

Hydroformylations

Hydroformylation and related reactions have been the subject of intense activity recently. Three papers have been published, using different techniques, all of which contribute to highly active and selective routes to functional molecules from simple starting materials.

Amines from alkenes, CO and hydrogen

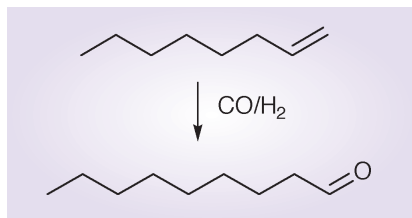
A new, highly atom economic and selective route to primary and secondary amines has been developed by researchers from Celanese in Oberhausen and the University of Rostock. Burkhard Zimmerman, Jürgen Herwig and Matthias Beller (*Angew. Chem., Int. Ed.*, 1999, **38**, 2372) have shown that a combination of Rh and Ir can selectively convert alkenes to amines *via* hydroformylation, imine formation and reduction of the imine. The reaction is carried out using water soluble phosphine ligands, allowing a two-phase reaction to take place, with excellent catalyst separation after completion of the reaction. Selectivity problems to be overcome include *n* : iso hydroformylation, aldol condensation and reduction of aldehyde, and primary : secondary amine formation. The choice of ligand allows control over *n* : iso selectivity; sulfonated triphenylphosphine gives reasonably high proportions of the *n*-isomer (76–87%). Primary : secondary amine ratios can be influenced by the ratio of ammonia : alkene, with 9 : 1 being the best achieved. Additionally, the relative polarities of the aqueous and organic phases can be adjusted such that the initially formed primary amine can be more rapidly transferred to the organic phase (and thus away from the catalyst), avoiding the formation of secondary amine. In this way a 96% selectivity to primary amine can be achieved. The use of sulfonated binaphthyl-phosphine

ligands allows a much higher degree of control, with *n* : iso ratios of 99 : 1 being achieved, and selectivities of 99 : 1 secondary amine being achievable at a 2 : 1 ratio of alkene to ammonia.

Water-soluble phosphine ligands

A further example of the use of water-soluble phosphine ligands in hydroformylations has been described by the group of Piet van Leeuwen (*Chem. Commun.*, 1999, 1633).

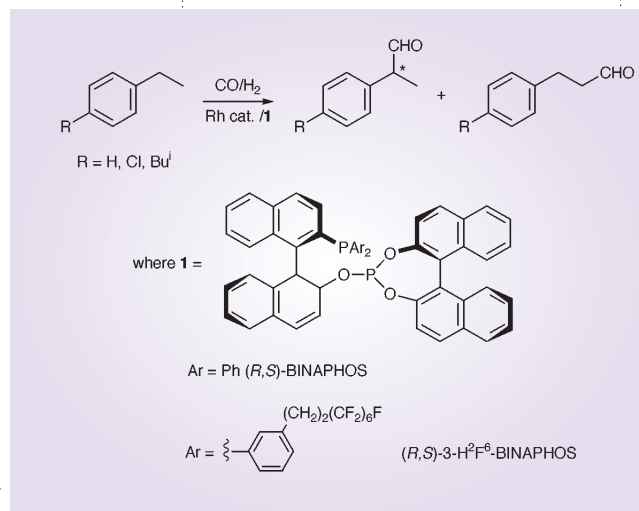
Their approach is based on the supported aqueous phase concept first described by Mark Davis (*Nature*, 1989, **339**, 454). A rhodium complex, based on the sulfoxantphos ligand, was shown to be active in the hydroformylation of alkenes with high *n* : iso ratios. Using pure alkene as substrate and solvent increased rates, which were significantly slower with *e.g.* toluene as solvent, and good rates of conversion could be achieved, with relatively high *n* : iso ratios. No loss of Rh into the liquid phase was detected, and catalysts could be reused several times with no loss in performance.



