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Trapping of Free-Radicals in the Oxidation of Ethers, Aldehydes and Alkanes by Dimethyldioxirane.

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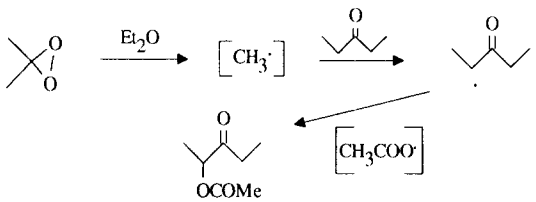
Abstract: Alkyl, α-oxyalkyl and acyl radical intermediates in the oxidation of alkanes, ethers and aldehydes by dimethyldioxirane are trapped by protonated quinolines and a free-radical chain is suggested for the α-acetoxylation of ketones.

The remarkably selective oxidation of several classes of organic compounds by dimethyldioxirane (DMD) accounts for numerous applications[1] reported during the last years. Very recently[2] we have obtained evidences concerning a free-radical mechanism in the oxidation of alkanes by DMD, which can be considered a very selective hydrogen abstracting species for both enthalpic and polar reasons; the stereoselectivity would be determined by an "oxygen rebound" mechanism, in contrast with the "O-insertion" mechanism suggested by the main research groups[1]. Recently[3] it has been reported that ethers can induce the free-radical decomposition of DMD; no mechanism was suggested for this induction, but in the presence of 3-pentanone the formation of 2-acetyloxy-3-pentanone was explained by the free-radical mechanism of Scheme 1

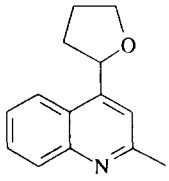


Scheme 1

The same mechanism has been suggested[4] for the thermal decomposition of DMD in the presence of ketones.. Now this mechanism is quite inconsistent on the grounds of the rate constant[5] (> 10^9 s^{-1}) of the unimolecular decarboxylation of the acetoxyl radical, so that a cross-coupling between the $CH_3COO\cdot$ radical and other carbon-centered radical outside the solvent cage is kinetically forbidden. On the other hand, the oxidation of ethers by DMD was shown[6] to be quite selective for α-C-H bonds and a free-radical mechanism was excluded owing to this high selectivity and to the absurd assumption that all the oxygen-centered radicals must have similar selectivity[6] (actually these selectivities are quite different, being $ROO\cdot > R_2C(OH)O\cdot >> RO\cdot >> HO\cdot$).

In order to obtain evidences about the mechanism of this oxidation we have attempted to trap the possible intermediate carbon-centered radicals by protonated heteroaromatic bases, which, in addition to the great synthetic potentiality, represent a powerful diagnostic criterion for the interception of nucleophilic free-radicals, due to the high reactivity and selectivity[7].

Attempts, carried out in acetone solution with DMD and Et_2O or THF in the presence of quinoline or 4-methylquinoline and CF_3COOH at room temperature led to trapping of small amounts (~ 1%) of methyl radical, while the main reaction products (50-60% yield) were the N-oxides of the heteroaromatic bases, likely formed by the electrophilic attack of DMD on the heterocyclic nitrogen atom. However, N-oxidation appears to be particularly sensitive to steric effects as it is considerably reduced with 2-methylquinoline under the same conditions: in this case the oxidation of ethers prevails. With Et_2O (Et_2O 10 mmol, DMD 1 mmol, quinaldine 1 mmol, CF_3COOH 1 mmol in 5 mL of acetone at 0°C), in addition to quinaldine N-oxide (12%) and ethanol, acetaldehyde and acetic acid as previously reported[3], also significant amounts of dimethylquinoline (1.2 %) and 2-methyl-4-ethylquinoline (3.2 %) were formed. With THF under the same conditions at 50°C quinaldine N-oxide (23%), 2,4-dimethylquinoline (3.2 %) and the substituted quinoline **1** (2.8%) were obtained, in addition to the oxidation products **2** and **3** already reported[6].



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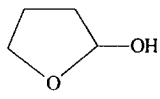

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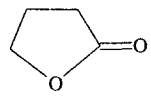

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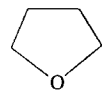

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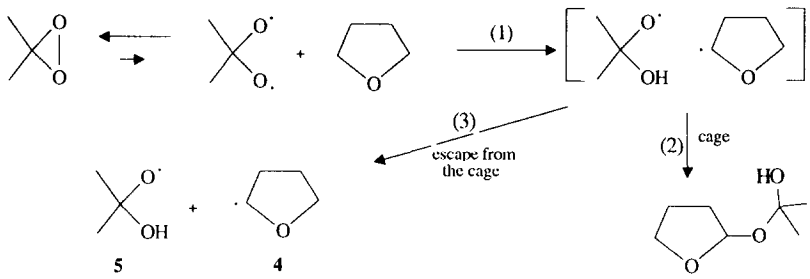
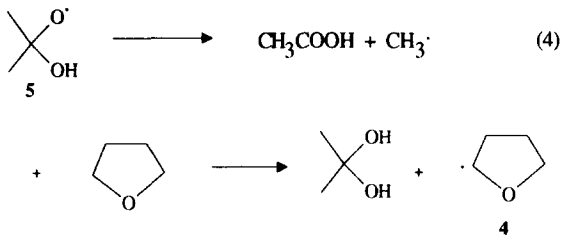
Thus methyl and ethyl, and respectively methyl and α-tetrahydrofuranyl (**4**) radicals are certainly formed in the oxidation of Et_2O and THF by DMD. We suggest that these results may be explained by the free-radical mechanism of Scheme 2.



