Induced Homolysis of Dimethyldioxirane by Alkanes and Alkyl Radicals in Oxidation Processes. The Dramatic Role of Molecular Oxygen and Radical Inhibitors

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The oxidation of alkanes by dimethyldioxirane is dramatically affected by the presence of molecular oxygen and radical inhibitors, supporting the hypothesis of a free-radical mechanism for these extraordinarily selective reactions; the factors affecting the free-radical selectivity are suggested.

The extraordinary regio-, chemo- and stereo-selectivity in the oxidation of alkanes by dimethyl (DMD) and other dioxiranes has led many research groups to exclude a free-radical mechanism, and a poorly defined 'oxenoid O-insertion' has been suggested for these reactions.[1] For example, it has been reported[1a,b,2] that the selectivity in the oxidation of toluene, ethylbenzene and cumene by DMD is not consistent with a free-radical mechanism, because it is considerably higher compared with the selectivity shown by the $Bu^tO^{\cdot}$ radical. We have recently[3] reported evidence concerning the involvement of free radicals in these oxidations. Here we report the dramatic effects of molecular oxygen and radical inhibitors, which strongly support a free-radical mechanism for these reactions.

When oxidations of cyclohexane, adamantane, ethylbenzene and cumene are carried out at room temperature in acetone solution, the reaction products and the conversions of the alkanes are quite different depending on whether the reaction is carried out under an oxygen or a nitrogen atmosphere. In the absence of oxygen the conversions of the alkanes (R–H) are lower and the alkyl acetates (RO–COMe) are the main or significant reaction products, while in the presence of oxygen the formation of acetates is substantially suppressed. In the latter case, the alcohols, or the ketones when a $-CH_2-$ group is oxidized, are mainly formed, and the conversions increase. The results are reported in Table 1.

We explain these results by the homolysis of DMD induced by the alkane (Scheme 1).

The formulation shown in Scheme 1 does not necessarily mean that a real pre-equilibrium of DMD is present, but it is related to the homolysis induced by the alkane. The radical pair gives rise to a cross-coupling in the solvent cage, while the radicals which have escaped from the cage initiate a free-radical chain process by induced homolysis of DMD [eqns. (1)–(3)]. The formation of esters has not been observed until now in the numerous reports[1] of alkane oxidation by DMD. Cyclohexanone and acetophenone are mainly obtained with cyclohexane and ethylbenzene because the alcohols initially formed are much more reactive than the starting alkanes.[3] With cumene minor amounts of acetophenone are formed, in addition to cumyl alcohol, probably by β-scission of a cumyloxy radical intermediate.

Careful NMR and GC-MS analyses reveal the presence of methane, methyl acetate, methanol and acetoxyacetone, in addition to the reaction products reported in Table 1, in the absence of oxygen. We explain the formation of these products by the competitive chain processes of eqns. (4)–(7).

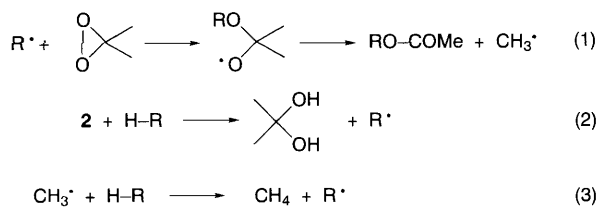
The oxygen intercepts all the carbon-centred radicals [eqn. (8)], suppressing the chain processes of eqns. (1)–(7).

