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Osmium-Catalyzed Oxidative Transformation of Alkenes to α-Ketols with Peracetic Acid

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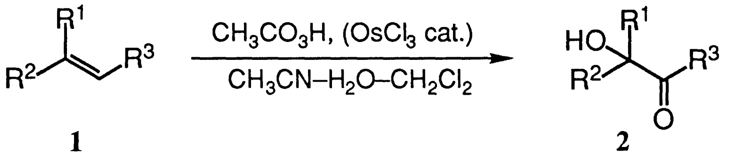
The $OsCl_3$-catalyzed oxidation of alkenes with peracetic acid at room temperature gives the corresponding α-ketols, which are important building units for synthesis of biological active compounds.

Recently, we found osmium-catalyzed cytochrome P-450 type oxidation of β-lactams with peracetic acid proceeds highly efficiently to give 4-acetoxy-β-lactams.[1)] In this reaction, non-porphyrin oxo-osmium species generated from osmium complexes and peracetic acid is a key intermediate for specific oxygenation of amides at the unactivated α-position of nitrogen. During the course of our study on the reactivity of oxo-osmium species towards alkenes, we have found that novel catalytic oxidative transformation of alkenes to α-ketols proceeds highly efficiently. Thus, the $OsCl_3$-catalyzed oxidation of alkenes **1** with peracetic acid in an aqueous solution under mild conditions gives the corresponding α-ketols **2** as depicted in Eq. 1.[2)] This reaction is quite different from the OsO_4-promoted oxidation of alkenes, giving *cis*-1,2-diols.[3)]

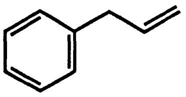
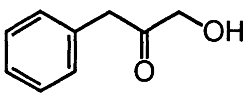
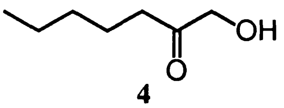
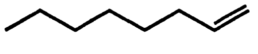
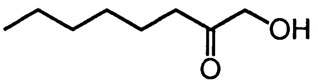
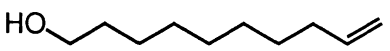
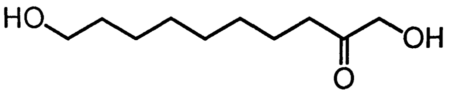
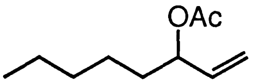
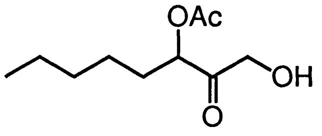
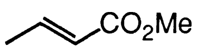
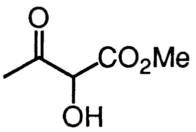
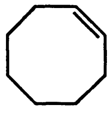
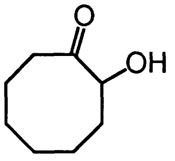
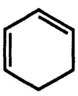
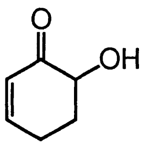
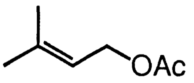
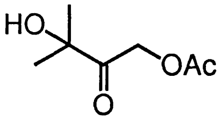


1 **2** (1)

α-Ketols are versatile synthetic intermediates and partial structures of various biologically active compounds such as cortisone acetate[4)] and adriamycin acetate.[5)] The methods for synthesis of α-ketols from mono-oxygenated compounds such as enol ethers[6)] and enolates[7)] have been studied extensively; however, those from alkenes are limited to the oxidations with $KMnO_4$-$CuSO_4 \cdot 5H_2O$[8)] and with isobutylaldehyde / O_2 in the presence of OsO_4 and bis(3-methyl-2,4-pentanedionato)nickel(II) catalysts in anhydrous THF.[9)] The present reaction provides a general and efficient method for the preparation of α-ketols from a variety of alkenes.

Osmium trichloride has been proven to be an effective catalyst. The two-phase aqueous system is required for the present reaction. Without water, cleavage of carbon-carbon double bonds of alkenes occurs to give carboxylic acids predominantly. Typical experimental procedure is exemplified by the oxidation of 1-heptene (**3**). To a stirred mixture of **3** (0.491 g, 5.00 mmol), $OsCl_3 \cdot 3H_2O$ (0.018 g, 0.05 mmol, 1 mol%), acetonitrile (5.0 mL), water (5.0 mL), and dichloromethane (5.0 mL) was added a 30% solution of peracetic acid in ethyl acetate (2.54 g, 10.0 mmol) dropwise at room temperature over a period of 2 h. After stirring for additional 3 h, the reaction mixture was poured into a 5% Na_2SO_3 solution in water to decompose excess peroxide and extracted with dichloromethane (25 mL x 5). The combined extracts were washed with brine (50 mL) and dried