Hydroformylation in compressed carbon dioxide

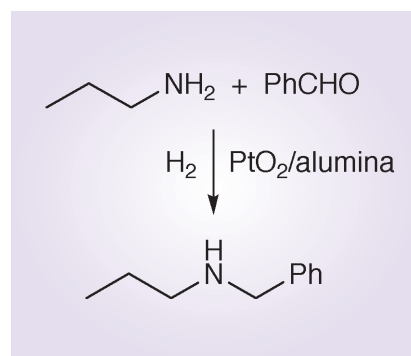
The use of supercritical and near-supercritical carbon dioxide as an environmentally benign solvent is the subject of an increasing number of articles. Walter Leitner and Giancarlo Francio of the Max Planck Institut für Kohlenforschung in Mülheim an der Ruhr have recently published details of a hydroformylation using perfluoro-substituted BINAPHOS-Rh as a catalyst in liquid or supercritical carbon dioxide (*Chem. Commun.*, 1999, 1663). The synthesis of the complex ligand is described, as is use of its Rh complex as an active catalyst in the hydroformylation of styrene. Good enantioselectivities were achieved, and high regioselectivities (in favour of the

iso product—compare with the earlier methods which favour the *n*-isomer) were found.



New, water-soluble form of Adam's catalyst

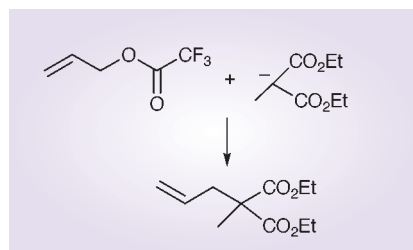
Manfred Reetz and Michael Koch of the Max Planck Institut für Kohlenforschung, Ruhr, Germany, have reported the preparation of a new, water soluble, form of Adams Catalyst, which is made simply by stirring an aqueous solution of PtCl_4 in the presence of a carbobetaine $[\text{C}_{12}\text{H}_{25}(\text{CH}_3)_2\text{N}^+(\text{CH}_2)_3\text{CO}_2^-]$ and excess NaOH (*J. Am. Chem. Soc.*, 1999, **121**, 7933). Adams Catalyst is a high surface area form of PtO_2 , which is normally prepared by reaction of H_2PtCl_6 with NaNO_3 at 450°C , and is an excellent hydrogenation catalyst. The new form of the catalyst is colloidal, with particle sizes of 1.8 ± 0.3 nm. This colloidal PtO_2 could be easily immobilised onto alumina supports, forming catalysts which are highly active in the reductive amination of benzaldehyde by *n*-propylamine. A similar procedure was used to prepare a water soluble bimetallic platinum–ruthenium oxide colloid. Although these new materials are water soluble, no attempt to use them as catalysts in aqueous solution was reported.





Dendrimeric catalysts in flow reactors

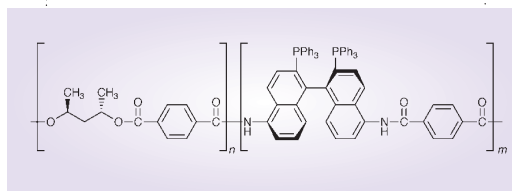
A group from the Netherlands led by Piet van Leeuwen has developed a novel dendrimeric Pd catalyst which can be used in a continuous flow membrane reactor (*Chem. Commun.*, 1999, 1623). These catalysts are derived from carbosilanes with terminal phosphines. The dendrimers are large enough to be recovered by nanofiltration, and contain Pd-phosphine complexes on their outer surface. These catalysts are active in the allylic alkylation reaction, where *e.g.* allyl trifluoroacetate was reacted with sodium diethyl methylmalonate, with the displacement of the trifluoroacetate. Batch reactions resulted in excellent activity under mild conditions, and continuous reaction using a molecular weight cut-off membrane led to initially excellent results, but reduced activity after a few cycles. Retention of catalyst in the reactor was excellent, and the reasons for the reduction in activity are currently being examined. Nonetheless, this approach does hold promise for immobilised and active Pd catalysts.



