Oxygenation of alkanes with hydrogen peroxide catalysed by osmium complexes

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Efficient oxidation of alkanes, including methane and ethane, with H_2O_2 in the presence of catalytic amount of an Os complex in MeCN (addition of nitrogen-containing heterocycles significantly enhances the yield of the products) or in $MeCO_2H$ gives the corresponding ketones and alcohols.

Unlike aromatic and olefinic hydrocarbons, alkanes are known to exhibit only negligible reactivity in reactions with a variety of normal reagents and the yields of the products are usually low, especially in the case of light saturated hydrocarbons (methane, ethane and propane).[1] Osmium compounds, particularly OsO_4, oxidize unsaturated hydrocarbons and some other organic compounds stoichiometrically and catalyse their oxygenations with various reagents.[2,3]

Here, we report that soluble osmium derivatives, especially $OsCl_3$, catalyse efficiently the oxygenation of saturated hydrocarbons with hydrogen peroxide. All reactions[4] were carried out at 80 °C. The oxidation of cycloheptane (0.4 mol dm^{-3}) in MeCN with H_2O_2 (1.0 mol dm^{-3}) in the presence of $OsCl_3$ (1.0×10^{-3} mol dm^{-3}) gave after 3 h cycloheptanol (0.05 mol dm^{-3}) and cycloheptanone (0.013 mol dm^{-3}), the total turnover number (TON) being 63. Addition of a small amount of pyridine (0.125 mol dm^{-3}) gave rise to a noticeable increase in the yield and to the predominant formation of the ketone (after 90 min: cycloheptanol, 0.020 mol dm^{-3}; cycloheptanone, 0.092 mol dm^{-3}; TON, 112). Other nitrogen-containing heterocycles also promote the oxidation: for example, the reaction with *n*-heptane in the presence of 3-methylpyrazole (Fig. 1) affords predominantly isomeric ketones (after 60 min total concentration 0.028 mol dm^{-3}) as well as isomeric alcohols (total 0.04 mol dm^{-3}). Heptanal has been detected only in negligible concentration. The reaction is accompanied by non-productive H_2O_2 decomposition to give molecular oxygen, and the oxidation decreases when hydrogen peroxide concentration becomes low (after approximately 1 h, as shown in Fig. 1). By varying the additive, it is possible to control the ketone/alcohol ratio (Table 1). Lower alkanes can be easily oxidized in MeCN, if pyridine is added to the reaction solution (Table 2). In contrast to methane which is the least reactive hydrocarbon in this reaction and affords methanol as the main product, ethane and propane give mainly carbonyl compounds and only smaller amounts of alcohols with TON values of 102 and 150, respectively.

The selectivities of the alkane oxidations catalysed by $OsCl_3$ are higher than those determined for analogous hydroxylations by the systems 'H_2O_2–$h\nu$' and 'H_2O_2–$FeSO_4$' as well as 'H_2O_2–VO_3^-–pyrazinecarboxylic acid (PCA)'[7] which are believed to produce free hydroxyl radicals (Table 3). It is noteworthy that selectivities significantly increase when pyridine is added to the reaction solution. Moreover, while the oxidation of *cis*-decalin with H_2O_2–$OsCl_3$ in MeCN occurs without retention of the configuration (the *trans/cis* ratio of the products formed being more than unity), in the presence of

