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Oxidation of Alkyl and Aryl Iodides, Phenylacetaldehyde and Alkenes by Dimethyldioxirane. Reaction Products and Mechanism.

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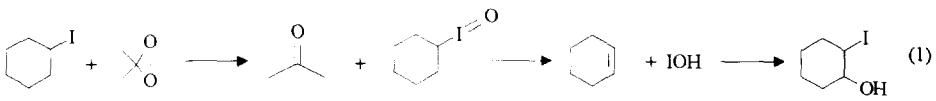
Abstract - Alkyl and aryl iodides are smoothly oxidized to iodosoderivatives and phenylacetaldehyde is oxidized to phenylacetic acid or benzyl acetate by dimethyldioxirane depending on the presence or not of oxygen. These results and the epoxidation or the allylic oxidation of alkenes by the same reagent are explained by a general free-radical mechanism.

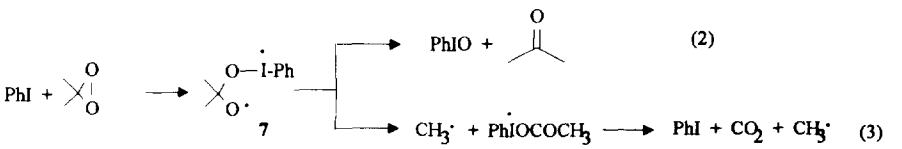
Recently, we[1] have reported evidences concerning the free-radical nature of the oxidation of alkanes, ethers and alcohols by dimethyldioxirane (DMD) in contrast with the main research groups[2] , which exclude a free-radical mechanism. A recent report[3] on the formation of alkenes and epoxides from alkyl iodides and DMD prompts us to report the different results obtained in the oxidation of alkyl and aryl iodides by DMD and the behaviour of phenylacetaldehyde and alkenes with the same reagent, together with a general free-radical interpretation of all these results. Aryl iodides smoothly react with DMD at 0°-20°C in acetone to give mainly, depending on the amount of DMD, Ar-IO (**1**) or Ar-IO_2 (**2**), which precipitate from the solution. In the presence of acetic acid, the corresponding iodosoacetate, Ar-I$(OAc)_2$ (**3**), are formed.

Cyclohexyl iodide mainly gives trans-2-iodocyclohexanol (**4**) and minor amounts of 1,2-cyclohexanediol (**5**), while in the presence of acetic acid the trans-2-iodocyclohexyl acetate (**6**) is the main reaction product. The formation of these products can be related to the instability of the alkyliodoso derivatives, which eliminate hypoiodous acid IOH, whose trans addition on the alkene gives the reaction product (eq.1) (Table 1).

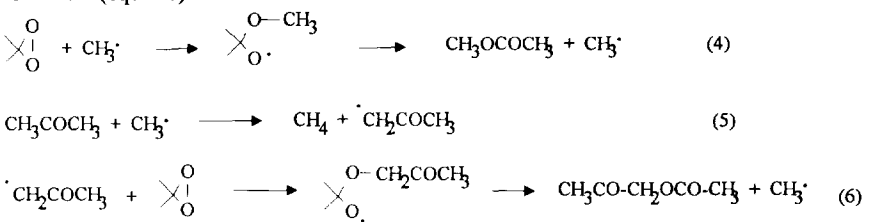


(1)

The different results with DMD in the recent report[3] can be explained by the proximity, in this case, of the trifluoromethylsulfonyl group, which deactivates the double bond towards the electrophilic addition. As concerns the reaction mechanism, the electrophilic oxidation of iododerivatives by peroxides (i.e. metachloroperbenzoic acid, MCPBA) is well documented[4]. We have, however, considered the possibility that a free-radical mechanism could be operating also in this case, on the ground of the fact that iododerivatives appear to react very rapidly (10^6 - 10^9 M^{-1} s^{-1} at r.t.) with both oxygen- and carbon-centred radicals[5]. In order to achieve mechanistic evidences, we have carefully analyzed by NMR the reaction solution and we have identified significant amounts of methyl acetate , methanol, acetoxyacetone, clearly suggesting that methyl radical is formed by induced free-radical decomposition of DMD (eq. 2)

