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Regioselective Alkene Carbon–Carbon Bond Cleavage to Aldehydes and Chemoselective Alcohol Oxidation of Allylic Alcohols with Hydrogen Peroxide Catalyzed by [*cis*-Ru(II)(dmp)$_2$(H$_2$O)$_2$]$^{2+}$ (dmp = 2,9-dimethylphenanthroline)

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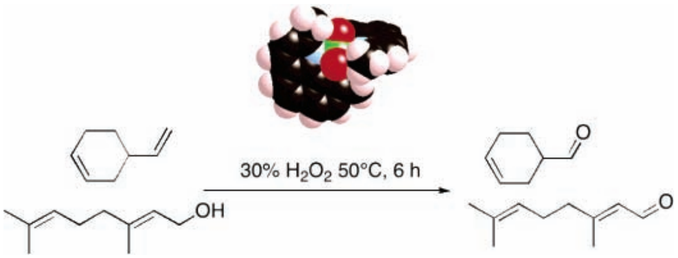
ABSTRACT



[*cis*-Ru(II)(dmp)$_2$(H$_2$O)$_2$]$^{2+}$ (dmp = 2,9-dimethylphenanthroline) was found to be a selective oxidation catalyst using hydrogen peroxide as oxidant. Thus, primary alkenes were very efficiently oxidized via direct carbon–carbon bond cleavage to the corresponding aldehydes as an alternative to ozonolysis. Secondary alkenes were much less reactive, leading to regioselective oxidation of substrates such as 4-vinylcyclohexene and 7-methyl-1,6-octadiene at the terminal position. Primary allylic alcohols were chemoselectively oxidized to the corresponding allylic aldehydes, e.g., geraniol to citral.

The use of hydrogen peroxide as an intrinsically environmentally benign oxidant has in recent years attracted considerable research attention in both the academic and industrial communities. One way to characterize this flurry of activity can be to differentiate between reactions by the type of reactive intermediate species formed and the ensuing mechanism of the oxygen transfer reaction. Probably the largest body of research deals with catalysis by high-valent metal compounds, predominantly Ti(IV), V(V), Mo(VI), W(VI), and Re(VII), that have in common the formation of reactive intermediate peroxo and/or hydroperoxo species.[1] A smaller but still significant body of research deals with the formation of high-valent metal-oxo species, mostly of Fe, Mn, Os, and Ru, and their use as reactive oxygen transfer agents.[2] These metal-oxo species are accessible through a variety of mono-oxygen donors including only in relatively few cases hydrogen peroxide. Often these types of metal complexes have relatively high redox potentials and so tend to considerably dismutate hydrogen peroxide; hydroxy and hydroperoxy radicals formed during the decomposition may lead to nonselective transformations.

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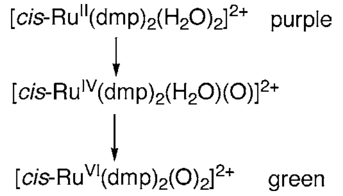
Oxidative alkene carbon−carbon bond cleavage reactions, classically carried out by ozonolysis or with permanganate, can be performed also catalytically with RuO_4/NaOCl, RuO_4/IO_4^- or with OsO_4/oxone[3] and using peroxotungstate complexes with H_2O_2 under relatively strongly acidic conditions.[4] Related *cis*-dihydroxylation of alkenes, usually performed with OsO_4[5] in the presence of various oxidants, has also been observed with some Fe, Ru, Mn, and Re complexes.[6] The Os-, Ru-, Mn-, and Re-based complexes seem to have in common the formation of reactive metal dioxo intermediates and probably react via 3 + 2 addition of the dioxo species to the alkene. Carbon−carbon bond cleavage with peroxotungstates appears to occur sequentially: epoxidation, hydrolysis to the *trans*-diol, and oxidation of the vicinal alcohol by the peroxotungstates.