Soluble polymer support for 'one-phase catalysis and two-phase separation'

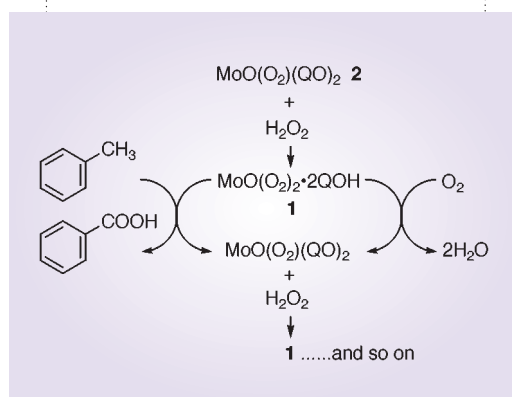
The combination of the advantages of heterogeneous and homogeneous catalysis is an important goal for green chemists, and several approaches, including the use of fluorous biphasic catalysis and ionic liquid biphasic, have achieved considerable success. Albert Chan and co-workers at the Hong Kong Polytechnic University, China, have tackled the problem from a different angle, by attaching their catalyst to a polymer backbone which is soluble under reaction conditions, but which precipitates on workup (*J. Am. Chem. Soc.*, 1999, **121**, 7407). A chiral phosphine was incorporated into a polyester and used to coordinate a ruthenium complex, to form an asymmetric hydrogenation

catalyst which was active in the reaction of 2-(6'-methoxynaphthyl)acrylic acid, giving quantitative conversions and enantiomeric excesses as high as 93.6%. Upon completion of the reaction (which was performed in 3:1 toluene-methanol), methanol was added, and the catalyst was precipitated, filtered and reused, retaining its activity for more than ten cycles.



Oxidation of alkylaromatics using air and hydrogen peroxide

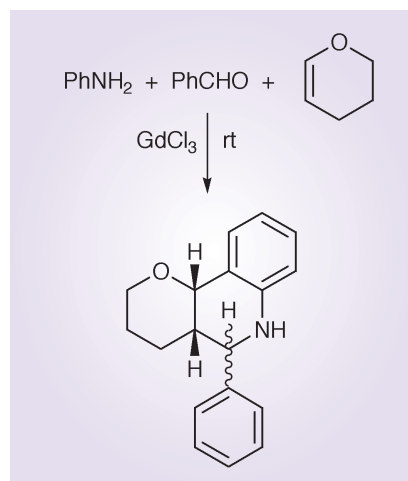
The search for simple and efficient systems for the conversion of alkylaromatics into oxygenated derivatives is an important theme, with many approaches being investigated. Particularly valuable would be a system which could use clean, cheap oxidants such as air or hydrogen peroxide as primary oxidant, but which avoids the need for high temperatures and pressures, and corrosive solvent/promotor mixtures. Ramgopal Bhattacharyya and co-workers from Jadavpur University in Calcutta have discovered a distorted molybdenum species which can oxidise compounds such as toluene and *o*-xylene to the corresponding acids under mild conditions (*Chem. Commun.*, 1999, 1627). Their catalyst is based on a molybdenum-quinoline complex which contains a 2-peroxo ligand and an oxo ligand. In the presence of oxygen and hydrogen peroxide, the complex functions as an effective catalyst for the oxidation of toluene to benzoic acid, *o*-xylene to phthalic acid and *p*-xylene to *p*-toluic acid. Conditions are mild, with reactions proceeding to high yield in refluxing acetonitrile in only a few hours. Turnover numbers are typically 1000+. Running



the reactions with only one of the two oxidants results in significantly reduced performance.

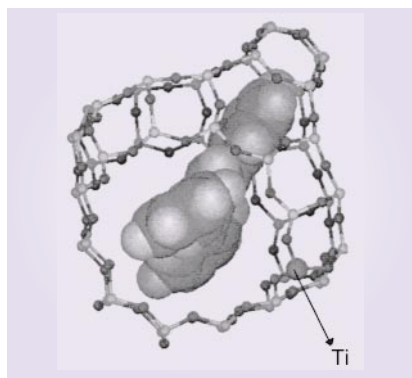
One-pot preparation of quinolines catalysed by lanthanide chloride

The aza-Diels-Alder reaction of *N*-arylimines with olefins is an important method for the preparation of tetrahydroquinoline derivatives, a class of compounds which exhibit anti-inflammatory and other biological activities. Meihua Xie and colleagues from the Chinese Academy of Sciences, Shanghai, have reported a simple one-pot reaction between an amine, benzaldehyde and dihydropyran or dihydrofuran, which offers advantages over existing methods (*J. Org. Chem.*, 1999, **64**, 6462). The new method avoids having to prepare and purify the arylimine beforehand, which may be tricky because imines are prone to hydrolysis. The reaction requires a lanthanide chloride catalyst (GdCl₃ worked best)—previous methods have used BF₃, Co₂(CO)₈ or Ni(CO)₄—and proceeds in a variety of solvents, including THF, DCM, diethyl ether and acetonitrile. The highest reported yield was 86%.