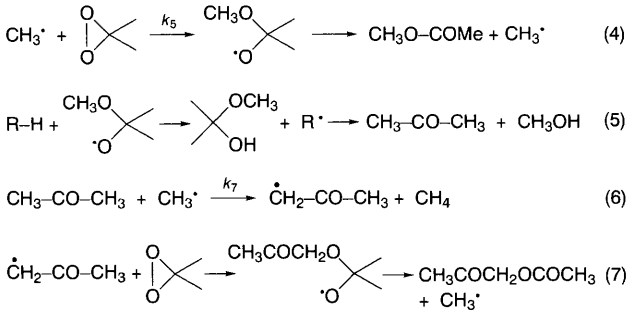
The peroxy radicals do not induce homolysis of DMD according to reactions similar to eqns. (1), (4) and (7), while, on

Table 1 Oxidation of alkanes (R–H) by DMD in acetone

R–H	Conversion[a] (%)	R–OH + Ketone (%)[a]	ROCOMe (%)[a]	Reaction time/h
Adamantane[b]	21	1-Ad-OH (32) 2-Ad-OH (0.6)	1-Ad-OCOMe (54.8) 2-Ad-OCOMe (12.6)	72
Adamantane[c]	47	1-Ad-OH (96) 2-Ad-OH (1.8)	1-Ad-OCOMe (1.6) 2-Ad-OCOMe (0.6)	72
Adamantane[d]	39	1-Ad-OH (96) 2-Ad-OH (1.7)	1-Ad-OCOMe (1.9) 2-Ad-OCOMe (0.4)	72
Adamantane[e]	Trace	Trace	Trace	72
Cumene[c]	39	Cum-OH (91) Acetophenone (8)	1	22
Cumene[b]	9	Cum-OH (16)	84	2.5
Cumene[b]	14	Cum-OH (32) Acetophenone (3)	65	22
Cumene[f]	8	Cum-OH (8)	92	1
Cumene[f]	18	Cum-OH (33) Acetophenone (5)	62	72
Cyclohexane[b]	25	R-OH (31) Cyclohexanone (36)	33	48
Cyclohexane[c]	32	TNR-OH (36) Cyclohexanone (64)	Trace	48
Ethylbenzene[b]	20	R-OH (36) Acetophenone (50)	14	48
Ethylbenzene[c]	46	R-OH (25) Acetophenone (75)	Trace	48

[a] General procedure: conversions of alkane based on DMD; the overall yields based on the converted alkane are in the range 94–96%; small amounts of unidentified products are present; the reported results are relative yields of the two main products. [b] Nitrogen was bubbled in 10 ml of an 0.1 mol dm^{-3} solution of DMD in acetone, prepared according to ref. 7, at room temperature; 1 mmol of alkane was added and the closed flask was kept at room temperature for the time reported; the solution was analysed by GLC and GC-MS, identifying the reaction products by comparison with authentic samples. [c] As in *b* with the difference that oxygen was bubbled and the flask was kept under 1 atm of oxygen pressure at room temperature. [d] As in *b* in the presence of 0.5 mmol of *p*-benzoquinone. [e] As in *b* in the presence of 0.5 mmol of TEMPO (**3** is formed in 60% yield based on TEMPO). [f] As in *b* with a 4:1 ratio of cumene:DMD.

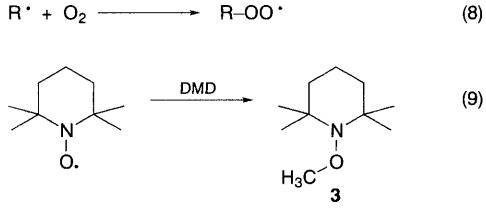




the other hand, they do not sustain effective auto-oxidation chains, because the peroxy radical is unreactive at room temperature towards the solvent (acetone) and the rate constants for hydrogen abstraction from alkanes (2.6×10^{-4} and 1.6×10^{-1} dm^3 mol^{-1} s^{-1}, respectively, for cyclohexane and cumene at 30 °C) do not allow significant amounts of hydroperoxide to be formed, due to the very low concentration of RH. The fate of the peroxy radical is probably identical to the termination processes in auto-oxidation. In any case, the radicals escaping from the solvent cage do not appear to be doing so in large amounts. Thus, the cage coupling of Scheme 1 is the main reaction in the presence of O_2. This is reflected in the different regioselectivity of hydroxylation (determined by Scheme 1) and acetoxylation [determined by Scheme 1, eqns. (2), (3) and (5)] of adamantane and in the lower covnersion of alkanes in the absence of oxygen, because DMD is also consumed by reactions (4) and (7), which do not involve the alkanes. Under a nitrogen atmosphere the ratio (alcohol + ketone):ester increases for long reaction times, probably owing to small amounts of oxygen.