Table 1. $OsCl_3$-Catalyzed Oxidation of Alkenes to α-Ketols with Peracetic Acid[a)]

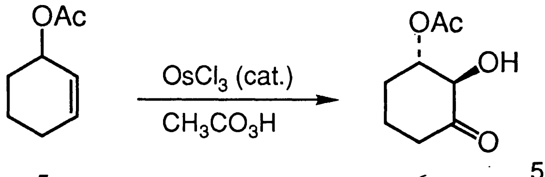
Run	Substrate	Product[b)]	Yield /%[c)]
1			62[d)]
2	 **3**	 **4**	72
3			88
4			55[d)]
5			60
6			58
7			60[d)]
8			52
9			72

a) The reaction was carried out as described in the text. b) The structure of the product was determined by IR, NMR, and Mass spectral data, and elemental analysis. c) Isolated yield based on the starting alkene. d) $OsCl_3$ (3 mol%) was used.

over $MgSO_4$. Removal of the solvent followed by short column chromatography on SiO_2 (hexane / ethyl acetate = 5 / 1) gave 1-hydroxy-2-heptanone (**4**) (0.469 g, 72%) as a colorless liquid.

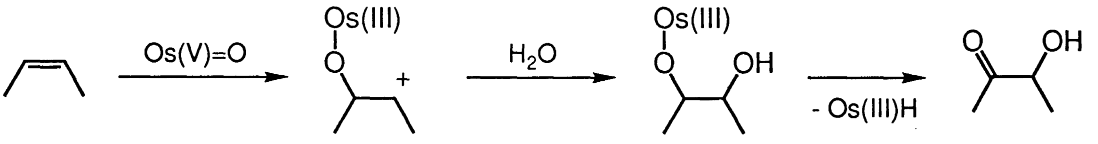
The representative results of the $OsCl_3$-catalyzed oxidation of alkenes are summarized in Table 1. Both cyclic and acyclic alkenes are converted into the corresponding α-ketols efficiently in the presence of 1-3 mol% of $OsCl_3$ catalyst. Importantly, the oxidation of monosubstituted olefins proceeds smoothly to give α-ketols with high regioselectivity (runs 1-5). Generally, the conversions of monosubstituted olefins to the corresponding α-ketols are difficult because of their lower reactivities. Indeed, similar treatment with $RuCl_3$ catalyst[10] results in recovery of the starting materials. Electron deficient olefins such as methyl crotonate can be also converted into the corresponding α-ketol (run 6). The reaction of olefinic alcohols proceeds selectively without loss of hydroxy groups (run 2). The oxidation of 1,3-cyclohexadiene gave 6-hydroxy-2-cyclohexen-1-one regioselectively (run 8).

One important feature of the present reaction is high regio- and / or stereoselection arising from chelation effect of neighboring substituents such as acetoxy group. Typically, the oxidation of 3-acetoxy-1-cyclohexene (**5**) proceeds with chemo- and stereoselectivities to give (2*R**,3*S**)-3-acetoxy-2-hydroxycyclohexanone (**6**, 50%) as a single diastereomer. This reaction will be highly useful for synthesis of sugar derivatives.



5 **6** 50%

The reaction can be rationalized by assuming three pathways which involve direct formation of α-ketols from alkenes (path A), formation of epoxides followed by ring opening (path B), and formation of 1,2-diols and subsequent partial oxidation (path C). The following control experiments for the oxidation of 4-octene exclude path B and path C: i) 4,5-Epoxyoctane was recovered completely under the reaction conditions. ii) The oxidation of 4,5-octanediol under the reaction conditions gave only a small amount (10%) of 5-hydroxy-4-octanone. Although it is premature to discuss the precise mechanism at the present stage, the reaction can be rationalized by assuming an intermediacy of oxo-osmium(V) species,[1] which is similar to the oxo-ruthenium species generated from low valent ruthenium and peroxides.[10-12] Thus, the reaction of Os(III) complexes with peracetic acid gives Os(V)=O species,[1] which undergoes reaction with alkenes to give cationic species **7**.[13] Addition of oxo-osmium species to 1-alkenes would proceed regioselectively, because steric repulsion between the osmium metal and the substituent of 1-alkenes is larger than that between oxygen atom of the oxo-osmium and 1-alkenes. Nucleophilic attack of water to **7** and subsequent β-elimination of osmium(III) hydride species would give α-ketols. Osmium(III) hydride would be reoxidized with peracetic acid to complete the catalytic cycle. The high reactivity towards less reactive 1-alkenes is due to higher electrophilicity of Os(V)=O



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species in comparison with Ru(V)=O species.[10)]

Work is in progress to provide definitive mechanistic information and to apply our method to other systems.

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