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RUTHENIUM-CATALYZED C-H BOND ACTIVATION
OXIDATION OF BRIDGED BICYCLIC AND TRICYCLIC ALKANES

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ABSTRACT : Catalytic oxidation (hydroxylation) with RuO_4 generated in situ occurs preferentially in tertiary position with retention of configuration on various bicyclic or tricyclic alcanes.

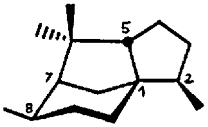
Oxidative functionalization of alkanes either directly with oxygen or with other oxidizing reagents into functionalized organic molecules is of great interest since hydrocarbons are important feedstocks on the industrial scale. Moreover, such functionalization of alkanes, which generally require heterogeneous reactions, high temperatures and pressures occur without great selectivity (1). For this purpose, selective catalytic processes under milder conditions are desirable, especially in the case of more complex molecules.

Within the widespread development in this area during these latter years (2) ruthenium complexes emerge as a new promising and efficient catalysts for the functionalization of hydrocarbons (3).

We report here (see Table) the preliminary results obtained during our investigations on ruthenium catalyzed oxidation of bicyclic [2.2.1] alkanes showing that hydroxylation occurs selectively at the exo position of tertiary carbons. Similar observations were made on bridged tricyclic alkanes featuring the cedrane skeleton which are of interest in the perfume industry.

Oxidation of 2-methyl-norbornane 1 (as a mixture of endo/exo isomers 3/1 ratio) gives selectively 2-methyl-exo-2-norbornanol 2 in 90 % yield (based on the endo isomer) leaving the exo isomer unchanged (entry 1). Similarly, 2-ethyl-norbornane 3 (as a mixture of endo/exo isomers 65:35 ratio) is selectively oxidized to 2-ethyl-exo-2-norbornanol 4 in 57 % (based on the endo isomer). No other isomeric alcohol has been detected (entry 2). In contrast, under identical oxidation conditions, no reaction is observed with tricyclic derivatives 5 or 6 where hydroxylation into tertiary exo positions is impossible (entry 3 and 4).

The bridged tricyclic cedrane skeleton features four tertiary C-H bonds but two of these (C_5-H & C_7-H) are more hindered than C_2-H and C_8-H. The Ruthenium-catalyzed oxidation of cedrane 7 and derivatives 10, 12,14 and 16 also occurs stereoselectively under mild condition on tertiary positions.



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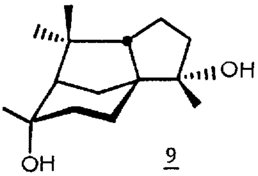

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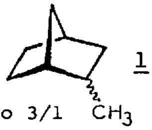
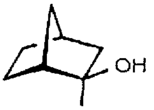
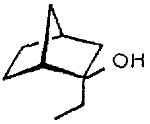
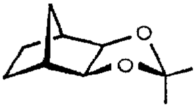
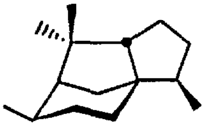
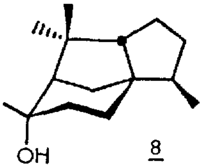
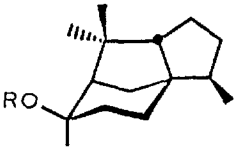
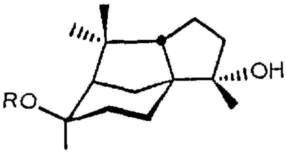
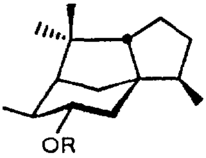
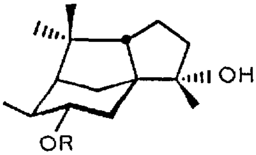
Cedrane 7 (4) was directly oxidized at room temperature to epi-cedrol 8 in 69 % isolated yield (entry 5). In this case, the ruthenium-catalyzed oxidation proved to be more selective than the dry ozonisation technique since the latter oxidizes both C_2-H and C_8-H giving diol 9 in 18 % yield (5).