To the best of our knowledge highly regioselective C−C bond cleavage of alkenes favoring less nucleophilic double bonds has never been reported, although such regioselective epoxidation has been observed in few instances.[7]

About a decade ago Drago and co-workers[8] reported on the oxidation of [*cis*-Ru(II)(dmp)$_2$(H_2O)$_2$]$^{2+}$ (dmp = 2,9-dimethylphenanthroline)[9] with hydrogen peroxide to the *cis*-ruthenium(VI)dioxo species, [*cis*-Ru(VI)(dmp)$_2$(O)$_2$]$^{2+}$, via the intermediate [*cis*-Ru(IV)(dmp)$_2$O(H_2O)]$^{2+}$ (Scheme 1).[10,11]

Scheme 1. Formation of [*cis*-Ru(VI)(dmp)$_2$(O)$_2$]$^{2+}$ from [*cis*-Ru(II)(dmp)$_2$(H_2O)$_2$]$^{2+}$ with Hydrogen Peroxide



Our initial studies with [*cis*-Ru(VI)(dmp)$_2$(O)$_2$]$^{2+}$ showed that it reacted very poorly with cyclohexene but surprisingly reacted easily with 1-octene to yield *n*-heptanal. This unusual reactivity profile of [*cis*-Ru(VI)(dmp)$_2$(O)$_2$]$^{2+}$ led us to explore the catalytic properties of [*cis*-Ru(II)(dmp)$_2$(H_2O)$_2$]$^{2+}$ with hydrogen peroxide as oxidant. In lieu of a crystal structure of [*cis*-Ru(VI)(dmp)$_2$(O)$_2$]$^{2+}$, a computer-generated structure via DFT calculation, Figure 1 (see Supporting Information for computational details), showed that the methyl substituents on phenanthroline highly masked the oxygen ligands and lent credibility to a hypothesis that [*cis*-Ru(VI)(dmp)$_2$(O)$_2$]$^{2+}$ may, in fact, be a regioselective oxidant.

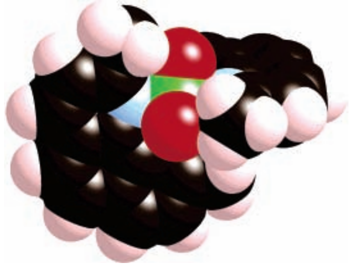


Figure 1. CPK representation of the computer-generated structure of [*cis*-Ru(VI)(dmp)$_2$(O)$_2$]$^{2+}$: Ru = green, N = blue, C = black, O = red, H = pink.

The oxidation of a series of alkenes and dienes with aqueous hydrogen peroxide catalyzed by [*cis*-Ru(II)(dmp)$_2$(H_2O)$_2$]$^{2+}$ is presented in Table 1.

As may be observed from Table 1, the [*cis*-Ru(II)(dmp)$_2$(H_2O)$_2$]$^{2+}$/H_2O_2 system is highly regioselective for the oxidative cleavage of alkenes to aldehydes with a relative reactivity of 1-octene > 2-methyl-1-heptene ≫ *trans*-2-octene ≫ 2-methyl-2-heptene and styrene > β-methylstyrene. Importantly, this relative reactivity leads to the highly selective oxidation of 1,4-hexadiene, 7-methyl-1,6-octadiene, 4-vinylcyclohexene, and limonene at the terminal alkene position. A very unusual phenomenon that was observed was the reduced reactivity of 4-vinylcyclohexene and limonene compared to vinylcyclohexane, which is as reactive as

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(10) The [*cis*-Ru(II)(dmp)$_2$(H_2O)$_2$]$^{2+}$ compound was prepared with a PF_6 counteranion.

(11) We were also able to confirm, by ESI-MS, the formation of [*cis*-Ru(IV)(dmp)$_2$(O)(Cl)]$^{1+}$ and then [*cis*-Ru(VI)(dmp)$_2$(O)$_2$]$^{2+}$ from the dichloro precursor [*cis*-Ru(II)(dmp)$_2$(Cl)$_2$]. Peaks attributable to the molecular clusters were observed at m/z = 559 and 550, respectively.

