Molecule-Induced Homolysis versus "Concerted Oxenoid Oxygen Insertion" in the Oxidation of Organic Compounds by Dimethyldioxirane

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Evidence for a molecule-induced homolysis of dimethyldioxirane by several classes of organic compounds (alkanes, alkenes, ethers, alcohols, aldehydes, iododerivatives) is reported. Carbon-centered radicals, arising from alkanes, ethers, and aldehydes, are trapped by $CBrCl_3$ or protonated quinolines. The dramatic influence of oxygen in these reactions, as well as the formation of products of induced homolysis of the dioxirane by carbon-centered radicals (CH_4, CH_3OH, CH_3COOCH_3, $ROCOCH_3$, $CH_3COOCH_2COCH_3$), strongly supports a radical mechanism. With alkenes and iodo derivatives the induced homolysis would lead to diradical intermediates, whose very fast fragmentation would prevent detection, but circumstantial evidence supports a radical mechanism.

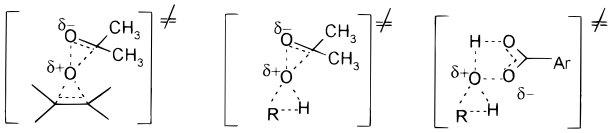
Introduction

Dioxiranes represent a class of oxidants of great current fashion for the oxidation of organic compounds. While this interest is undoubtedly justified from the theoretical standpoint, it is less so for synthetic and practical purposes, despite the excessive emphasis given to the synthetic applications of these oxidations[1] and of the potential accessibility of the simplest member of the series, dimethyldioxirane (DMD), from acetone and potassium monoperoxysulfate (tradename Curox or Caroate). Actually, DMD is an expensive reagent because it is obtained in about 5% yield from Caroate[2] (78 g of Caroate is consumed to prepare 1 g of DMD); moreover, it is unstable, due to a fast radical chain decomposition which can be initiated at room temperature by traces of occasional impurities, and most oxidations carried out with DMD can be achieved by simpler and cheaper oxidants.

Several classes of organic compounds have been oxidized by DMD or similar dioxiranes and some specific behaviors are strictly related to the oxidation mechanism.

In preliminary papers we[3] have reported evidence that the oxidation of a variety of organic compounds (alkanes, alcohols, ethers, aldehydes, alkenes, and alkyl iodides) by DMD can be explained by radical mechanisms. These reports were in clear contrast with the widely accepted mechanism[1] of "concerted oxenoid oxygen insertion", which postulates a butterfly type transition state (structure **1**) for the oxidation of alkenes, similar to the one originally suggested by Bartlett[4] for the alkene epoxidation by peracids.

LFER studies[5,6] would indicate similar concerted electrophilic transition states also for the oxidation of alkanes both by DMD and by peracids (structures **2** and **3**).



1 **2** **3**

This dualism (concerted oxygen insertion versus radical mechanism) is not limited to DMD, but it is quite general (aromatic peracids,[6] perfluorooxaziridines,[7] Gif reaction,[8] cytochrome P450,[9] and metalloporphyrin catalysis and other metal salt complexes[10]). We have recently reported evidence that also with peracids,[11] Gif reaction,[12] and metalloporphyrin catalysis[13] the oxidation of alkanes can be explained by radical mechanisms.

In a recent report[14] numerous authors have criticized our mechanistic conclusions by stating that "the epoxidation and oxygen insertion into alkane C−H bonds by DMD do not involve detectable radical pathways"; moreover, these authors reported that some of our experimental results could not be reproduced.

In this paper we report the developments of our preliminary data, experimental details, and further

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Table 1. Reaction of Adamantane with DMD in the Presence of $CBrCl_3$[a]

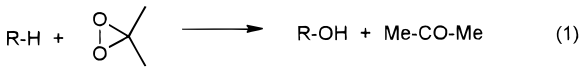
$CBrCl_3$ (mmol)	conversion (%)[b]	**1** (%)	**2** (%)	**3** (%)	**4** (%)	**5** (%)	**6** (%)
0.1	57	12.2	2.3	0.7	77.2	1.1	1.8
0.2	63	23.1	4.3	1.4	62.6	0.8	1.2
0.4	68	37.4	6.8	2.2	53.1	0.8	0.9
0.6	72	42.1	7.6	2.4	46.2	0.6	0.5
0.8	75	46.4	8.5	2.7	38.3	0.5	0.4
1.0	76	51.1	9.1	3.0	34.0	0.4	0.3
2.0	80	56.8	13.7	3.3	24.1	0.3	0.1

[a] **1** = 1-bromoadamantane, **2** = 2-bromoadamantane, **3** = 1-chloroadamantane, **4** = 1-adamantanol, **5** = 2-adamantanol, **6** = 2-adamantanone. [b] Conversion of adamantane based on DMD (4 mmol of adamantane are reacted with 1 mmol of DMD).

results, which, in our opinion, strongly support the radical character of several oxidations by DMD.

Results and Discussion

Oxidation of Alkanes. The oxidation of unactivated C−H bonds is a subject of great interest both from the theoretical and the applicative standpoint. A variety of oxidants and catalytic processes have been utilized.[6−10] As concerns the oxidation by DMD, the overall reaction eq 1 is very exothermic because the energies of the newly formed bonds are considerably higher than those of the broken ones.



The energy of the O−O bond in DMD is very low, due to ring strain: it has been evaluated[15] at about 10 kcal mol^{-1}. Despite the large exothermicity, the reaction is highly regio-, chemo-, and stereoselective.[1] These and other mechanistic features (kinetics, isotope effect) have induced most authors to exclude the intermediate formation of radicals. The high sensitivity to polar effects in the oxidation of alkanes by DMD and by aromatic peracids ($\rho = -2.76$ in the oxidation of substituted cumenes by DMD[5] and $\rho^* = -2.2$ in the oxidation of substituted alkanes by aromatic peracids[16]), in addition to a high degree of configurational retention, would support a concerted electrophilic mechanism for both oxidants (structures **2** and **3**). We have recently reported evidence pointing out that the oxidation of alkanes by aromatic peracids is a radical process and that the high regio-, chemo-, and stereoselectivity must be ascribed to enthalpic, polar, and cage effects.[11]

Our preliminary results,[3] which are now more completely developed and reported in detail, supporting a "radical oxygen rebound" mechanism[3a] in the oxidation of alkanes by DMD were based on the following reactions.

