Organic Process Research & Development **1998**, *2,* 64–65

Highlights from the Literature

Some Items of Interest to Process R & D Chemists and Engineers, Selected by the Editor

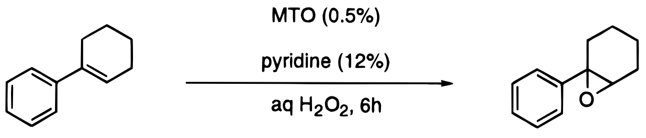
It is a long time since I have read one issue of a journal (apart from OPRD, of course) which has so much of interest to process R & D chemists and engineers as issue No. 23 in Vol. 36 (1997) of *Angewandte Chemie, International Edition in English.* A. Gansäuer (p 2591) discusses the use of methyl trioxorhenium (MTO) catalysed epoxidation of olefins, recently reported by the groups of Sharpless (*J. Am. Chem. Soc.* **1997**, *119*, 6189) and Herrmann (*J. Organomet. Chem.*, in press). MTO is touted as a reagent to replace *m*-chloroperbenzoic acid, which has a number of disadvantages in the laboratory and is normally not used on large scale. The Sharpless procedure uses aqueous hydrogen peroxide and dichloromethane as solvent in a two-phase mixture with pyridine and MTO and can be run at high concentration, and with simple product isolation. Epoxides are formed in high yield (Scheme 1).

The addition of tertiary amines such as pyridine is to suppress the ring opening of the epoxide by the acidic MTO$-$H$_2$O$_2$ complex, but of course the pyridine gets oxidised (and therefore partially consumed) during the reaction. The two-phase reactions used by Herrmann and Sharpless have the advantage that the pyridine *N*-oxide, which Gansäuer suggests is detrimental to catalyst activity, remains in the aqueous layer. Substituted pyridines such as 3-cyanopyridine are also effective (*Chem. Commun.* **1997**, 1565).

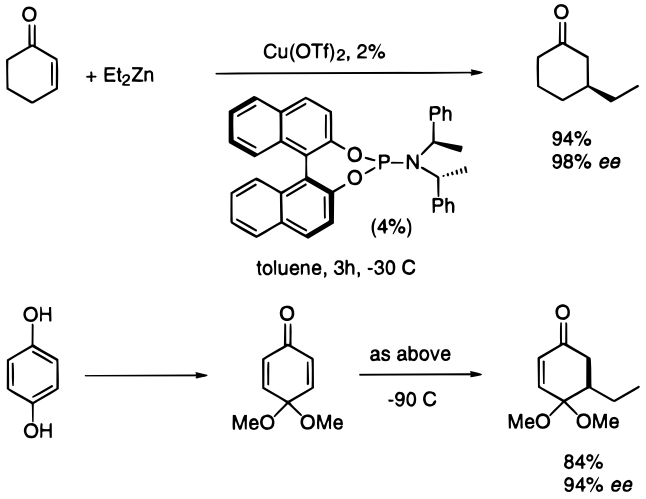
It was thus surprising to find that 2,2-bipyridine *N,N′*-dioxide was also an effective additive, whereas other *N*-oxides, such as isoquinoline *N*-oxide or pyridine *N*-oxide, were ineffective when used at the level of 1.2 mol %, with MTO at 1 mol % [Nakajima, M. *Tetrahedron Lett.* **1998**, *39* (1$-$2), 87]. Obviously this looks destined for a new approach to asymmetric epoxidation of simple olefins, and preliminary results have appeared (Nakajima, M. *Tetrahedron: Asymmetry* **1997**, *8*, 341).

The work of Herrmann's group at the Technical University of Munich is being carried out in collaboration with Hoechst Corporate R & D in Frankfurt, who recognise the potential industrial applications of alkylrhenium oxides (for a review, see: Herrmann, W. A.; et al. *Acc. Chem. Res.* **1997**, *30*, 169). The synthesis of MTO and analogues is normally carried out by direct alkylation of Re$_2$O$_7$, which is extremely moisture sensitive. Herrmann's group now reports the synthesis of alkylrhenium oxides directly from the more accessible perrhenates in high yields, in a one-pot reaction, without the need to exclude air or moisture [Herrmann, W. A. *Angew. Chem., Int. Ed. Engl.* **1997**, *36* (23), 2652]. The industrial advantage is that perrhenates are formed as degradation products in MTO-catalysed processes, and the new method offers an easy recycling opportunity.

Scheme 1



Scheme 2



In the same issue, B. L. Feringa et al. (p 2620) describe catalytic enantioselective 1,4-addition of dialkylzinc compounds to enones in the presence of copper triflate and binaphthol-derived phosphorous amidites, where the amino component derives from one enantiomer of bis(1-phenylethyl)amine. High yields and ee's generally in the 93$-$98% range are obtained with cyclic enones and dienones (Scheme 2).

