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DECOMPOSITION OF DIOXIRANES INDUCED BY DIALKYL ETHERS

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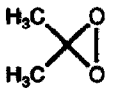
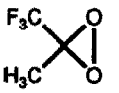
Abstract: Simple dialkyl ethers (*i.e.* diethyl or dihexyl ether), in addition to undergo oxidative cleavage by reaction with methyl(trifluoromethyl)dioxirane or dimethyldioxirane, induce the decomposition of these oxidation reagents in a concentration dependent manner. The identification of compounds derived from reactions with species such as $CH_3^{\cdot}$ or $CF_3CO_2^{\cdot}$ suggests that the above decomposition is a radical chain process.

Key words: Ether, radicals, dimethyldioxirane, methyl(trifluoromethyl)dioxirane.

The advantages of dioxiranes as oxidation reagents in organic synthesis, i.e. easy of preparation and manipulation, high reactivity under neutral conditions, broad scope of substrates and simple work-up procedures, account for their numerous applications reported during the last years. Thus, oxidation of heteroatoms, epoxidation of double bonds or oxygen insertion into C-H bonds are representative examples of the reactivity of these compounds [1]. Among dioxiranes, dimethyldioxirane (DMD) has been the most widely used reagent, although the unique reactivity exhibited by methyl(trifluoromethyl)dioxirane (TFMD) has led to remarkable and selective synthetic transformations [1c,2].

DMD   TFMD

Despite the oxidation properties of TFMD, its use has been somewhat restricted due to a "classical" problem encountered in its preparation. Thus, it was known that some commercially available 1,1,1-trifluoropropanone (TFP) batches did not afford TFMD when treated with caroate under the conditions described by Mello *et al.*[3]. Occasionally, the pale yellow solution containing the dioxirane could be collected at -70 °C, but the color disappeared when the temperature raised to approximately -20 °C, with the concomitant loss of the oxidation power. In addition, the TFP samples that did not give rise to stable TFMD solutions caused also the deactivation of DMD when added to acetone solutions of this compound, although this deactivation took place at a slower rate. These facts suggested the presence of an impurity in the fluorinated ketone which would be the species responsible for the observed decomposition of both dioxiranes. This impurity could not be removed from TFP either by distillation or by different drying procedures. However, when we performed a partition of TFP among water and CCl_4 (which is the method used by Adam *et al.* for obtaining TFMD solutions free from TFP [4]), we observed that the impurity was concentrated into the organic layer, which allowed its identification by NMR and GC. The impurity resulted to be *diethyl ether* (Et_2O), probably arising from the method used for the preparation of TFP. The concentration of Et_2O in the fluorinated ketone sample was estimated within 1-2% (ca. 0.2 M, ^1H NMR) in the different batches analyzed. On the other hand, the addition of this amount of Et_2O to a stable solution of TFMD led to the immediate decomposition of this dioxirane, which confirmed our hypothesis [5].This

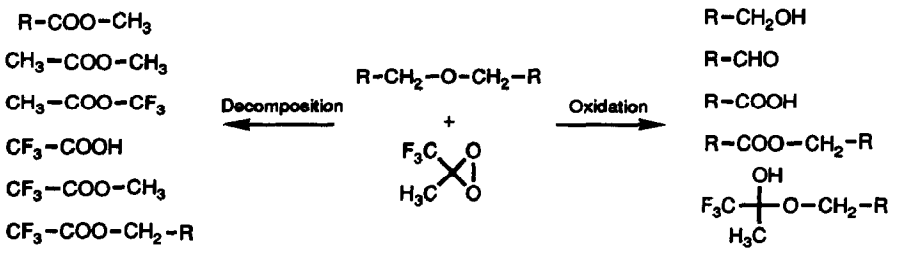
finding prompted us to study with a more detail the behaviour of TFMD in front of simple dialkyl ethers. For this purpose we chose Et_2O and dihexyl ether (Hex_2O) as model substrates, and the preliminary results obtained are also reported in the present communication.

Regarding the stability of dioxiranes, Singh and Murray reported that the thermal decomposition of DMD in solution of mixtures of different ketones leads to the formation of acetyloxyketones. A mechanism involving hydrogen atom abstraction from the ketones promoted by the radical species generated in the decomposition of DMD, with further reaction of the ketone radical intermediate with acyloxy radicals derived from homolysis of the dioxirane, would account for the formation of the observed esters [6]. On the other hand, Adam *et al.* studied the thermal and photochemical induced decomposition of TFP-free solutions of TFMD. The detection of methyl and trifluoromethyl esters of acetic and trifluoroacetic acids supported the hypothesis of a radical chain process initiated by attack of CH_3 and CF_3 radicals over TFMD to give α-alkoxy-α-alkoxyl radical intermediates, which would afford the ester derivatives by β-alkyl fragmentation [4]. More recently, the same group reported the decomposition of TFMD induced by catalytic amounts of iodide anion; in this case, a catalytic cycle takes place with the exclusive formation of TFP and superoxide ion [7].