Table 1. Oxidation[e] of Alkenes and Dienes with 30% H_2O_2 Catalyzed by [*cis*-Ru(II)(dmp)$_2$(H_2O)$_2$]$^{2+}$

substrate	product	conversion, mol %	selectivity, mol %
1-octene	*n*-heptanal	80	>99
1-heptene	*n*-hexanal	85	>99
1-hexene	*n*-pentanal	95	>99
E-2-octene	*n*-hexanal	18	>99
2-Me-1-heptene	2-heptanone	73	>99
2-Me-2-heptene	no product		
1,4-hexadiene	3-pentenal	84	90[a]
7-Me-1,6-octadiene	6-Me-5-heptenal	87	85[b]
vinylcyclohexane	cyclohexane-carboxaldehyde	88	99
4-vinylcyclohexene	cyclohexene-4-carboxaldehyde	21	97[c]
limonene	4-acetyl-1-Me-cyclohexene	11	95[c]
styrene	benzaldehyde	92	>99
β-methylstyrene	benzaldehyde	71	>99
allyl chloride	2-chloroethanal	60	78[d]
methylacrylate	methylglyoxylate	37	97
methyl methacrylate	methylpyruvate	21	92

[a] 10% reaction at both double bonds. [b] 15% selectivity to 7-methyl-6,7-epoxy-1-octene. [c] the remaining products were ene-ols and ene-ones formed on the cyclohexyl ring. [d] 22% epichlorohydrin. [e] Reaction conditions: 1 M substrate, 0.01 M [*cis*-Ru(II)(dmp)$_2$(H_2O)$_2$]$^{2+}$ in acetonitrile at 55 °C; 10 equiv of 30% H_2O_2 added in 10 portions over 8 h. Analysis was by GC and GC−MS including use of reference standards when available and using chlorobenzene (0.1 M) as internal standard (mass balance was 100 ± 5%). It should be noted that the cleavage reaction at the terminal alkene moiety led also to formation of formaldehyde (GC and NMR) and traces of formic acid (GC).

1-octene. One possible but unproven explanation is that the more nucleophilic cyclohexenyl moiety may preferably interact with the [*cis*-Ru(VI)(dmp)$_2$(O)$_2$]$^{2+}$ intermediate, which does not, however, lead to C−C bond cleavage for steric reasons. Some support for this idea may be drawn from the observations that (a) addition of nonreactive 2-methyl-2-heptene as a competitive substrate to reactive 1-octene leads to inhibition of the oxidation of 1-octene (∼2% conversion versus 55% with 1-octene alone after 3 h; reaction conditions as in Table 1); (b) the lifetime of the [*cis*-Ru(VI)(dmp)$_2$(O)$_2$]$^{2+}$ is limited; that is, the catalytic system shows relatively significant H_2O_2 dismutation activity (10 equiv of H_2O_2 are expended on a reaction that requires 3 equiv of H_2O_2); and (c) the only products observable in the oxidation of cyclohexene as substrate are 2-cyclohexen-1-ol (34%) and 2-cyclohexen-1-one (66%) at a ∼5 mol % conversion under reaction conditions noted in Table 1. Such allylic oxidation products are also observable as minor byproducts in the oxidation of 4-vinylcyclohexene and limonene.

It should be noted that trace amounts of epoxide formed in most of the reactions are *not* intermediate products on the way to the formation of the cleaved oxidation products; both octene oxide and 1,2-octanediol are completely inert under reaction conditions. It is likely that the additional mono-oxo intermediate species, [*cis*-Ru(IV)(dmp)$_2$(H_2O)(O)]$^{2+}$, also formed in the [*cis*-Ru(II)(dmp)$_2$(H_2O)$_2$]$^{2+}$/H_2O_2 system is the species responsible for epoxide formation.[7] In fact, when the reaction was carried out in methanol as a coordinating solvent (1 M 1-octene, 0.01 M [*cis*-Ru(II)(dmp)$_2$(H_2O)$_2$]$^{2+}$ in methanol at 55 °C; 10 equiv of 30% H_2O_2 added in 10 portions over 8 h), the product ratio was 62 mol % 1-octene oxide and 38 mol % heptanal and its hemiacetal. Notable also is the observation that when the reaction is carried out in acetonitrile, no significant formation of carboxylic acids was observed via further oxidation of the aldehydes. However, if the reaction is carried out in acetone, some acid is formed. For example, 1 M 1-octene 0.01 M [*cis*-Ru(II)(dmp)$_2$(H_2O)$_2$]$^{2+}$ in acetone at 55 °C with addition of 10 equiv of 30% H_2O_2 in 10 portions over 8 h yielded a product distribution of 78% heptanal and 22% heptanoic acid at a 92% conversion. Finally, it is worth pointing out that even electron-poor alkenes substituted with electron-withdrawing groups at the allylic position (allyl chloride, methylacrylate, and methyl methacrylate) were moderately reactive and also yielded mostly products emanating from C−C bond cleavage.