Similary oxidation of cedrol 10 affords diol 11 in 29 % isolated yield (entry 6) and other more polar unidentified products. The same diol 11 was obtained by dry ozonisation according to Mazur's procedure in 50 % yield (5). Cedryl acetate 12 affords the acetate alcohol 13 in 53 % isolated yield (entry 7). Compound 13 had been previously obtained in 63 % by dry ozonisation (5, 6).

Oxidation of neoisocedranol acetate 14 (entry 8) or carbonate 16 (entry 9) gives selectively hydroxylated products in C-2 position in moderate yields. No oxidation products in C-8 position have been detected in these cases as a result of steric hindrance of the polar substituent on C-9.

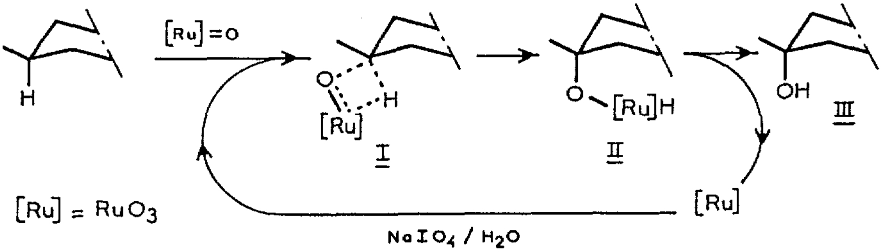
Our results show that a stereoselective ruthenium catalyzed oxidation occurs at the exo position of tertiary carbons on alkanes featuring the bicyclo [2.2.1] heptane skeleton. Similarly, stereoselective oxidations of cedrane derivatives occur with retention of configuration. At this stage the informations concerning this oxidation mechanism are scarce, but netherless significative. The oxidation process is sensitive to steric hindrance, and the accessible tertiary C-H bonds are the most reactive (8). Finally hydroxylation occur preferentially on C-H bonds which might be weakened by stereoelectronic factors (increase of C-H antibonding electronic population by appropriate overlap with a trans antiparallel electron rich C-C bond). The stereoselectivity observed, and the absence of rearrangement products (7) arising from bicyclic [2.2.1] alkanes do not favour the mechanism proposed for oxidation of cyclic saturated hydrocarbons involving carbonium ions as intermediates (3b). Although, homolytic C-H bond cleavage has been proposed for oxidation of cycloalkanes (3d), we suggest a mechanism involving an activation of C-H bond by the highly electrophilic oxidizing ruthenium tetroxide with formation of a four-centered transition state I

Table : Catalytic Oxidation of Bicyclic and Tricyclic Alkanes with RuO_4

Entry	Substrate	$NaIO_4$ (nb.equiv.)	Reaction Conditions	Product(s)	Yield^b (%)
1	 1 endo/exo 3/1	4	55°C, 20h	 2	90
2	 3 endo/exo 65/35	4	60°C, 27h	 4	57
3	 5	4	85°C, 22h	no reaction	
4	 6	4	90°C, 18h	no reaction	
5	 7	4	rt, 30h	 8	69
					
6	10 R = H	4	70°C, 1d	11 R = H	29
7	12 R = Ac	4	55°C, 1d	13 R = Ac	53
					
8	14 R = Ac	7	55°C, 5d	15 R = Ac	33
9	16 R = CO_2Me	7,5	50°C, 3d	17 R = CO_2Me	35

a : All reactions were carried out with the following conditions:
Substrate : RuCl3 = 1 : 0.02 (mmol)
CCl4 : CH3CN : H2O = 2 : 2 : 3 (mL).

b : Isolated yields. All new compounds have been fully characterized by spectroscopic analysis and elemental composition has beeen established by combustion analysis.



Reductive elimination on the resulting alkoxy-ruthenium hydride II releases the tertiary alcohol III and the reduced species RuO_3 (9), the later is then reoxidized with sodium metaperiodate, thus rendering the process catalytic relatively to ruthenium.

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