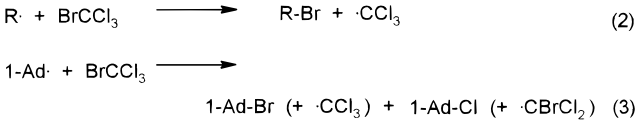
(a) When the oxidation of alkanes by DMD was carried out at room temperature in the presence of variable amounts of $CBrCl_3$, halogenation competes with oxidation of the alkane,[3a] the halogenation increasing with the concentration of $CBrCl_3$ (Tables 1 and 2). The fact that with cyclohexane and adamantane the halogenated compounds are cyclohexyl bromide and 1-bromo, 1-chloro-, and 2-bromoadamantane indicate beyond any doubt that

Table 2. Oxidation of Cyclohexane with DMD in the Presence of $CBrCl_3$[a]

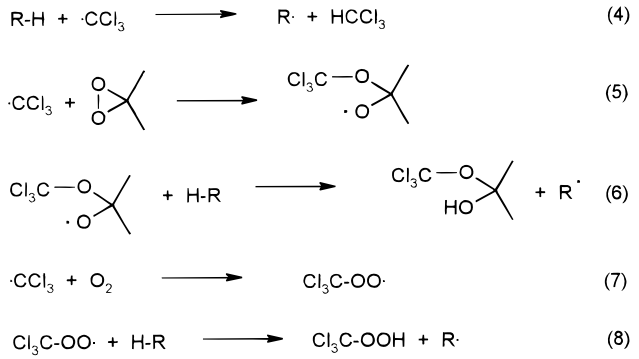
$CBrCl_3$ (mmol)	conversion (%)[b]	**7** (%)	**8** (%)	**9** (%)
0.1	30.3	35.1	24.4	40.6
0.2	32.1	47.7	23.2	29.1
0.4	46.8	58.4	20.3	21.3
0.6	52.2	65.6	18.8	15.6
0.8	58.3	71.5	16.3	12.2
1.0	63.2	79.9	13.1	7.0
2.0	65.4	89.1	7.7	3.2
4.0	70.7	94.7	5.2	traces

[a] **7** = cyclohexyl bromide, **8** = cyclohexanol, **9** = cyclohexanone. [b] Conversions based on DMD (cyclohexane 4 mmol, DMD 1 mmol)

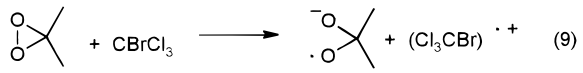
cyclohexyl and adamantyl radicals are involved in the halogenation: cyclohexyl and 2-adamantyl radicals only abstract bromine atoms (eq 2), whereas 1-adamantyl radical abstracts both bromine and chlorine atoms (eq 3).[16,17]



•CCl_3 or •$CBrCl_2$ can induce several radical chain processes[3a,18]



The fact that in the absence of DMD no reaction takes place under the same conditions clearly indicates that DMD induces the radical halogenation of alkanes. An explanation, recently suggested[19] for our results, involves an electron-transfer process between DMD and $CBrCl_3$ (eq 9).



This explanation is really surprising: the electron-transfer from a strongly electron-deficient substrate with high oxidation potential, such as $CBrCl_3$, to DMD appears extremely unlikely.

(b) When the oxidation of cyclohexane or adamantane by DMD was carried out in the presence of quinaldine or lepidine and CF_3COOH, quinaldine *N*-oxide and lepidine *N*-oxide were the main reaction products, alkane oxidation was significant, and small amounts of quino-

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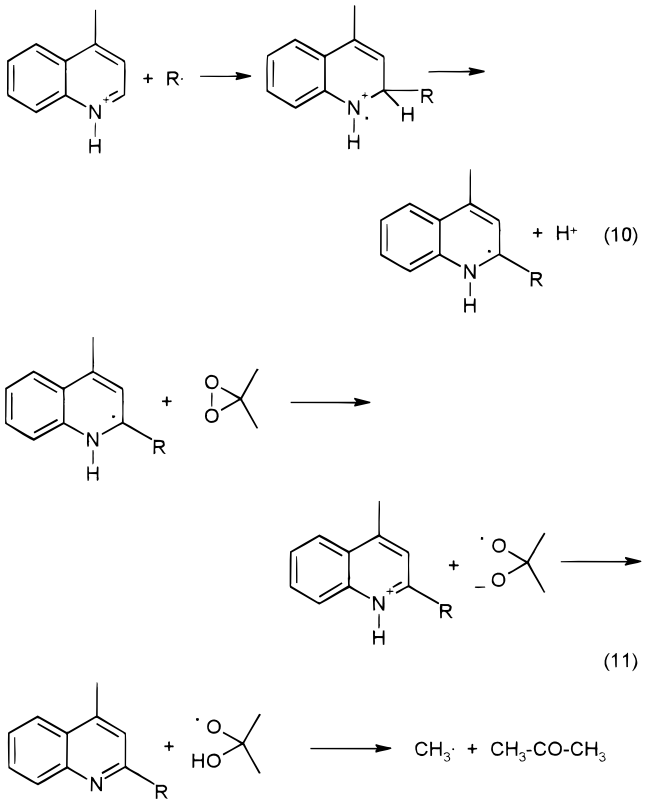
(19) Curci, R.; Dinoi, A.; Fusco, C.; Lillo, M. A. *Tetrahedron Lett.* **1996**, *37*, 249.

Table 3. Oxidation of Alkanes under Oxygen (Procedure A) or under Argon (Procedure B) Atmosphere

alkane (RH)	convn (%)[a]	ROH (%) + ketone (%)	ROCOMe (%)	proc
cyclohexane	34.4	cyclohexanol 2.7 cyclohexanone 72.3	traces	A
cyclohexane	18.7	cyclohexanol 3.1 cyclohexanone 53.6	35.3	B
cumene	41.1	ROH 91.7	traces	A
cumene	12.6	ROH 9.6	86.3	B
ethylbenzene	57	ROH 2.4 Ph-CO-Me 74.8	traces	A
ethylbenzene	18.2	ROH 2.2 PhCOMe 53.6	16.4	B
adamantane	63	1-AdOH 96.3 2-AdOH 1.7	traces	A
adamantane	38	1-AdOH 52.4 2-AdOH 0.8	1-MeCOOAd 37.0 2-MeCOOAd 8.2	B

[a] Conversion of the alkane.

lines, substituted in the 2- and 4-positions by methyl, cyclohexyl, and adamantyl groups, were also obtained.[3b] The only reasonable explanation for the formation of these compounds involves the reaction of cyclohexyl, adamantyl, or methyl radicals with protonated quinolines[20] (eqs 10 and 11).