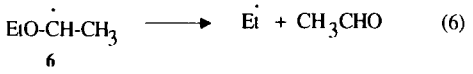
5 4

Scheme 2

The radical pair mainly reacts in the solvent cage, leading to the oxidation products **2** and **3**. The electrophilic radical **5**, escaped from the cage, is known to undergo competitive β-scission[8] (eq.4) and selective hydrogen abstraction from the α-C-H bonds of THF (eq.5)[9].

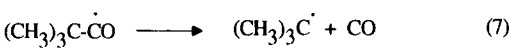


The nucleophilic methyl and tetrahydrofuranyl (**4**) radicals are trapped outside the solvent cage by quinaldine. Et_2O gives ethyl radical, in addition to methyl radical (eq.4), because it is known[10] that the α-ethoxyethyl radical **6** undergoes β–scission (eq.6)



Similar results were obtained in the oxidation of acetaldehyde by DMD at 0°C under the same conditions: acetic acid is the main reaction product, but significant amounts of quinaldine-N-oxide (7%), 2,4-dimethylquinoline (4.1%) and 2-methyl-4-acetylquinoline (4.2%) are formed, indicating that methyl and acetyl radicals are certainly involved outside the solvent cage and strongly supporting that the oxidation of acetaldehyde to acetic acid takes place through the acetyl radical according to Scheme 2.

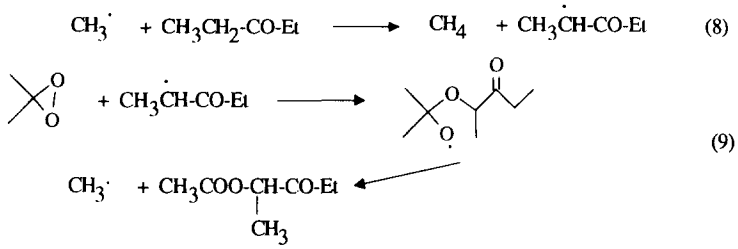
To obtain further support about the intermediate formation of acyl radicals in the oxidation of aldehydes we have investigated the oxidation of pivalaldehyde, because the pivaloyl radical undergoes a fast decomposition, giving t-butyl radical (eq.7)



However, it is known[11] that t-butyl radical attacks rapidly and selectively only position 2 on quinoline, so that quinaldine could not be utilized as trap; by using lepidine at 0°C under the same conditions we mostly obtained lepidine N-oxide (60%), but also small but significant amounts of 2-t-butyl-4-methylquinoline (0.4%) and 2-pivaloyl-4-methylquinoline (1.1%), indicating that pivaloyl and t-butyl radicals are formed from the aldehyde.

Alkyl radicals were also trapped in the oxidation of alkanes in the presence of quinaldine. With cyclohexane the following products are formed, respectively at 0°C and at 50°C: cyclohexanol (6.1 and 10.2 %), quinaldine-N-oxide (28.5 and 22.8 %), 2,4-dimethylquinoline (3.6 and 2.4 %), 2-methyl-4-cyclohexylquinoline (0.6 and 2.2 %). With adamantane and lepidine at 50°C the reaction products are: 1-adamantanol (29.1%), lepidine-N-oxide (62.6 %), and 2(1-adamantyl)-4-methylquinoline (2.9 %) with 61% conversion based on DMD: The fact that only position 1 of adamantane is involved in the oxidation and in the heteroaromatic substitution is a strong evidence that both reaction products arise from 1-adamantyl radical.

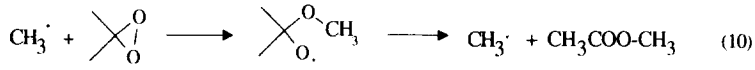
Since the mechanism of Scheme 1 is highly unlikely, and on the grounds of the results reported in this Letter, we suggest that the α-acetoxylation of ketones by DMD, induced by ethers[3] or through thermal[4] decomposition, can be rationalized by the radical chain of eqs. 8 and 9



(8)

(9)

The hydrogen abstraction from the α-C-H bonds of the ketone is favoured by polar (CH_3· is a nucleophilic radical) and enthalpic effects. The kinetic length of the chain should increase with temperature. A competitive free-radical chain (eq.10) leads to methyl acetate.



(10)

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