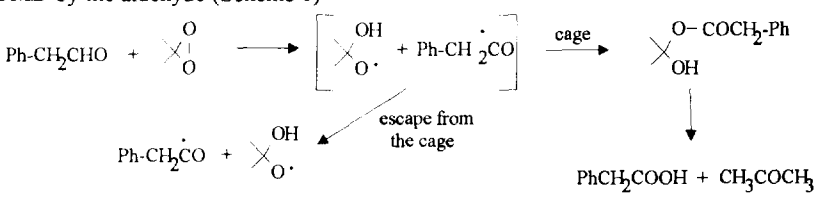


The biradical 7 would mainly collapse to the iodosoderivative (eq.2) due to the highly favoured enthalpic effect (formation of two new bonds) and to a minor extent to methyl radical (eq.3), which would induce a chain decomposition of DMD (eqs.4-6)



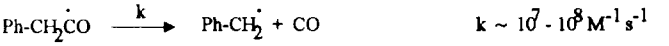
Thus, small amounts of methyl radical formed according to eq.3 could induce a large decomposition of DMD (eqs. 4-6). Further circumstantial evidence for a free-radical mechanism was obtained from competitive oxidations of iodobenzene and quinoline by DMD and MCPBA in acetone solution: both oxidants oxidize the substrate respectively to iodosobenzene and quinoline N-oxide. However, in competitive experiments under the same conditions, with equimolecular amounts of iodobenzene and quinoline, the reactivity is dramatically reversed, in the sense that with DMD only iodobenzene is oxidized, while with MCPBA only quinoline is oxidized, in spite of its reduced reactivity due to the relevant protonation by the acidic oxidant. Since quinoline is mainly oxidized by an electrophilic process, it appears highly unlikely that such a dramatic inversion of reactivity could occur if also the oxidation of iodobenzene by DMD would take place by an electrophilic oxidation. On the opposite, this result is well explained if we assume that MCPBA acts in both cases as an electrophilic reagent, while DMD oxidizes iodobenzene by a fast induced homolysis (eq.2) and quinoline by a much slower electrophilic process.

The oxidation of phenylacetaldehyde by DMD at 20°C provides further strong evidence of a free-radical mechanism. In the presence of oxygen, phenylacetic acid is the only reaction product and conversions are high (75%), while in nitrogen or argon atmosphere under the same conditions the oxidation of phenylacetaldehyde is practically inhibited (only 6% conversion, with the formation of 67% benzyl acetate and 33% phenylacetic acid). At 60°C under nitrogen atmosphere, the conversion increases to 16% with formation of 87% benzyl acetate and 13% phenylacetic acid. Under the same conditions in the presence of oxygen and in the absence of DMD no substantial oxidation of phenylacetaldehyde occurs. In the absence of oxygen, DMD mainly decomposes to methyl acetate, methanol and acetoxyacetone. We explain these results by the induced homolysis of DMD by the aldehyde (Scheme 1)



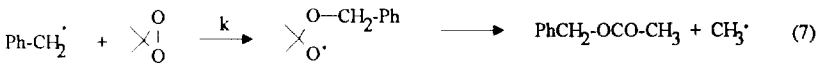
Scheme 1

The acyl radical escaped from the cage undergoes fast decarbonylation[6] (eq.3)



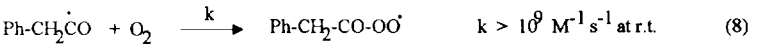
$$Ph\text{-}CH_2\dot{C}O \xrightarrow{k} Ph\text{-}CH_2^{\cdot} + CO \qquad k \sim 10^7 - 10^8\ M^{-1}s^{-1}$$

The benzyl radical induces a chain decomposition of DMD giving benzyl acetate (eqs. 7 and 4-6)



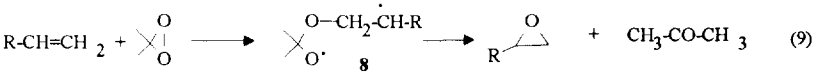
$$Ph\text{-}CH_2^{\cdot} + \underset{O}{\overset{O}{\times}} \xrightarrow{k} \underset{O^{\cdot}}{\overset{O\text{—}CH_2\text{-}Ph}{\times}} \longrightarrow PhCH_2\text{-}OCO\text{-}CH_3 + CH_3^{\cdot} \qquad (7)$$