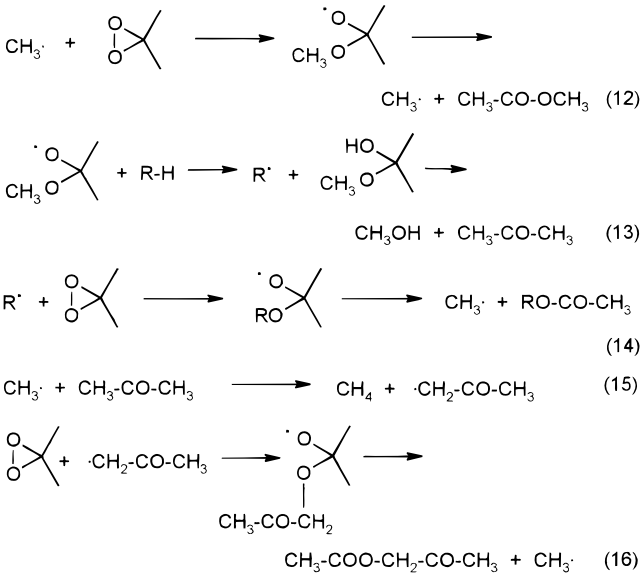
(c) The presence of oxygen has a dramatic influence on the oxidation of alkanes by DMD,[3c] as the results of Table 3 indicate. The reproducibility of these results is strictly related to a careful elimination of even the smallest traces of oxygen. The absence of oxygen has several consequences never before described in the numerous reports[1] on alkane oxidation by DMD:

(1) Relevant amounts of ROCOMe were formed in addition to ROH, which is formed in eq 1, whereas CH_4, MeOH, MeCOOMe, and $MeCOOCH_2COMe$ were all formed from DMD.

(2) The hydroxylation of the alkane is much more selective than its acetoxylation; thus, with adamantane the ratio 1-AdOH/2-AdOH is >50, whereas the ratio 1-AdOCOMe/2-AdOCOMe is about 4.

(3) The conversions of alkanes are significantly lower in the absence of oxygen.

The formation of CH_4, MeOH, MeCOOMe, and $MeCOOCH_2COMe$ in the absence of oxygen can be reasonably explained only by radical chains, which involve Me•, R•, and $•CH_2COMe$ radicals according to eqs 12−16.



We can evaluate a rate constant of 2.7×10^3 M^{-1} s^{-1} for eq 15 from the known absolute rate constant of hydrogen abstraction from EtCOEt[21] (7.4×10^4 M^{-1} s^{-1}) by Me• and from the relative rates of hydrogen abstraction MeCOMe:EtCOEt (1:27)[22] always by Me•. At low conversion of DMD it was therefore possible to approximately evaluate the relative rates of eqs 12 and 15 from the amounts of MeOH + MeCOOMe generated by the induced homolysis of DMD by Me• (eqs 12 and 13) and from the amount of $MeCOOCH_2COMe$ generated by hydrogen abstraction from acetone by Me• (eqs 15 and 16). Reaction 12 appears to be >500 times faster than reaction 15; thus, the induced homolysis of DMD by Me• is very fast, $>10^6$ M^{-1} s^{-1}. If we consider that the β-scission of alkoxyl radicals[23,24] (for cumyloxyl radical, rate constants ranging from 2.6×10^5 to 1.9×10^6 s^{-1} at 30 °C has been reported[24] for the β-scission in several solvents) and the hydrogen abstraction by alkoxyl radicals from C−H bonds are also fast processes (for cyclohexane a rate constant of 1.0×10^6 M^{-1} s^{-1} has been reported),[24] the kinetic length of the radical chain of eqs 12−16 must be rather high. This means that a large quantity of DMD is consumed by small amounts of chain-initiating radicals.

(20) Minisci, F. *Top. Curr. Chem.* **1976**, *62*, 1; Minisci, F. *Substituent Effects in Free-Radical Chemistry*; Viehe, H., Ed.; D. Reidel: Dordrecht, 1986; p 391. Minisci, F.; Fontana, F.; Vismara, E. *Heterocycles* **1989**, *28*, 489. Minisci, F.; Fontana, F.; Vismara, E. *J. Heterocycl. Chem.* **1990**, *27*, 79.

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(22) Singh, M.; Murray, R. W. *J. Org. Chem.* **1992**, *57*, 4263.

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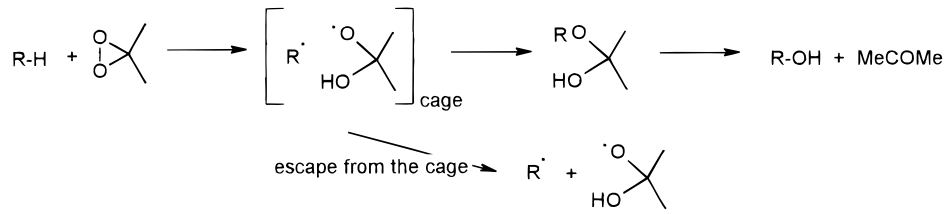
(24) Avila, D. V.; Brown, C. E.; Ingold, K. U.; Lusztyk, J. *J. Am. Chem. Soc.* **1993**, *115*, 466.

Scheme 1



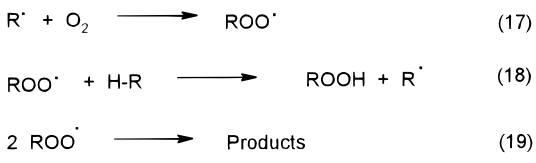
All these results (a−c) show beyond any doubt that radicals are involved in the oxidation of alkanes by DMD.

The crucial mechanistic problem concerns the question: is the oxidation of alkanes by DMD strictly related to the radical chains described by eqs 2−16 or are these radical reactions competitive chain processes independently initiated by DMD? In other words, either the initial reaction of the alkane with DMD leads to radicals, which on one hand determine the alkane oxidation and on the other hand initiate the radical chains of eqs 2−16, or there are two completely different independent mechanisms, a "concerted oxenoid oxygen insertion", which does not involve radicals, and the radical chains of eqs 2−16, induced by DMD and due to accidental impurities or to reactions such as eq 9, as has been recently suggested.[19]

Our interpretation involves an "induced homolysis" of DMD by the alkane[3c,d] with formation of a radical pair, whose coupling in the solvent cage leads to the oxidation products; radicals escaping from the cage can initiate the radical chains of eqs 2−16 (Scheme 1).