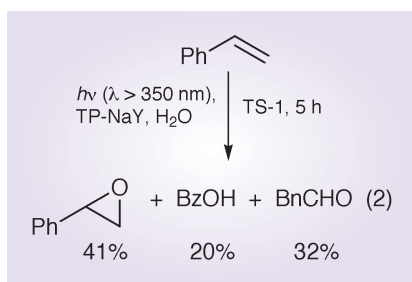


Photocatalysis within zeolite cages

The use of photocatalysis is potentially a very clean methodology. Avelino Corma, Hermegildo Garcia and co-workers from the University of Valencia have developed the concept using photosensitisers encapsulated in zeolites as a system for the epoxidation of alkenes using just water and light (*Chem. Commun.*,



1999, 1641). This remarkable system relies on the generation of hydroxyl radicals from water using the excited state of the photosensitiser 2,4,6-triphenylpyrylium cation inside a Ti containing zeolite. Remarkably, the sensitiser is not destroyed by the water or the hydroxyl radicals formed, as is the case in bulk water where it is rapidly hydrolysed, but allows the effective conversion of alkenes to epoxide to occur.



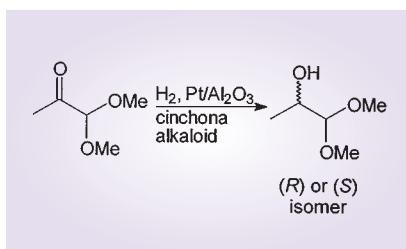
Catalyst life extended in ionic liquids

Concerns have been raised that since homogeneous catalysts only have limited life spans, the widespread interest in developing catalytic protocols using aqueous and ionic liquid solvents is unnecessary. Peter Wasserscheid and his team at the Institut für Technische Chemie und Makromolekulare Chemie in Aachen, Germany, have been investigating the hydroformylation of methyl 3-pentenoate, a precursor to adipic acid and many other products, using rhodium based catalysts (*J. Catal.*, 1999, **186**, 481). They have compared the activity of the catalysts under homogeneous conditions in toluene and dichloromethane and using the ionic liquid [BMIM][PF₆] (1-butyl-3-methylimidazolium hexafluorophosphate). In the reactions carried out in organic solvents deactivation of the catalysts takes place rapidly whereas in the reactions conducted in the ionic liquid the catalyst remains active for

considerably longer periods with turnover numbers typically 600% greater.

Enantioselective hydrogenations using cinchona-modified catalysts

Two groups have independently reported identical results relating to the selective reduction of α -hydroxy acetals using cinchona-modified Pt/Al₂O₃ catalysts. M. Bartok *et al.* (*Chem. Commun.*, 1999, 1725) and M. Studer *et al.* (*Chem. Commun.*, 1999, 1727) have extended the use of this method to the reduction of dimethyl acetals. The products are valuable synthetic equivalents to α -hydroxy-aldehydes. The method in the best cases produces high enantioselectivities (up to 97%) and good rates of reaction, and is reported to be simpler and more cost-effective than other methods. The conversion of the products to other valuable synthons was also demonstrated.



Aerobic oxidation

In a recent communication (*Chem. Commun.*, 1999, 1591) Roger Sheldon and colleagues at the Delft University of Technology in The Netherlands describe RuCl₂(PPh₃)₃-TEMPO as an effective catalyst for the aerobic oxidation of non-activated aliphatic alcohols and a broad range of other alcohols to aldehydes and ketones. RuCl₂(PPh₃)₃ on its own was a poor catalyst for these reactions, but the addition of TEMPO, itself not active as a catalyst, led to a substantial increase in activity. This is one of the most reactive catalysts reported to date for the aerobic oxidation of (aliphatic) alcohols.

