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Vanadyl acetylacetonate as peroxide activator in osmium-catalyzed dihydroxylation of olefins by hydrogen peroxide

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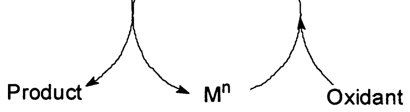
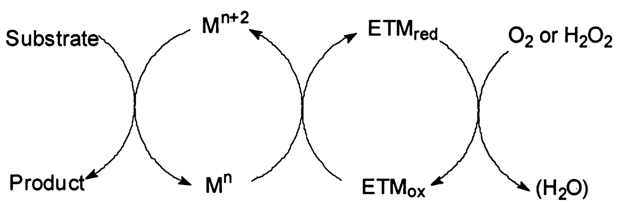
Abstract—Olefins are selectively and efficiently oxidized to vicinal *syn*-diols by aqueous hydrogen peroxide using a coupled catalytic system consisting of osmium tetroxide, vanadyl acetylacetonate and *N*-methylmorpholine. © 2001 Published by Elsevier Science Ltd.

Oxidation reactions using clean oxidants such as molecular oxygen or aqueous hydrogen peroxide are highly attractive from an environmental point of view. Direct oxidation of organic substrates by these oxidants is normally slow, but in the presence of suitable substrate-selective redox catalysts oxidation can take place and the reduced form of the redox catalyst is reoxidized by O_2 or H_2O_2 (Scheme 1).[1,2] In many selective catalytic oxidations, however, the energy barrier is too high for the direct oxidation of the reduced form of the catalyst by O_2 or H_2O_2. Nature efficiently reduces this energy barrier in biological redox process, by having one or several relaying redox-couples (*electron-transfer mediators*, ETMs) between the substrate-selective catalyst and the terminal oxidant (Scheme 2).[3] This principle is also applied in several synthetically useful transition-metal catalyzed processes, e.g. the Wacker process[4,5] and the aerobic 1,4-oxidation of 1,3-dienes.[5,6] We have previously reported on a relayed triple catalytic redox system for the osmium-catalyzed dihydroxylation of olefins using aqueous hydrogen peroxide.[7,8]

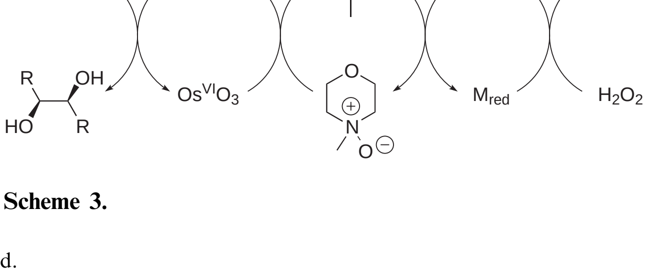


Scheme 1.



Scheme 2.

The osmium-catalyzed dihydroxylation of olefins is a highly efficient process for the formation of *syn*-diols.[9] In this process, osmium(VIII) is reduced to osmium(VI) upon reaction with the olefin, forming an osmium(VI) glycolate. A catalytic amount of osmium tetroxide can be used if a suitable reoxidant is present, which oxidizes osmium(VI) back to the active reagent. Synthetically useful reoxidants are *N*-methylmorpholine *N*-oxide (NMO) (Upjohn process)[10] or potassium ferricyanide.[11] Recently molecular oxygen was employed as oxidant at a higher pH.[12] In our previous studies we have shown



Scheme 3.

Keywords: osmium-catalyzed dihydroxylation; hydrogen peroxide; vanadyl acetylacetonate.

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Table 1. Dihydroxylation of *trans*-5-decene by H_2O_2[a]

Entry	$VO(acac)_2$ (mol%)	OsO_4 (mol%)	NMM (mol%)	Time (h)	Yield (%)[b]
1	0	2	0	26	10
2	0	2	23	16 (8+8)[c]	72 (58)[d]
3	1	2	0	12 (4+8)[c]	26
4	2	2	10	12 (4+8)[c]	45
5	2	2	23	16 (8+8)[c]	89
6	2	0	23	12 (4+8)[c]	0

[a] The reactions were performed on a 1 mmol scale employing H_2O_2 (1.5 equiv., 30% aqueous) and 2 equiv. of tetraethylammonium acetate (TEAA) in acetone (3.8 ml) and water (1.2 ml) at room temperature.

[b] Isolated yields.

[c] The first figure in the parenthesis corresponds to the addition time of aqueous hydrogen peroxide, the latter to further reaction time after the addition.

[d] Without 2 equiv. of (TEAA).

that NMO can be generated from *N*-methylmorpholine (NMM) and aqueous hydrogen peroxide in the presence of catalytic amounts of a biomimetic flavin.[7,8,13] By employing this methodology, a catalytic H_2O_2-based dihydroxylation was developed involving reoxidation of Os(VI) to Os(VIII).[7,8] The flavin is an efficient ETM but rather unstable, so we looked for more robust mediators which would work in the triple catalytic dihydroxylation system (Scheme 3).