We have emphasized[3c] the fact that only a few radicals escape from the solvent cage, because the radical pair is necessarily generated in a singlet state and small amounts of air oxygen inhibit the radical chains; the kinetic lengths of these chains in the absence of oxygen are, however, high enough to allow a considerable amount of DMD to react.

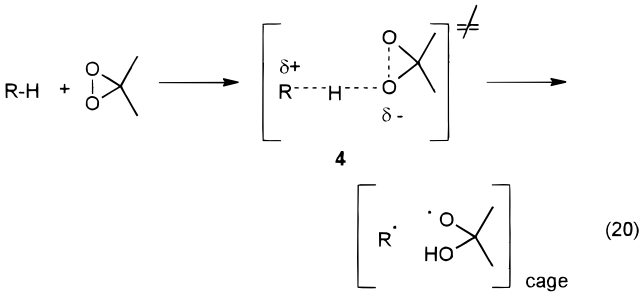
The inhibition by oxygen is due to the formation of peroxyl radicals[3c] (eq 17), which, under the reaction conditions, are unable to effectively sustain the chain, because the hydrogen abstraction from the alkane (eq 18) (10^{-3}−10^{-2} M^{-1} s^{-1}) is too slow at room temperature.[3c] The fate of peroxyl radicals is then a bimolecular self-reaction, as in classical autoxidation processes[25] (eq 19).



The high degree of configurational retention is due to the fast coupling of the singlet radical pair in the cage.

Adam and Curci[14,19] have repeatedly stated that we interpret the alkane oxidation by DMD by a *radical chain mechanism*, quoting ref 3c; *this is completely incorrect.* In ref 3c we clearly report that in the presence of air oxygen only the coupling of the radical pair in the cage takes place. In the absence of oxygen, radical chain processes occur, but they concern different reactions (eqs 2−16) and form different reaction products.

The old concept of molecule-induced homolysis was thoroughly developed by one of the fathers of radical chemistry, Walling,[26] in his works concerning the reactions of peroxides and alkyl hypochlorites with alkenes, alkynes, and electron-rich substrates, such as amines. As far as we know, the molecule-induced homolysis of peroxides by alkanes was never previously observed or suggested. We believe that this induced homolysis is reasonable on the basis of thermochemical evaluations: two bonds, R−H in the alkane and O−O in DMD, are broken and a strong O−H bond is formed; for tertiary C−H bonds the process is almost thermoneutral. With other peroxides, which have energies >30 kcal mol^{-1} for the O−O bonds, the molecule-induced homolysis is too endothermic to take place; the induction, on the opposite, is possible with alkenes, due to the much lower energy of the π bond. The transition state for the induced homolysis by alkanes is shown by structure **4** (eq 20).



This transition state does not involve a "concerted oxygen insertion", but it has a clear-cut radical character with some charge separation (as for the classical polar effect in radical reactions). This may well explain the high regio- and chemoselectivity: the marked discrimination among primary, secondary, and tertiary C−H bonds depends on the fact that hydrogen abstraction is largely endothermic in the first two cases; on the other hand, the high sensitivity to the electron availability of the C−H bond is related to the polar effect. The high regioselectivity in the hydroxylation of adamantane (1-Ad-OH/2-Ad-OH > 50) and the much lower selectivity in acetoxylation (1-Ad-OCOMe/2-Ad-OCOMe ∼ 4) clearly indicate that hydrogen abstraction from Ad-H takes place by two different mechanisms: the slow induced homolysis for the alcohol (Scheme 1) and mainly the fast eq 13 for the ester.

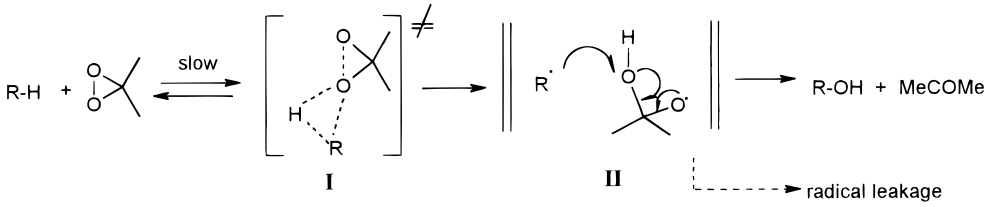
After the publication of our preliminary results, an attempt has been reported[14,19] to reconcile the "concerted" and radical mechanisms (Scheme 2).

The explanation given to Scheme 2 is, in our opinion, contradictory and ambiguous; the reaction is considered

(25) Walling, C. *Active Oxygen in Chemistry;* Foote, C. S., Valentine, J. S., Greenberg, A., Liebman, J. F., Eds.; Blackie Academic Professional: New York, 1995; p 24.

(26) Walling, C.; Chang, Y. W. *J. Am. Chem. Soc.* **1954**, *76*, 4878; Walling, C.; Heaton, L.; Tanner, D. D. *J. Am. Chem. Soc.* **1965**, *87*, 1715.

Scheme 2



"an essentially concerted oxenoid mechanism of insertion (**I**); in the rate-determining step, this should present no *distinct* radical nor carbenium ion character, but after the transition state some radical character develops (**II**)" [19]

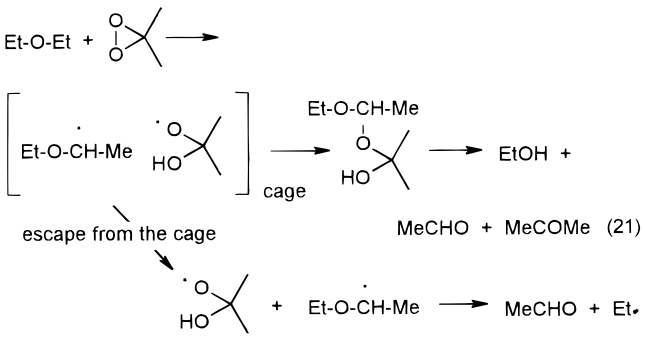
The contradiction concerns the fact that a "concerted mechanism of insertion" does not involve, by definition, any intermediate; moreover, a transition state with no charge separation cannot explain the high influence of polar effects. If **II** is a radical pair, we do not understand why it should have only some radical character (a radical is a well-defined species, characterized by an unpaired electron) and why the coupling of the radical pair should fail to occur, while a hydroxyl transfer takes place. If **II** is not a radical pair, it becomes to us a mysterious species, as one transition state cannot, by definition, give different reactions. Structure **II** would then give either hydroxyl transfer or a radical leakage, competitively. Yet, it is also stated that "the oxygen insertion into alkanes by DMD does not involve detectable radical pathways";[14] in this case we do not understand the meaning of "radical leakage". Besides, the collapse of the concerted transition state **I** into products is much more favorable on enthalpic grounds than would be its evolution to a radical pair. It appears to us that this attempt to reconcile concerted and radical mechanisms does not work, as the two mechanisms are alternative. To verify if the radical chains of eqs 12−16 are really initiated by radicals, escaped from the cage according to Scheme 1, and not by accidental initiation, we have carefully investigated the decomposition of DMD. We conducted several experiments, both under argon and under oxygen, in the presence as well as in the absence of adamantane, at room temperature (20 °C), by always using the same solution of DMD, to avoid the possibility that radical-chain-initiating impurities could affect the results.