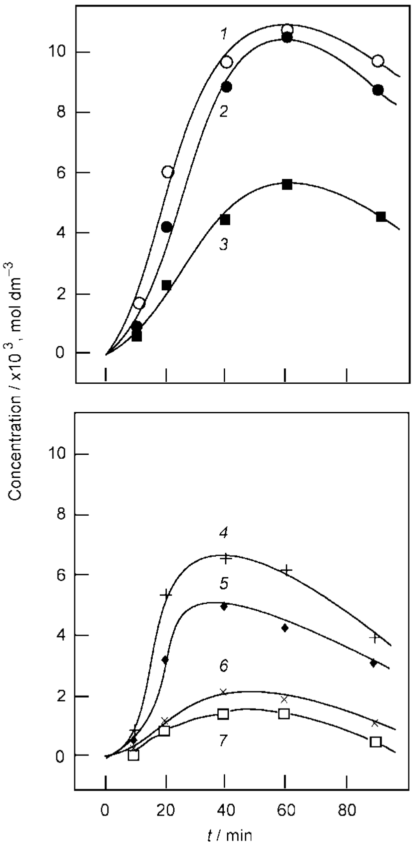

Fig. 1 Accumulation of heptan-2-one (*1*), heptan-3-one (*2*), heptan-4-one (*3*), heptan-2-ol (*4*), heptan-3-ol (*5*), heptan-4-ol (*6*) and heptan-1-ol (*7*) in the *n*-heptane (0.4 mol dm^{-3}) oxidation with H_2O_2 (1.0 mol dm^{-3}) catalysed by $OsCl_3$ (10^{-3} mol dm^{-3}) in MeCN in the presence of 3-methylpyrazole (0.12 mol dm^{-3}) at 80 °C.

Table 1 Oxidation of cycloheptane (0.4 mol dm^{-3}) with H_2O_2 (1.0 mol dm^{-3}) in MeCN (80 °C, 2 h)[4]

		Products/mol dm^{-3}		
Catalyst	Additive	Cyclo-heptanol (OL)	Cyclo-heptanone (ONE)	Ratio OL/ONE
$OsCl_3$	2,5-Dichloropyridine	0.076	0.014	5.4
$OsCl_3$	None	0.049	0.010	4.9
$OsCl_3$	2,2′-Bipyridine	0.059	0.026	2.3
Na_2OsCl_6	3,5-Dimethylpyrazole	0.022	0.026	0.85
Na_2OsCl_6	3-Methylpyrazole	0.030	0.070	0.45
$OsCl_3$	3-Methylpyrazole	0.035	0.077	0.45
$OsCl_3$	Pyridine	0.020	0.092	0.2

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Table 2 Oxygenation of lower alkanes (H_2O_2 = 1 mol dm^{-3}, $OsCl_3$ = 1 × 10^{-3} mol dm^{-3}, py = 0.125 mol dm^{-3}; MeCN 80 °C, 1.5 h)[4]

Alkane (pressure/bar)	Products/mol dm^{-3}
Methane (40)	CH_3OH (0.017); HCHO (3.0 × 10^{-5})
Ethane (20)	CH_3CHO (0.08); CH_3CH_2OH (0.022)
Propane (6)	CH_3CH_2CHO (0.034); CH_3COCH_3 (0.054); $CH_3CH(OH)CH_3$ (0.018); $CH_3CH_2CH_2OH$ (0.044)
n-Butane (2)	$CH_3CH_2CH_2CHO$ (0.011); $CH_3COCH_2CH_3$ (0.026); $CH_3CH(OH)CH_2CH_3$ (0.011); $CH_3CH_2CH_2CH_2OH$ (0.002)

Table 3 Selectivities of alkane oxidations by various systems

Substrate	System	Selectivity[a]
n-Heptane		C(1) : C(2) : C(3) : C(4)
	H_2O_2–$h\nu$ in MeCN	1.0 : 7.3 : 6.3 : 8.1
	H_2O_2–$FeSO_4$ in MeCN–H_2O	1.0 : 5.0 : 4.8 : 4.6
	H_2O_2–$OsCl_3$ in MeCN	1.0 : 11.8 : 9.8 : 3.5
2,2,4-Trimethylpentane		1° : 2° : 3°
	H_2O_2–$h\nu$ in MeCN	1.0 : 1.75 : 6.2
	H_2O_2–$FeSO_4$ in MeCN–H_2O	1.0 : 2.75 : 6.0
	H_2O_2–Bu_4NVO_3–PCA in MeCN	1.0 : 3.0 : 4.8
	H_2O_2–$OsCl_3$ in MeCN	1.0 : 2.2 : 8.7
	H_2O_2–$OsCl_3$ in MeCN–py (0.125 mol dm^{-3})	1.0 : 2.1 : 18.3
cis-Decalin		*trans*/*cis*
	H_2O_2–$h\nu$ in MeCN	1.3
	H_2O_2–$h\nu$ in py	1.9
	H_2O_2–$FeSO_4$ in MeCN–H_2O	3.4
	H_2O_2–Bu_4NVO_3–PCA in MeCN	2.1
	H_2O_2–$OsCl_3$ in MeCN–py (0.125 mol dm^{-3})	1.2
	H_2O_2–$OsCl_3$ in MeCN–py (6.25 mol dm^{-3})	0.56
	H_2O_2–$OsCl_3$ in $MeCO_2H$	0.26