There are several transition metal complexes that activate hydrogen peroxide and thus would be capable of replacing the flavin in the dihydroxylation reaction. Methyltrioxorhenium (MTO)[14] reacts readily with aqueous hydrogen peroxide and is a very efficient catalyst for a number of oxidation reactions, e.g. epoxidation[15] and *N*-oxidation of amines[16] and pyridines.[17] In an initial experiment, we found that MTO efficiently catalyzes hydrogen peroxide oxidation of NMM to NMO. However, replacing the flavin for MTO in the dihydroxylation of *trans*-5-decene resulted in only 50% yield of the diol. This is comparable to yields isolated from reaction mixtures containing no other mediators but NMM. The MTO catalyst is known to be stable under acidic reaction conditions but in basic reaction media, under oxidative conditions, it decomposes into methanol and catalytically inert perrhenic acid.[18] A plausible explanation for the poor results obtained in the dihydroxylation reaction using MTO as ETM is decomposition of the rhenium catalyst due to the rather high pH of the reaction media. Vanadium complexes represent another class of transition metals, which are known to activate hydrogen peroxide.[19] Vanadyl acetylacetonate ($VO(acac)_2$) was found to catalyze the formation of NMO from NMM,[20] although at a lower rate than that observed for the MTO-catalyst. We then examined the use of $VO(acac)_2$ as an ETM in the osmium-catalyzed dihydroxylation of *trans*-5-decene (Table 1).

Performing the dihydroxylation reaction using a catalytic amount of osmium tetroxide and aqueous hydrogen peroxide as oxidant resulted in a very low yield of *syn*-decane-5,6-diol (entry 1, Table 1). When a catalytic amount of NMM is present in the reaction mixture and hydrogen peroxide were added slowly (8 h) the yield of the diol increased to 72% (entry 2, Table 1). The peroxo complex of the $VO(acac)_2$ is not efficiently reoxidizing osmium(VI), which is reflected by the low yield obtained in the absence of NMM (entry 3, Table 1). The best result in the selective dihydroxylation of *trans*-5-decene was obtained using $VO(acac)_2$ (2 mol%), OsO_4 (2 mol%), NMM (23 mol%) and adding hydrogen peroxide slowly (8 h) to the reaction mixture (entry 5, Table 1). Slow addition of the oxidant is necessary to avoid overoxidation of the diol, with the formation of the parent α-hydroxyketone as a major product. Increasing the amount of $VO(acac)_2$ to 4 mol% does not improve the reaction. In a control experiment without osmium tetroxide no formation of diol was observed (entry 6, Table 1). Addition of 2 equivalents of tetraethylammonium acetate (TEAA), thereby increasing the rate of osmium-glycolate hydrolysis,[21] proved to be beneficial for the yield of the diol (entry 2, Table 1).

The optimized conditions obtained for the dihydroxylation of *trans*-5-decene were applied to other olefins and the results are summarized in Table 2.[22] In all entries the background reaction, i.e. direct oxidation of either NMM or Os(VI) with aqueous hydrogen peroxide, is slower than when the vanadium catalyst is present. Employing vanadium(V)oxide as ETM resulted in yields similar to those obtained with $VO(acac)_2$ (entries

Table 2. Dihydroxylation of olefins by H_2O_2[a]

Entry	Olefin	% Yield of diol[b]	
		Method A	Method B
1	*trans*-2-Octene	36	70 (80)[c]
2	*trans*-4-Octene	51	83
3	*trans*-5-Decene	72	89 (89)[c]
4	Cyclohexene	52	66
5	Styrene	69	83
6	α-Methylstyrene	77	86

[a] The reactions were carried out employing 1 mmol of olefin, 0.02 equiv. of OsO_4, 0.23 equiv. of NMM, 2 equiv. of TEAA, and H_2O_2 (1.5 equiv., 30% aqueous) in acetone (3.8 ml) and water (1.2 ml). Method A: no $VO(acac)_2$. Method B: 0.02 equiv. of $VO(acac)_2$.

[b] Isolated yields.

[c] With 0.04 equiv. of V_2O_5 as vanadium source.

1 and 3, Table 2). A preliminary result performing the dihydroxylation reaction on styrene in the presence of the cinchona-based ligand $(DHQD)_2PHAL$ shows the formation of (1*R*)-1-phenyl-1,2-ethanediol in 65% yield and 80% enantiomeric excess.

In conclusion, by using $VO(acac)_2$ and NMM as co-catalysts the osmium catalyzed dihydroxylation of olefins can be performed efficiently and with high selectivity with aqueous hydrogen peroxide as the terminal oxidant. Further studies on the enantioselective dihydroxylation using this triple catalytic system are under investigation.

Acknowledgements

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22. Typical experimental procedure exemplified for the dihydroxylation of styrene (Table 2, entry 4): Styrene (1 mmol) was dissolved in acetone (3.8 ml) and water (1.2 ml) at room temperature. To this mixture was added NMM (23 μl, 0.23 mmol), tetraethylammonium acetate (522 mg, 2 mmol), and $VO(acac)_2$ (5.4 mg, 0.02 mmol). To this stirred mixture was added OsO_4 (250 μl, 0.02 mmol) followed by 1/5 of the H_2O_2 (1/5×150 μl, 30% aqueous, 1/5×1.5 mmol). The reaction mixture was stirred for 20 minutes and the rest of the H_2O_2 was introduced over a period of 8 h using a syringe pump. When the addition was complete the resulting solution was stirred for an additional 8 h. Quenched by addition of $Na_2S_2O_4$ (120 mg) and magnesium silicate (240 mg). After 2 h of stirring the mixture was diluted with ethyl acetate and filtered through a pad of Celite, and the Celite bed was washed thoroughly with ethyl acetate. The solvent was removed and the residue was purified by flash chromatography using a mixture of pentane/EtOAc (80:20) to afford 1-phenyl-1,2-ethanediol (0.114 g, 83%).