In the absence of adamantane, DMD is not significantly decomposed after 6 h, either under argon or under oxygen. In the presence of adamantane under argon 76% of DMD reacts in 6 h and the reaction products are 1-adamantanol (27%), traces of 2-adamantanol (<1%), 1-acetoxyadamantane (18.8%), and 2-acetoxyadamantane (4.2%); the balance of the reacted DMD is completed by CH_4, MeOH, MeCOOMe, and $MeCOOCH_2COMe$. In the presence of adamantane under oxygen, 71% of DMD reacts in 6 h and the reaction product is mostly 1-adamantanol (>90%), with small amounts of 2-adamantanol and 1- and 2-acetoxyadamantane.

Since 1- and 2-acetoxyadamantane, CH_4, MeOH, MeCOOMe, and $MeCOOCH_2COMe$ (on the whole 65% of the reacted DMD) are certainly formed under argon by a radical mechanism (eqs 12−16), while in the absence of adamantane under the same conditions no reaction occurs, the only reasonable explanation of these results (Occam's razor) involves the induced homolysis of DMD by adamantane. The few radicals escaping the cage initiate the radical chains of eqs 12−16, which are broken by the presence of a small amount of oxygen.

Oxidation of Ethers and Alcohols. Dialkyl ethers are very easily oxidized by DMD in the α-position.[27] It has been reported that "the high selectivity for the observed α-functionalization speaks for a nonradical C−H insertion. In fact, also some β-attack would be expected in a classical pathway involving RO• radicals; for instance, approximately 13% attack at β-CH_2 was found for the reaction of THF with HO•".[27] This statement is really surprising, because it is well-known that oxygen-centered radicals selectively attack the α-position of alkyl ethers, with the exception of HO• radical, which is an extremely reactive and unselective species, mainly for enthalpic reasons. The facile α-autoxidation of ethers is notorious because of the production of hazardous peroxides.[28]

Again, when we carried out the oxidation of diethyl ether or of THF by DMD in the presence of protonated quinaldine, N-oxidation was the main reaction but small amounts of methyl, ethyl and α-tetrahydrofuranyl radicals were trapped by the heterocyclic ring. Methyl radical is generated from DMD by reactions similar to eqs 12,14, 16; α-tetrahydrofuranyl radical is originated by hydrogen abstraction from THF and ethyl radical comes from diethyl ether[29] according to eq 21.



Also in this case, when the reaction was performed under argon in the presence of diisopropyl ether or cyclohexanol, the main reaction products (CH_4, MeOH, MeCOOMe, and $MeCOOCH_2COMe$) came from the radical decomposition of DMD; if diethyl ketone was added to the reaction mixture, the α-acetoxy derivative (EtCO-CH(Me)OCOMe) was a significant reaction product (Et-COEt is 27 times more reactive than acetone toward methyl radical).[22] Since in the absence of diisopropyl ether or of cyclohexanol the same solution, under the same conditions, does not give decomposition of DMD,

(27) Curci, R.; D'Accolti, L.; Fiorentino, M.; Fusco, C.; Adam, W.; Gonzalez-Nunez, M. E.; Mello, R. *Tetrahedron Lett.* **1992**, *33*, 4225.
(28) ref 25 pag.29.
(29) Minisci, F.; Coppa, F.; Fontana, F.; Zhao, L. *Gazz. Chim. Ital.* **1993**, *123*, 613.

the reasonable conclusion is that diisopropyl ether and cyclohexanol induce the homolysis of DMD. Because of enthalpic and polar effects, ethers and alcohols induce the homolysis of DMD more effectively than do the corresponding alkanes; e.g. cyclohexanol is about 10^3 times more reactive than cyclohexane.[3a]

The radical decomposition of dioxiranes, induced by alkyl ethers, has also been recently reported by other authors,[30] although they did not suggest a mechanism to explain the formation of radicals; besides, their interpretations are not consistent with the reactivity of the involved species: for instance, the formation of the acetoxyl derivatives has been explained by cross-coupling between acetoxyl and alkyl radicals (eq 22).

$$R^{\cdot} + {}^{\cdot}OCOMe \longrightarrow R\text{-}OCOMe \qquad (22)$$

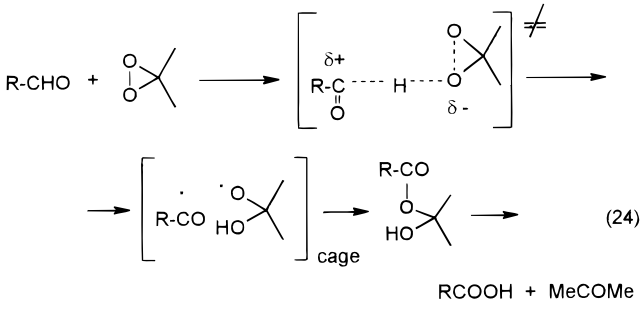
This cross-coupling, however, can be excluded by the fact that the Ingold−Fischer "persistent radical effect"[31] is not fulfilled (both radicals are transient) and, above all, by the high rate constant ($>10^9$ s^{-1}) of the unimolecular decarboxylation of the acetoxyl radical (eq 23)

$$MeCOO^{\cdot} \xrightarrow{k} Me^{\cdot} + CO_2 \qquad (23)$$
$$k > 10^9\ s^{-1}$$

The only reasonable mechanism for the formation of the acetoxyl derivative is the one depicted in eq 14.

The conclusion is that ethers and alcohols are oxidized by DMD through a mechanism which is identical with the one operating for alkanes, the only differences being the contribution of polar effects and the lower bond strength and the correspondingly lower activation energy for the reaction of the α-C−H bond in ethers and alcohols.