In the following paper, P. Knochel *et al.* (p 2623) expand on the use of perfluorinated solvents for organometallic processes when the catalyst is also perfluorinated. At temperatures of around 60 °C, organic solvents are miscible with the perfluorinated solvents, but at room temperature or below, a two-phase system is obtained. Separation of the product from the catalyst and recycling of the catalyst are thus possible. This avoids the problem of contamination of the product (and sometimes of the reactor by metal residues), which may need further processing to remove low levels of metal (see OPRD, Vol. 1, No. 4).

Thus cross coupling between acylzinc bromides and acyl iodides proceeds in a toluene$-$C$_8$F$_{17}$Br mix with Pd(dba)$_2$ and (p-C$_6$F$_{13}$C$_6$H$_4$)$_3$P as catalyst in 89$-$99% yield. The

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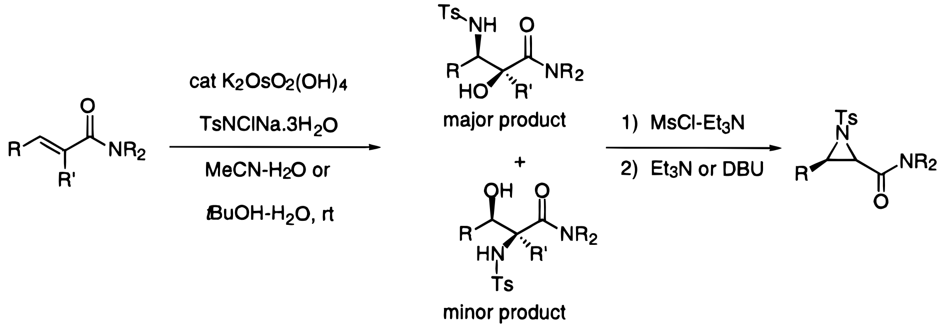
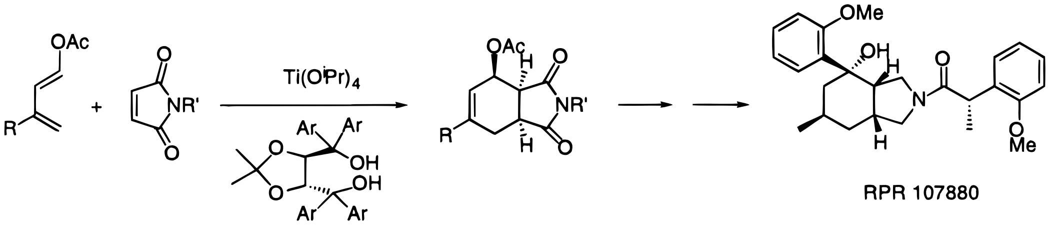
Scheme 3



Scheme 4



catalyst can be reused several times with little change in yield and can be used at lower levels (0.15 mol %) than $(Ph_3P)_4Pd$. The phosphine ligand was easily prepared from *p*-iodoaniline in three steps.

The simple workup and catalyst recycling offer possibilities for large-scale use, but economics will depend on the cost of the perfluorinated solvent and its efficient recycling as well as the cost of the catalyst.

The collection of eminent scientists in the same issue of *Angew. Chem., Int. Ed. Engl.* continues with contributions from B. Trost (p 2635) on the asymmetric synthesis of α-alkylated amino acids using readily available azlactones as starting materials and B. Sharpless with a further improvement in procedures for aminohydroxylation of α,*β*-unsaturated carbonyl compounds (p 2637).

Using cinnamamides, rather than esters, or Weinreb amides, the regioselectivity of the process can be controlled, and high yields of products can be obtained using chloramine T hydrate, and potassium osmate (as little as 0.1 mol %) as catalyst in a one- or two-phase reaction medium (Scheme 3). The reaction works well at high concentration and is rapid, and workup is straightforward. If the product is insoluble in *t*-BuOH solvent, then simple filtration leads to high-purity product, whereas for soluble products MeCN is the preferred solvent, and the product is isolated by extraction. The two procedures have been demonstrated on a 10−20-g scale and no doubt will soon be working on a kilogram scale, too.

Two further catalysts of potential industrial application have also been reported. The group of Jacobs at Leuven, Belgium, has designed a novel, heterogeneous, strongly basic catalyst in which a guanidine base is covalently coupled to an inorganic siliceous mesoporous support. This catalyst is excellent for Michael additions under mild conditions [*Angew. Chem., Int. Ed. Engl.* **1997**, *36* (23), 2661].

H. Bienaymé from Rhone-Poulenc, St. Fons, France, also reported in the same journal (p 2670) the use of ligand-controlled asymmetric Diels−Alder cycloaddition in the synthesis of substance P antagonist RPR 107880. The key fragment of this molecule is a perhydroindole with four stereocentres; three of the four centres were constructed in one step from substituted 1-acetoxybutadiene and a maleimide derivative using titanium isopropoxide and a chiral diol. The reaction was optimised to give cycloadducts in 96% yield and 97% ee, which could be upgraded to optical purity in a single recrystallisation (Scheme 4). (See also: *Tetrahedron* **1997**, *53*, 9637.)

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Editor

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