Since less accessible double bonds are not oxidized using the [*cis*-Ru(II)(dmp)$_2$(H_2O)$_2$]$^{2+}$/H_2O_2 catalytic system and aldehyde oxidation to carboxylic acids can be prevented by choice of solvent, it was recognized that primary allylic alcohols may be chemoselectively oxidized to the corresponding allylic aldehydes. Usually oxidation of primary allylic alcohols with hydrogen peroxide is chemoselective to reaction at the double bond because oxidation of primary alcohols are more difficult; catalytic oxidation reactions at

Table 2. Oxidation[d] of Primary Allylic Alcohols with 30% H_2O_2 Catalyzed by [*cis*-Ru(II)(dmp)$_2$(H_2O)$_2$]$^{2+}$

substrate	product	conversion, mol %	selectivity, mol %
3-Me-2-buten-1-ol	3-Me-2-butenal	90	95
trans-2-hexen-1-ol	*trans*-2-hexenal	82	88[a]
cis-2-hexen-1-ol	*cis*-2-hexenal	87	81[a]
cis-3,7-diMe-2,6-octadien-1-ol (nerol)	*cis*-3,7-diMe-2,6-octadienal (neral)	83	>99
trans-3,7-diMe-2,6-octadien-1-ol (geraniol)	*trans*-3,7-diMe-2,6-octadienal (geranial)	85	>99
farnesol[b]	farnesal[c]	86	>99

[a] The remaining observed product was butanal. [b] Mixture of isomers 95% *trans,trans*- and *trans,cis*-3,7,10-trimethyl-2,6,10-dodecatrien-1-ol. [c] Mixture of isomers 95% *trans,trans*- and *trans,cis*-3,7,10-trimethyl-2,6,10-dodecatrienal. [d] Reaction conditions 1 M substrate, 0.01 M [*cis*-Ru(II)(dmp)$_2$(H_2O)$_2$]$^{2+}$ in acetonitrile at 55 °C; 15 equiv of 30% H_2O_2 added in 10 portions over 12 h. Analysis was by GC and GC−MS including use of reference standards when available and using chlorobenzene (0.1 M) as internal standard (mass balance was 100 ± 5%).

the alcohol position are usually effected by use of other oxidants, e.g., hypochlorite or molecular oxygen.[12] In Table 2 are presented the results for the oxidation of a series of primary allylic alcohols with aqueous hydrogen peroxide catalyzed by [*cis*-Ru(II)(dmp)$_2$(H$_2$O)$_2$]$^{2+}$.

From the results shown it Table 2, one may observe that high to very high chemoselectivity was obtained in the oxidation of primary allylic alcohols to the correspondinding allylic aldehydes without loss of stereoselectivity at the double bond positions. For allylic alcohols with more hindered alkene moieties such as in geraniol, nerol, and farnesol and to a slightly lesser degree for 3-methyl-2-buten-1-ol, there was practically no carbon−carbon bond cleavage observed. For less hindered double bonds such as those in *cis*- and *trans*-2-hexen-1-ol, chemoselectivity was slightly reduced (80−90%) and some butanal was formed. In the oxidation of 1-octen-3-ol, as expected, there was only 50% chemoselectivity to the ketone product. Further, recalling that the double bond of cyclohexene is resistant to oxidation, the oxidation of 2-cyclohexen-1-ol in fact only yielded 2-cyclohexen-1-one as the observed product (97% conversion, >98% selectivity. The regioselectivity observed in the simple alkene oxidations was indeed translated to chemoselectivity in the oxidation of primary allylic alcohols.

In summary, it was found that the known [*cis*-Ru(II)(dmp)$_2$(H$_2$O)$_2$]$^{2+}$ compound appears to have a hindered active site. This led to the use of [*cis*-Ru(II)(dmp)$_2$(H$_2$O)$_2$]$^{2+}$ as a regioslective catalyst for alkene carbon−carbon bond cleavage with hydrogen peroxide to form aldehydes with signficant preference for primary alkenes. This regioselectivity manifested itself also in the chemoselective oxidation of primary allylic alcohols to the corresponding allylic aldehydes.

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Supporting Information Available: Experimental details on the oxidation reactions and computational studies. This material is available free of charge via the Internet at http://pubs.acs.org.

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