Oxidation of Aldehydes. The oxidation of acetaldehyde, pivalaldehyde, and phenylacetaldehyde by DMD in the presence of air oxygen mainly leads to the corresponding carboxylic acids with high selectivity. Polar and enthalpic factors suggested that the molecule-induced homolysis could be still easier in these cases (eq 24)



$$\text{RCOOH + MeCOMe} \qquad (24)$$

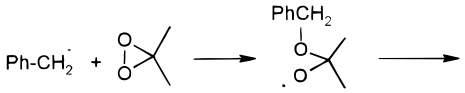
The coupling of the radical pair in the cage gives the carboxylic acid. The induced homolysis is more exothermic by 5−6 kcal mol^{-1} compared to tertiary C−H bonds in alkanes, due to the lower energy of the C−H bond in the aldehyde group. Protonated quinaldine and lepidine have been once again utilized in the oxidation of acetaldehyde and pivalaldehyde to intercept radicals outside the solvent cage. Acetic and pivalic acids were the main reaction products when the reaction was carried out in the presence of oxygen; lepidine *N*-oxide was formed in significant amount (7−10%), and minor amounts (1−4%) of 2,4-dimethyl-, 2-acetyl-4-methyl-, 2-pivaloyl-4-methyl-, and 2-*tert*-butyl-4-methylquinoline were also obtained. Thus methyl, pivaloyl and *tert*-butyl radicals are certainly involved in the oxidation. *tert*-Butyl radical clearly arises from the unimolecular decarbonylation of pivaloyl radical (eq 25).

$$Me_3C\text{-}\dot{C}{=}O \longrightarrow Me_3\dot{C} + CO \qquad (25)$$

A careful investigation has been carried out for the oxidation of phenylacetaldehyde by DMD, to recognize the origin of these radicals; again, the same solution of DMD in acetone has been utilized for all the experiments. In the presence of oxygen, phenylacetic acid was the only reaction product from the aldehyde (81% conversion of DMD, 75% yield of phenylacetic acid in 6 h at 20 °C); under the same conditions, in the absence of DMD, no substantial oxidation of phenylacetaldehyde occurs. Under argon atmosphere, at 20 °C for 6 h, DMD was converted for 78%, but the conversion of phenylacetaldehyde was only 6% (4% gave benzyl acetate and 2% phenylacetic acid); most of the DMD was converted into CH_4, MeOH, MeCOOMe, and $MeCOOCH_2COMe$. At 60 °C under argon the conversion of DMD was complete, but phenylacetaldehyde conversion only increased up to 16%, with formation of benzyl acetate (14%) and phenylacetic acid (2%). In the absence of phenylacetaldehyde at 20 °C under argon, no substantial decomposition of the same solution of DMD occurred. The only reasonable mechanism for the formation of benzyl acetate involves the fast decarbonylation[32] of the acyl radical outside the cage (eq 26)

$$Ph\text{-}CH_2\text{-}\dot{C}{=}O \xrightarrow{k} Ph\text{-}CH_2^{\cdot} + CO \qquad (26)$$
$$k = 0.5\text{-}1 \times 10^7\ s^{-1}$$

The benzyl radical induces the chain decomposition of DMD, giving benzyl acetate (eq 27)



$$PhCH_2\text{-}OCOMe + Me^{\cdot} \qquad (27)$$

These results indicate beyond any doubt that phenylacetaldehyde induces the radical decomposition of DMD under argon because only a small amount of phenylacetic acid is obtained, while all the reaction products come from the radical reaction of DMD.

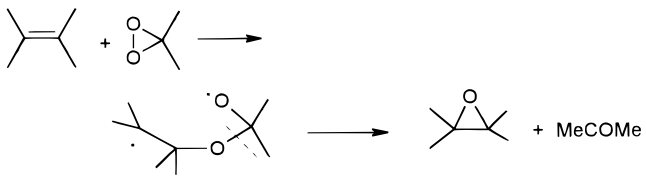
The presence of a small amount of air oxygen inhibits the radical chain processes, favoring the formation of phenylacetic acid, as in the oxidation of alkanes, ethers, and alcohols. Thus, the oxidation mechanism of all these classes of organic compounds by DMD is basically identical, due to the molecule-induced homolysis of DMD by C−H bonds of relatively low energy and high electron availability. The relevant fact is that the numerous authors who investigated the oxidations by DMD did not realize that the success of these reactions was strictly

(30) Ferrer, M.; Sanchez-Baeza, F.; Casas, J.; Messeguer, A. *Tetrahedron Lett.* **1994**, *35*, 2981.

(31) MacFaul, P. A.; Arends, I. W. C. E.; Ingold, K. U.; Wayner, D. D. M. *J. Chem. Soc. Perkin 2* **1997**, 135. Fischer, H. *J. Am. Chem. Soc.* **1986**, *108*, 3925. Bravo, A.; Bjørsvik, H. R.; Fontana, F.; Liguori, L.; Minisci, F. *J. Org. Chem.* **1997**, *62*, 3849.

(32) Lunazzi, L.; Ingold, K. U.; Scaiano, J. C. *J. Phys. Chem.* **1983**, *87*, 528.

Scheme 3



related to the presence of a small amount of air oxygen in the reaction medium.

Oxidation of Alkenes. The molecule-induced homolysis of peroxides and other electron-deficient reagents with weak bonds (e.g. O−Cl, O−Br) by alkenes has been thoroughly investigated.[26] The very weak peroxidic bond in DMD (about 10 kcal mol^{-1}) suggested that the induced homolysis should be much easier compared with common peroxides, i.e., more exothermic by at least 20 kcal mol^{-1}. Thus we considered the possibility that also the epoxidation of alkenes by DMD could be explained by the molecule-induced homolysis according to Scheme 3.

On the other hand, if an induced homolysis of DMD occurs with alkanes, ethers, alcohols, and aldehydes, the process should be extremely more favored with alkenes, due to the weak π bond and the high electron availability.

This hypothesis has been recently challenged:[14] "Mechanistically more relevant is the fact that, were a radical DMD epoxidation to apply, (Scheme 3), cycloadducts should be formed, since it is well established that a diradical intermediate of this type would preferentially cyclize rather than undergo fragmentation.[33] The cyclization would have essentially no activation energy, whereas as much as 10−15 kcal mol^{-1} would be required for the fragmentation, because a relatively strong C−O bond is broken and a strained product (epoxide) formed".[14] Now this thermochemical evaluation is *completely erroneous* and the report of ref 33 is *quite incorrect*. The authors clearly mistake the C−O bond energy of a molecule for that of the same bond in the β-position to a radical; this is an elementary concept in radical chemistry. Actually, the C−O bond, broken in Scheme 3, is an extremely weak bond (<20 kcal mol^{-1}) and the C−O bond formed (epoxide) is >60 kcal mol^{-1}. Thus the fragmentation of the diradical in Scheme 3, with formation of the epoxide and of acetone, is exothermic by at least 40 kcal mol^{-1}; this means, for a radical β-scission, no activation enthalpy.