Molecular oxygen, by intercepting all carbon-centred radicals, avoids both the decarbonylation of the acyl radical (eq.8) and the chain decomposition of DMD (eqs. 4-6), while it does not appear to induce homolysis of DMD.



$$Ph\text{-}CH_2\dot{C}O + O_2 \xrightarrow{k} Ph\text{-}CH_2\text{-}CO\text{-}OO^{\cdot} \qquad k > 10^9\ M^{-1}s^{-1}\ \text{at r.t.} \qquad (8)$$

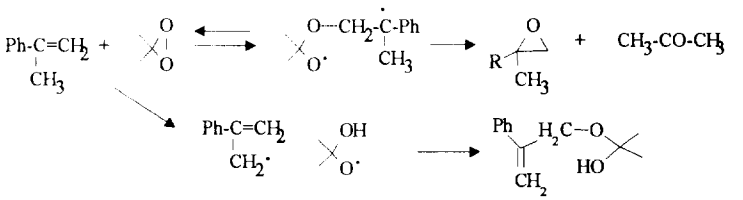
All these and previous[1] results suggested that alkenes could much more easily induce the homolysis of DMD and that epoxides could be formed by a free-radical mechanism (eq.9)



$$R\text{-}CH{=}CH_2 + \underset{O}{\overset{O}{\times}} \longrightarrow \underset{O^{\cdot}}{\overset{O\text{—}CH_2\text{-}\dot{C}H\text{-}R}{\times}} \quad \mathbf{8} \longrightarrow \underset{R}{\overset{O}{\triangle}} + CH_3\text{-}CO\text{-}CH_3 \qquad (9)$$

The high stereoselectivity[2] would be ascribed to the fast collapse of the biradical **8** (also this process is enthalpically favoured by the formation of two new bonds). This mechanism would be supported by the behaviour of oxygen-centered radicals with simple alkenes: alkoxy and peroxy radicals react by allylic hydrogen abstraction[7], while the benzoyloxy radical Ph-C(=O)-O· , structurally similar to the dioxyl radical $(CH_3)_2C(O\cdot)O\cdot$, adds to the double bond[8].

Also with alkenes, the relative rates of oxidation of cyclohexene and quinoline by DMD and MCPBA would support the free-radical mechanism of eq.9. In the competition with equimolar amounts of cyclohexene and quinoline, only cyclohexene epoxide is formed with DMD, while with MCPBA quinoline N-oxide is highly prevailing (87%). A further support to a free-radical mechanism is provided by the results obtained with α-methylstyrene: in addition to the epoxide (35%) and its rearranged derivative, α-phenylpropionaldehyde (51%), the allylic oxidation significantly occurs and the allylic alcohol, $Ph\text{-}C(CH_2OH){=}CH_2$ and the unsaturated aldehyde, $Ph\text{-}C(CHO){=}CH_2$ are formed respectively in 6% and 5% yields. We explain these results by the fact that the addition of alkoxy radicals to α-methylstyrene appears to be reversible[9], while the allylic hydrogen abstraction is irreversible, so that the latter reaction, even if slower, can compete with the epoxide formation (Scheme 2). With β-methylstyrene the radical addition is less reversible (formation of a secondary benzyl radical) and less than 1% of benzylic oxidation occurs. It would appear that when steric, polar or enthalpic effects make the radical addition to the double bond difficult, allylic hydrogen abstraction can compete[11].



Scheme 2

Table 1. - Oxidation of iododerivatives by DMD.

R-I	1 (%)	2 (%)	3 (%)	4 (%)	5 (%)	6 (%)
Ph-I[a]	26	13	--	--	--	--
p-MeO-Ph-I[b]	--	46	--	--	--	--
c-C_6H_{11}-I[b]	--	--	--	43	4	--
c-C_6H_{11}-I[c]	--	--	--	--	--	35
Ph-I[c]	--	--	56	--	--	--

[a]the alkyl iodide was dissolved at room temperature and under nitrogen atmosphere in a 0.09 M solution of DMD in acetone prepared according to the known procedure[10] (equimolar amounts of DMD and RI were used). After 5 hrs **1** and **2** were isolated by filtration and **3**, **4**, **5**, **6** analyzed by GLC and NMR and compared with authentic samples; [b]ratio DMD: RI 2:1; [c]as in (b) in the presence of 5 mol AcOH per mol of RI; yields based on converted RI are in the range 92-96%.

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