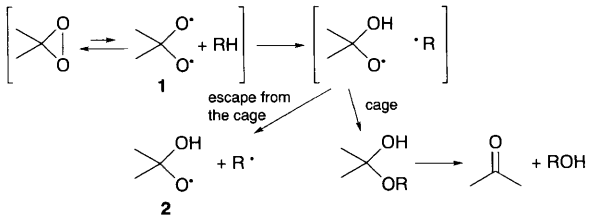
An effect similar to that caused by molecular oxygen occurs under a nitrogen atmosphere in the presence of *p*-benzoquinone: the formation of the acetates is suppressed, owing to the high rate constants[4] ($> 10^7$ dm^3 mol^{-1} s^{-1}) for the addition of alkyl radicals to the quinone ring.

The presence of TEMPO under a nitrogen atmosphere practically inhibits the oxidation of alkanes; it appears that TEMPO also induces the homolytic decomposition of DMD since the main reaction product arises from trapping of the methyl radical [eqn. (9)].



The mechanism of this induction will be discussed in a full paper. It appears that the previously reported results[1] were due to the activity of the air oxygen, which was neglected because a free-radical mechanism had been excluded.

An approximate value of k_5 has been established according to the following procedure: 1 mmol of adamantane was added at 20 °C to a solution of 1 mmol of DMD in 10 ml of acetone



Scheme 1

under a nitrogen atmosphere; after 1 h at 20 °C the solution was analysed by NMR (clean singlets for CH_4, CH_3OH, CH_3COOCH_3 and CH_3COOCH_2–$COCH_3$ at δ 0.15, 3.29, 3.58 and 4.70, respectively in acetone solution); a ratio of 3.2:0.8:1 has been determined for methyl acetate, methanol and acetoxyacetone, while the evaluation of methane was only qualitative, owing to its gaseous nature. It is possible to approximately evaluate at low conversions $k_5/k_7 = 544$ from the ratio (4:1) of CH_3COOCH_3:CH_3OH, arising from reactions (4) and (5), and CH_3COOCH_2–$COCH_3$ [from eqns. (6) and (7)] and the number of mmols of DMD (1) and acetone (136). Since k_7 can be evaluated at 2.7×10^3 dm^3 mol^{-1} s^{-1} from the known[5] rate constant (7.4×10^4 dm^3 mol^{-1} s^{-1}) for hydrogen abstraction by the methyl radical from diethyl ketone, this latter being about 27 times more reactive than acetone towards methyl radical,[6] a value of k_5 *ca.* 10^6 dm^3 mol^{-1} s^{-1} at 20 °C can be established.

The previous assumption[1,2] that the observed selectivity among toluene, ethylbenzene and cumene excludes a free-radical mechanism does not appear, in our opinion, to be justified. Apart from the fact that the relative rates were determined[2] by hydrocarbon consumption without the analysis of the reaction products, we can expect a radical such as **1** to be much more selective than a simple alkoxy radical for enthalpic as well as polar reasons: we can qualitatively evaluate the energy of the O–H bond in radical **2** as significantly lower than that of the O–H bond of an alcohol because the homolysis of the O–H bond in **2** gives DMD and a hydrogen atom. Moreover, the more unfavourable enthalpy associated with the presence of two oxygen atoms makes radical **1** much more electrophilic and therefore much more selective in hydrogen abstraction in relation to the electron availability of the C–H bond, compared to simple alkoxy radicals. These effects would explain the exceptional regio- and chemo-selectivity of the oxidation, while the very fast oxygen-rebound mechanism in the solvent cage [eqn. (3)] would explain the observed stereoselectivity.[2]

Our preliminary results for the oxidation of other classes of organic compounds (ethers, aldehydes, alkenes) suggest an induced homolysis of DMD also for these reactions.

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