Moreover, the cyclization of the diradical of Scheme 3 leading to the 1,3-dioxolane is, obviously, largely exothermic, but entropic factors would favor the fragmentation. Reference 33 only reports that the oxidation of fullerene-C_{60} by DMD leads to both the epoxide and the 1,3-dioxolane in a 1:1.5 ratio; the comments of the authors in ref 33 are "the determination of the mechanism of the formation of the epoxide and the dioxolane requires further studies". If we consider that small amounts of dioxolane were also formed during the epoxidation of simple alkenes, such as *cis*-3-hexene,[34] we believe that the results with fullerene[33] represent, on the opposite, a significant evidence of the induced homolysis also for epoxidation: the same diradical adduct of Scheme 3 would give cyclization in competition with fragmentation, because steric factors make the fragmentation less favorable in the case of fullerene diradical compared with simple alkenes. The fact that small amounts of 1,3-dioxolane were obtained in the epoxidation of *cis*-3-hexene also supports this interpretation because the cyclization is sterically more favorable for the cis than for the trans isomer.

An interesting point concerns the behavior of 1,1-diphenyl-2-vinylcyclopropane toward DMD;[14] the fact that the epoxide is the only reported reaction product would indicate that either an induced homolysis does not occur or the fragmentation of the diradical is faster than the cyclopropylcarbinyl rearrangement. Certainly the fragmentation of the diradical is more exothermic than the rearrangement, and this could explain both the lack of rearrangement and the high stereoselectivity. However, a question arises from the very high rate of fragmentation of the diradical: does it make any sense to distinguish between "induced homolysis" and "concerted oxygen insertion" with alkenes, considering the very short lifetime of the possible diradical in Scheme 3? We believe that the distinction still makes sense, even if the detection of the radical intermediate is quite a problem and the evidence can only be circumstantial. Actually, we consider the formation of 1,3-dioxolane, observed in some cases[33,34] in competition with the formation of the epoxide, as a significant, although indirect, proof of a radical mechanism. If the epoxidation mechanism is the same by DMD and by *m*-chloroperbenzoic acid (*m*-CPBA), namely an electrophilic concerted mechanism, we should expect, at least qualitatively, the same behavior with both reagents. To verify this aspect we have investigated the relative reactivities for the oxidation of cyclohexene and quinoline: cyclohexene epoxide and quinoline *N*-oxide were the only reaction products in separate experiments with both oxidants. However, in the competitive oxidation of equimolar amounts of cyclohexene and quinoline, only cyclohexene epoxide was formed by DMD, while with *m*-CPBA cyclohexene epoxide and quinoline *N*-oxide were formed in a 13:87 ratio, despite the reduced reactivity of quinoline, due to the broad extent of protonation by the peracid. Quinoline is oxidized by an electrophilic process and it appears unlikely that such a dramatic inversion of reactivity should occur if the epoxidation of cyclohexene by DMD would also take place by the same mechanism. This result, though, can be explained by assuming that *m*-CPBA acts as an electrophilic reagent toward both substrates, while DMD oxidizes cyclohexene through a fast induced homolysis and quinoline by a much slower electrophilic process.

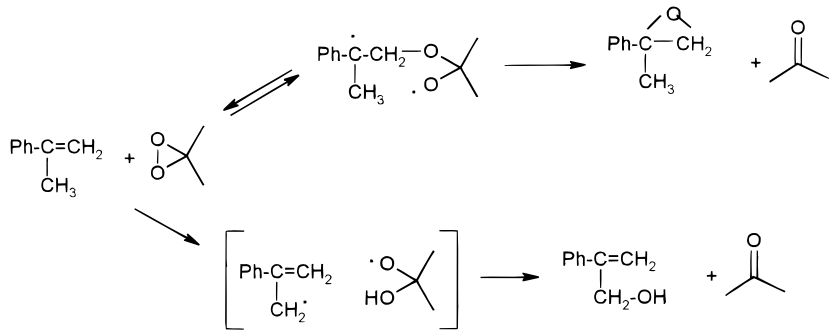
Further circumstantial evidence for a radical mechanism was provided by the results obtained with α-methylstyrene under nitrogen: the epoxide was obtained in 86% yield. The careful GC−MS analysis revealed the presence of minor amounts of 2-phenylpropenol and of 2-phenylpropenal. During the GC−MS analysis, part of the epoxide rearranges to α-phenylpropionaldehyde: this thermal rearrangement is well-known for styrene epoxide. We explain these results by a fast but reversible induced homolysis of DMD by the alkene, with which allylic hydrogen abstraction can compete to a small extent (Scheme 4).

It was recently reported[14] that the oxidation of α-methylstyrene by DMD exclusively gave the epoxide and that

(33) Elemes, Y.; Silverman, S. K.; Sheu, C.; Kao, M.; Foote, C. S.; Alvarez, M. M.; Whetten, R. L. *Angew. Chem., Int. Ed. Engl.* **1992**, *31*, 351.

(34) Murray, R. W.; Ramachandran, V. *Photochem. Photobiol.* **1979**, *30*, 187.

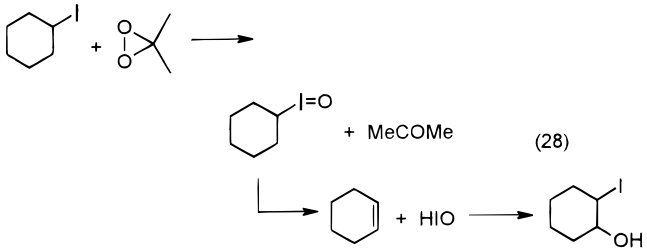
Scheme 4



attempts to detect minor amounts of 2-phenylpropenol and 2-phenylpropenal failed. Our preliminary results were reported without experimental details, which are now described in the Experimental section. On the other hand, our result is not unprecedented: the peroxyacid epoxidation of 4,4-dimethyl-D[5] steroids is straightforward,[35] while on the contrary, by using DMD the double bond is not attacked and only allylic oxidation occurs.