Concerning the reaction of dioxiranes with ethers, Curci *et al.* reported that acetals and ethers are oxidized by dioxiranes through α-CH insertion. The selectivity found for the hydroxylation into C-H bonds α to the ether moiety suggested that the reaction proceeded through a non-radical pathway. Among the substrates studied, there was only one dialkylether, that is CH_3-$(CH_2)_6$-O-$(CH_2)_6$-CH_3, and the identified products from its reaction with DMD were heptanol, heptanal and heptanoic acid, by using a 1:2.2 substrate:DMD molar ratio [8].

In our case, we determined as a 1.5:10 dialkyl ether:TFMD molar ratio the relative concentration of either Et_2O or Hex_2O needed to induce the complete deactivation of this dioxirane (30 min at -20 °C). In respect to the products formed in this decomposition process, when an enough amount of Et_2O (0.2 mmol) was added to 1 ml of a 0.6 M solution of TFMD in TFP at -20 °C for achieving the complete deactivation of this dioxirane, the ^1H and ^{19}F NMR analysis of the reaction mixture allowed the identification of ethanol, acetaldehyde, acetic acid, ethyl acetate, methyl acetate, trifluoroacetic acid, methyl trifluoroacetate, ethyl trifluoroacetate and trifluoromethyl acetate (Scheme I). While the first four components of this mixture could be originated from the oxidative cleavage of Et_2O (cf. ref. 8), the presence of the last compounds (*i.e.*, the fluorinated derivatives and methyl acetate) suggests that methyl and trifluoromethyl radicals had been also generated in the reaction medium. According to the results of Adam *et al.* mentioned above [4], the formation of these species occurs during the decomposition of the TFMD through a radical mechanism [9].

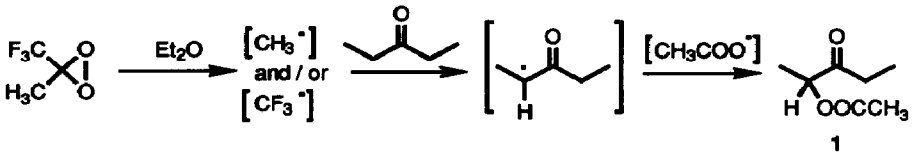
Scheme I



A similar experiment was carried out by using Hex_2O as substrate. In this case, the components of the crude reaction mixture could be analyzed by GC and by GC/MS. The comparison with authentic standards for most of the compounds present in the mixture supported the corresponding identifications. Thus, hexanol, hexanal, hexanoic acid, hexyl hexanoate and the hexyl hemiacetal of TFP were detected in the mixture (Scheme I). More important, the occurrence of markers of the radical decomposition of TFMD induced by the ethereal substrate, such as methyl hexanoate and hexyl trifluoracetate, could be also identified. Moreover, the ^{19}F NMR analysis of the reaction mixture showed a pattern with close resemblance to that obtained for the case of the Et_2O induced decomposition of TFMD, and again the presence of trifluoroacetic acid, methyl trifluoroacetate and trifluoromethyl acetate was observed. The identification of all these compounds leads to the same conclusion described above for the case of Et_2O.

An additional evidence of the intervention of radical species in the decomposition of TFMD induced by dialkyl ethers was obtained from the experiments carried out in the presence of 3-pentanone. Thus, the addition of 250 µl of a 0.13 M solution of Et_2O in 3-pentanone to the same volume of a 0.65 M solution of TFMD in TFP at -20 °C, led to the rapid decomposition of the dioxirane. The GC/MS analysis of the crude reaction mixture permitted the identification, among other compounds, of 2-acetyloxy-3-pentanone (**1**), which is the same product found by Singh and Murray in their experiments of thermolysis of DMD in the presence of the above ketone [6]. This result supports the hypothesis on an acetyloxy radical generation during the TFMD decomposition process (Scheme II).

Scheme II



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Finally, to test whether a decomposition process similar to that observed for TFMD could take place in the case of DMD, the addition of either Et_2O or Hex_2O in a 0.2 M concentration to an acetone solution of DMD (75-85 mM, prepared as described elsewhere [10] and maintained at 0 °C), was tested. Again, the oxidation reactivity of this dioxirane was lost, although the deactivation process was slower in comparison with that exhibited by TFMD [11]. In this case, the study on the influence of the Et_2O concentration on the DMD deactivation (Fig. 1) [12], did not permit the differentiation between the occurrence of a deactivation process based on a radical chain pathway, from that caused by the oxidative cleavage of the ethereal substrate. Nevertheless, the GC/MS identification of 2-acetyloxy-3-pentanone (**1**), among other compounds, in the crude reaction mixture obtained from the treatment of 1ml of a 80 mM solution of Et_2O in 3-pentanone with the same volume of a solution of 80 mM DMD in acetone for 20 h at 0 °C, indicated that the deactivation of DMD proceeds, at least to a certain

