Oxygen and Osmium—A New Alliance for Dihydroxylations?

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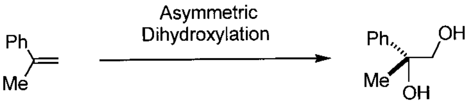
In the industrial production of monomers and chemical intermediates selective oxidation processes are used a great deal and, therefore, there is a great interest in these reactions. Although many of these processes are well established, there is still a need for further improvements, especially in the functionalization of nonactivated carbon–carbon double bonds.

Although the activation of oxygen is one of the main issues in biochemistry[1] as well as in homogeneous catalysis,[2] the use of molecular oxygen as a cooxidant in osmium-catalyzed dihydroxylation reactions has been ignored up until recently. However, publications now show increasing activity in this field of research.[3]

The oxidation of alkenes by osmium tetroxide has been well known for a long time and osmium is one of the most efficient transition metals for catalytic dihydroxylations. It is not just the possibility of an asymmetric version of this reaction that has attracted synthetic[4] and theoretical[5] chemists. Several cooxidants have been investigated in osmium-catalyzed dihydroxylations to replace the ferricyanide in the reoxidation of Os^{VI} to Os^{VIII}.[6] It was shown early on that oxygen can be used for this purpose, but the reoxidation is highly pH-dependent.[7] Usually these oxidations led to carboxylic acids but, under certain conditions, diols can be obtained.[8] Although it was already known that oxygen can add to several osmium complexes,[9] dioxygen is activated by this coordination and recently the first stable oxo complexes of osmium have been isolated.[10]

Krief and Colaux-Castillo have used selenoxides as cooxidants for Os^{VI}.[11] Earlier work by Krief's group had shown that the corresponding selenides can be easily oxidized by singlet oxygen, which is generated by irradiation in the presence of a sensitizer.[12] Therefore, the resulting selenoxides serve as an oxygen carrier in this reaction. By dihydroxylation of α-methylstyrene (**1**) in the presence of a chiral ligand 1,4-bis(dihydroquinidinyl)phthalazine [$(DHQD)_2PHAL$], diol **2** was obtained in similar selectivity and yield to that originally described by Sharpless using the AD-mix-β [Eq. (1)].[13] It is remarkable that even air can be used in this reaction, instead of oxygen, with almost equal efficiency.



1 **2** (1)

More direct is the approach from Beller et al. His team optimized the reaction conditions of the osmium-catalyzed dihydroxylation with oxygen as cooxidant and applied this method to the asymmetric version as well.[14] The drawback of overoxidation, described earlier for this system,[7] was solved by using a biphasic system. Careful investigation of the pH dependence of the reaction showed that at low pH no significant amount of diol was formed, probably because of the instability of the Os^{VI} state below pH 8. High conversions were found at pH 10.4.

As this is a ligand-accelerated reaction,[15] higher yields are obtained by using additional ligands. These can be either achiral, such as 1,4-diazabicyclo[2.2.2]octane (DABCO), or chiral ligands, such as $(DHQD)_2PHAL$. The selectivities are slightly lower than in the Sharpless and Krief procedures, probably due to the higher reaction temperature of 50 °C. If the reaction is performed at lower temperatures, or with lower oxygen pressures, the conversions are unsatisfactory. On the other hand, by using higher oxygen, or even air, pressures (3–5 bar), the catalyst loading can be lowered to 0.05 mol% and high selectivities can still be obtained.[16] The procedures of the different groups and their results for the dihydroxylation of α-methylstyrene (**1**) are summarized in Table 1.

Table 1. Comparison of the conditions for the reaction **1** → **2**.[a]

	$[K_2OsO_2(OH)_4]$/ $(DHQD)_2PHAL$	K_2CO_3	Cooxidant (quantity)	Solvent	T [°]	Yield [%]	*ee* [%]
Sharpless	0.2/1	300	$K_3Fe(CN)_6$ (300)	*t*BuOH/H_2O	0	90	94
Krief	0.4/1.1	30	$PhSeCH_2Ph$ (8), $^1O_2$	*t*BuOH/H_2O	12	89	96
Beller	0.5/1.5	—	O_2	*t*BuOH/phosphate buffer	50	96	80

[a] Quantities given in mol%.

The Beller group also extended their procedure to other, functionalized alkenes and obtained good to high selectivities with good yields. Interestingly, even tri- or tetrasubstituted alkenes can be dihydroxylated without the addition of methanesulfonamide, a requisite reagent in the Sharpless procedure for these alkenes.[16] The procedure developed by Krief and co-workers was also applied to other alkenes, and selectivities similar to the Sharpless procedure were obtained.[17]

Dioxygen is often used as a versatile cooxidant but usually only one oxygen atom is transferred during these oxidation reactions, leaving the other oxygen atom behind in a

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stoichiometric side product. This can be observed in various transition metal catalyzed reactions, as well as in enzymatic transformations. This is also true for the Krief procedure where water is generated as a stoichiometric side product.

In one of the first atom-efficient oxidation reactions, in which both oxygen atoms from dioxygen were incorporated into the substrate, ruthenium porphyrin catalysts were used for epoxidations of alkenes.[18] The Beller procedure runs along these lines, using both oxygen atoms for the dihydroxylation in an atom-efficient way. This procedure opens up perspectives for a preparation of diols without the production of side products—even on an industrial scale.

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