension of this work toward methane as a substrate. R. A. Periana (USC, Los Angeles, USA) reported the use of CH_4 to generate acetic acid in the metal-catalyzed oxidation with O_2 as well as the first efforts toward the establishment of a catalytic cycle for the O_2- oxidation of hydrocarbons starting from Ir alkoxides.

A further important area of oxidation chemistry (especially within the detergent industry) is bleaching catalysis, to which an entire section of lectures was devoted. There is great interest in the development of active metal catalysts, and the most prominent representative of these is $[(Me_3tacn)Mn(\mu\text{-}O)_3Mn(Me_3tacn)]^{2+}$ (tacn = 1,3,7-triazacyclononane). The talk given by J. R. Lindsay-Smith (University of York, UK) dealt with mechanistic investigations of this system, and R. Hage (Unilever, UK) introduced the general development of metal-mediated bleaching. The lecture given by G. Reinhardt (Clariant, Germany) made it clear that there is not, and never will be a panacea for the bleaching industry. Additional talks on this subject were given by G. Miracle (P&G, USA) and J. J. Dannacher (University of Basel, Switzerland).

Efficient systems for the oxidation of prochiral thioethers to enantiomerically pure sulfoxides were introduced by R. F. W. Jackson (University of Sheffield, UK) und C. Bolm (RWTH Aachen, Germany). Through systematic variation of the ligand, metal, and additives, enantiomeric excesses of up to 99.5% could be reached, making the procedure suitable for the synthesis of biologically active compounds. Y. Shi (CSU, Fort Collins, USA) reported equally impressive *ee* values and yields in his investigation of organocatalyzed epoxidations. His research group succeeded in finding chiral ketone catalysts, which are converted in situ by an external oxidant into dioxiranes, which in turn, effect an enantioselective oxygen transfer to olefin substrates. M. Beller (Leibniz Institute for Organic Catalysis (IFOK), Rostock, Germany) presented a novel chiral pyridine bisimidazoline ligand system, in which Ru complexes in conjunction with pyridine dicarboxylic acid give the highest reported *ee* values for a transition-metal-mediated epoxidation with H_2O_2. The talk by I. Hermans (University of Leuven, Belgium) gave rise to controversial discussions, as it dealt with autoxidation of hydrocarbons. The validity of the conventionally accepted mechanistic model of alcohol and ketone formation, was put into question based on current experimental and theoretical data; a new proposal was presented in which cyclohexylperoxyl radicals, for example, do not abstract hydrogen atoms from cyclohexane, but instead from cyclohexylhydroperoxide (→ketone).

There were many other interesting talks regarding mechanistic and preparative aspects of oxidation catalysts the discussion of which would significantly expand the scope of this report [A. Llobet (University of Barcelona, Spain), Y. Naruta (Kyushu University, Fukuoka, Japan), T. Geller (Bayer CropScience, Germany), J. P. Roth (Johns Hopkins University, Baltimore, USA), W. R. Thiel (University of Kaiserslautern, Germany), T. Funabiki (Doshisha University, Japan), C. Punta (University of Milan, Italy), I. Weinstock (City College New York, USA), Z. Gross (Technion, Haifa, Israel), C. Limberg (HU Berlin, Germany)]. The closing talk was given by R. A. Sheldon (TU Delft, The Netherlands), in which he discussed the imposing range of oxidation reactions that can be catalyzed by nitroxyl radicals.

Overall, the conference demonstrated that through the intense efforts of the past few years in the area of oxidation chemistry, many breakthroughs were made which, of course, have given rise to new questions and challenges. Among these, for example, the application of atmospheric oxygen for the selective oxidation of hydrocarbons remains an important goal. The mechanistic understanding was broadened, refined, and even renewed, and many novel systems can be developed from this. That oxidation chemistry—regardless of whether fundamental or technical questions are examined—is, as always, a very lively and rapidly developing research area was demonstrated impressively at ADHOC 2005. The pronounced emphasis on application was underscored by the fact that this year's meeting was, for the first time, organized jointly by both the industrial and academic spheres, and through the strong participation and generous support of industry (especially BASF).

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