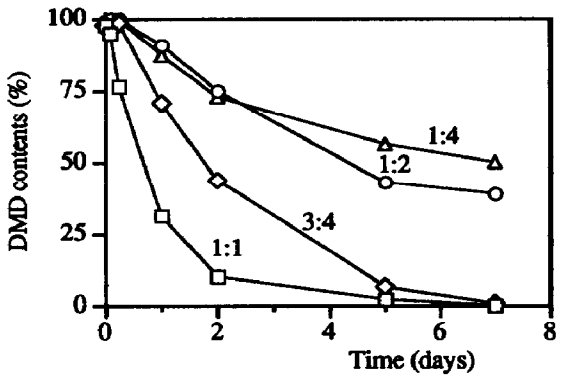

Figure 1. Time-course decomposition of DMD at different Et_2O:DMD molar ratios, in acetone soln. at 0 °C.

extent, through the radical chain mechanistic pathway shown in Scheme II for the case of TFMD.

In summary, we have presented different evidences that simple dialkyl ethers induce the decomposition of TFMD and DMD, and that this process takes place through the intervention of radical species derived from the ethereal substrate. The question that now emerges is related to the nature of these species; that is, whether they are originated from the ether itself or from a product derived from its oxidative cleavage. The different behavior observed in the deactivation of both dioxiranes suggests that the latter possibility could be more plausible. Investigations along this line are in progress in our laboratory [13].

Notes and References.

1. For recent reviews on these reagents, see a) Adam, W.; Curci, R.; Edwards, J. O. *Acc. Chem. Res.* **1989**, *22*, 205-211. b) Murray, R.W. *Chem. Rev.* **1989**, *89*, 1187-1201. c) Curci, R., in "Advances in Oxygenated Processes", A.L. Baumstark, Ed., JAI Press Inc., London, **1990**, pp 1-60. d) Adam., W.; Hadjiarapoglou, L. P.; Curci, R.; Mello, R. in *Organic Peroxides*; W. Ando, Ed.; Wiley, New York; **1992**, Chapter 4, pp 195-219.

2. D'Accolti, L.; Detomaso, A.; Fusco, C.; Rosa, A.; Curci, R. *J. Org. Chem.* **1993** *58*, 3600-3601, and references cited therein.

3 Mello, R.; Fiorentino, M.; Sciacovelli, O.; Curci, R. *J. Org. Chem.* **1988**, *53*, 3890-3891.

4. Adam, W.; Curci, R.; Gonzalez-Nuñez, M.E.; Mello, R. *J. Am. Chem. Soc.* **1991**, *113*, 7654-7658.

5. It should be pointed out that the different assays carried out to induce the decomposition of TFMD were performed using small (up to millimol range) amounts of reagents. In some cases, the observed decomposition processes were rapid, but not violent. However, the results reported herein advise for caution when handling dioxiranes in the presence of ethers.

6. Singh, M.; Murray, R.W. *J. Org. Chem.* **1992**, *57*, 4263-4270.

7. Adam, W.; Asensio, G.; Curci, R.; Gonzalez-Nuñez, M.E.; Mello, R. *J. Am. Chem. Soc.* **1992**, *114*, 8345-8349.

8. Curci, R.; D'Accolti, L.; Fiorentino, M.; Fusco, C; Adam, W.; Gonzalez-Nuñez, M.E.; Mello, R. *Tetrahedron Lett.* **1992**, *33*, 4225-4228.

9. It is worth of noting that solutions of TFP containing a 2% of Et_2O did not show the presence of these fluorinated and non fluorinated derivatives by NMR. On the other hand, when a conventional oxidation reaction with TFMD, such as epoxidation of *cis*-stilbene, was performed, the analysis of the crude reaction mixture showed only the presence of the expected epoxide and TFP. This result indicates that when TFMD acts as oxidation reagent, it does not lead to the formation of compounds derived from the generation of methyl or trifluoromethyl radical intermediates.

10. Adam, W.; Bialas, J.; Hadjiarapoglou, L. *Chem. Ber.* **1991**, *124*, 2377.

11. Preliminary assays carried out with different ethereal compounds showed that dimethoxyethane, dioxane or ^{t}butyl methyl ether did not induce the decomposition of DMD when tested under the same conditions. Conversely, THF afforded similar results to those observed for Et_2O.

12. The assay was performed as follows: to 1 ml of DMD soln. in acetone (75-85 mM) it was added 1 ml of an acetone soln. of Et_2O at the appropriate concentration, and the mixture was maintained at 0 °C, in the dark. Aliquots were taken at the given periods of time and DMD concentration was determined by using a GC analytical method based on the epoxidation of methyl citronellate in the presence of nitrobenzene as internal standard.

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