[a] Parameter C(1) : C(2) : C(3) is normalized (*i.e.* calculated taking into account the number of hydrogen atoms at each position) relative reactivities of hydrogens at carbon atoms 1, 2 and 3 of the alkane chain, respectively; parameter 1° : 2° : 3° is normalized relative reactivities of hydrogen atoms at primary, secondary and tertiary carbons, respectively; parameter *trans*/*cis* = [*trans*-decal-9-ol]/[*cis*-decal-9-ol], where [*trans*- and *cis*-decal-9-ol] are concentrations of *trans*- and *cis*-decal-9-ol formed in the oxidation, respectively.

pyridine the reaction becomes more selective, the *trans/cis* ratio decreasing with increasing pyridine concentration. It is important to note that in $MeCO_2H$ the reaction exhibits a high value of the *trans/cis* parameter (0.26) and the parameter $RC_{cis} = 100(c_{cis} - c_{trans})/(c_{cis} + c_{trans}) = 58\%$. The value of the *trans/cis* parameter for the system 'H_2O_2–$OsCl_3$' in $MeCO_2H$ is only slightly higher than that (*trans/cis* = 0.12) for the hydroxylation in MeCN by the system 'H_2O_2–$LMn^{IV}(O)_3$-$Mn^{IV}L^+$–$MeCO_2H$ (L = 1,4,7-trimethyl-1,4,7-triazacyclononane)' described recently.[8]

On the basis of the results obtained and especially taking into account the selectivity parameters, one may assume that oxidation by the system H_2O_2–$OsCl_3$ starts with hydrogen atom abstraction from the alkane by an oxo osmium complex, and the reaction occurs in a solvent cage. The alkyl radicals formed react then with dioxygen to generate the corresponding alkyl hydroperoxide which decomposes to afford the corresponding ketone and alcohol. The system described here can be considered as a model for the oxidations of C–H compounds catalysed by iron-containing enzymes, osmium being an iron homologue in the Periodic System. Indeed, oxidations with participation of cytochrome P-450, methane monooxygenase and chloroperoxidase are believed to begin with hydrogen atom abstraction by a high-valent iron oxo species.[1,9] Coordination of a nitrogen-containing heterocycle (and/or acetate) to osmium may produce a catalytically active oxo species surrounded with voluminous ligands, and the relatively high bond- and stereoselectivities of the alkane oxidation may be due in this case to the bulkiness of the ligands at the reaction centre.

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4 The oxidations of higher hydrocarbons were carried out in air in thermostated Pyrex cylindrical vessels with vigorous stirring. The total volume of the reaction solution was 5 or 10 mL. In a typical experiment, initially, a portion of 35% aqueous solution of hydrogen peroxide (Fluka) was added to the solution of the catalyst, substrate and heterocycle in acetonitrile (Fluka). The oxidations of lower alkanes were carried out in an stainless steel autoclave with intensive stirring (volume of the reaction solution was 5 mL and total volume of autoclave was 100 mL). Before the oxidation the autoclave was charged with the alkane under appropriate pressures. The reactions were stopped by cooling with ice and the reaction solution was analysed by GC (DANI-86.10; fused silica capillary column 25 m × 0.32 mm × 0.25 mm, CP-WAX52CB; integrator SP-4400). Comparison of the chromatograms of the reaction samples before and after their treatment with PPh_3 (for this method, see refs. 1(*a*),(*b*),5–8) demonstrated that concentrations of alkyl hydroperoxides were very low. The concentration of formaldehyde was measured spectrophotometrically after its transformation into 2,6-dimethyl-3,5-diacetyl-1,4-dihydropyridine as described previously.[6]

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