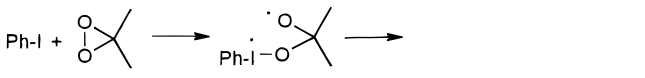
Oxidation of Iodo Derivatives. Aryl iodides smoothly react with DMD at 0−20 °C in acetone to give mainly ArIO or $ArIO_2$, depending on the amount of DMD; in the presence of AcOH the corresponding iodosoacetate, $ArI(OAc)_2$, is formed.[3d]

Cyclohexyl iodide mainly gives *trans*-2-iodocyclohexanol, while in the presence of AcOH *trans*-2-iodocyclohexyl acetate is formed;[3d] this is due to the instability of the alkyliodoso derivatives: they eliminate IOH, whose trans addition to cyclohexene gives the reaction products (eq 28)



(28)

The electrophilic oxidation of iodo derivatives by peroxides is well-documented.[36] We have, however, considered the possibility that a radical mechanism could be operating with DMD (eq 28), on the grounds that iodo derivatives appear to react very rapidly with oxygen- and carbon-centered radicals[37] (10^6−10^9 M^{-1} s^{-1} at rt).



Ph-I=O + MeCOMe (29)

The fragmentation of the diradical adduct is largely exothermic and it is almost certainly extremely fast; thus, also in this case, mechanistic evidence could only be circumstantial, as for the reaction with alkenes. Competitive reaction with iodobenzene and quinoline were carried out in acetone solution by DMD and by *m*-CPBA; both reagents oxidize the substrates to iodosobenzene and to quinoline *N*-oxide, respectively. However, in competitive experiments the reactivity is totally opposite, in that DMD exclusively oxidizes iodobenzene, while *m*-CPBA only attacks quinoline. The result is well-explained if we assume, as in the case of alkenes, that iodobenzene induces the homolysis of DMD according to eq 28.

Conclusions

The molecule-induced homolysis of DMD by alkanes, ethers, alcohols, and aldehydes, through hydrogen abstraction from relatively weak C−H bonds of high electron availability, is considered responsible for the oxidation of these classes of compounds. The oxidation occurs by cross-coupling of the radical pair in the solvent cage, while the few radicals escaping from the cage can initiate radical chains involving DMD. The effect of the presence of oxygen, $CBrCl_3$, or protonated quinoline supports this interpretation. It is suggested that an induced homolysis could occur also for the epoxidation of alkenes and for the oxidation of iodo derivatives, but in these cases the evidence is only circumstantial.

Experimental Section

General Methods. All the solvents and reagents were obtained from commercial sources and were used without further purification. The acetone solutions of DMD were prepared according to the literature procedure,[2] and the concentration of DMD was evaluated by iodometric titration. All the reaction products were commercially available or were previously prepared by different procedures in our laboratory, as was the case for the quinoline derivatives;[20] they were utilized for the qualitative identification (GC−MS) and the quantitative analysis (GC and NMR).

General Procedure for the Oxidation of Adamantane and Cyclohexane by DMD in the Presence of $CBrCl_3$. The hydrocarbon (4 mmol) was added at 20 °C to a solution of 1 mmol of DMD in 10.4 mL of acetone, prepared according to the known procedure,[2] and in which variable amounts of $CBrCl_3$ were dissolved, as reported in Tables 1 and 2. After 2 h, the solution was analyzed by GC and GC−MS. With adamantane six products were formed: 1-bromoadamantane (**1**), 2-bromoadamantane (**2**), 1-chloroadamantane (**3**), 1-adamantanol (**4**), 2-adamantanol (**5**), and 2-adamantanone (**6**). The products were identified by comparison with authentic commercial samples. The results are reported in Table 1. With cyclohexane the reaction products were cyclohexyl bromide (**7**), cyclohexanol (**8**), and cyclohexanone (**9**); the results are reported in Table 2.

In the absence of DMD under the same conditions no reaction took place.

(35) Marples, B. A.; Muxworthy, J. P.; Baggaley, K. H. *Tetrahedron Lett.* **1991**, *32*, 533.

(36) Davidson, R. I.; Kropp, P. J. *J. Org. Chem.* **1982**, *47*, 1904 and references therein.

(37) Minisci, F. In *Sulfur-Centered Reactive Intermediates in Chemistry and Biology*: Chatgilialoglu, C., Asmus, K. D., Eds.; NATO ASI Series A; Plenum Press: New York, 1990; Vol. 197, p 303 and references therein; Baciocchi, E.; d'Acunzo, F.; Galli, C.; Ioele, M. *J. Chem. Soc. Chem. Commun.* **1995**, 429.

Oxidation of Adamantane and Cyclohexane by DMD in the Presence of Protonated Quinaldine or Lepidine. The hydrocarbon (4 mmol), the heteroaromatic base (1 mmol), and CF_3COOH (1 mmol) were added to a solution of 1 mmol of DMD in 11.2 mL of acetone. The reaction was carried out at 0 °C for 8 h or at 50 °C for 1 h. The solution was analyzed by GC and GC−MS. With cyclohexane in the presence of quinaldine five products were formed, in the amounts reported in brackets respectively for 0 and 50 °C: cyclohexanol (4.3 and 6.4%), cyclohexanone (1.8 and 3.8%), quinaldine *N*-oxide (28.5 and 22.8%), 2,4-dimethylquinoline (3.6 and 2.4%), and 2-methyl-4-cyclohexylquinoline (0.6 and 2.2%). With adamantane in the presence of lepidine, lepidine *N*-oxide was the main reaction product at 50 °C (38.2%), 1-adamantanol was a significant reaction product (17.8%), and a small amount (1.8%) of 2-(1-adamantyl)-4-methylquinoline was also formed. The reaction products were identified by comparison with authentic commercial samples, with the exception of 4-cyclohexyl-2-methylquinoline and 2-(1-adamantyl)-4-methylquinoline, previously prepared by known procedures.[20]

Oxidation of Alkanes by DMD in the Presence and in the Absence of Oxygen. **General Procedure A.** A solution of 1 mmol of DMD in 10.8 mL of acetone was purged with oxygen for 10 min and then kept under oxygen for the duration of the experiment. Alkane (1 mmol) was added and the solution was kept at 20 °C for 8 h. The solution was directly analyzed by GC and GC−MS by using authentic samples for the identification and the quantitative analysis.

General Procedure B. The reaction was carried out as in method A, but the acetone solution was purged with argon and kept under argon for the duration of the experiments.

The results are reported in Table 3.

Complete Analysis of the Oxidation of Adamantane by DMD under Argon. The reaction was carried out as in method B with adamantane at 23 °C. After 6 h iodometric titration revealed that 76% of the DMD had reacted. GC analysis of the solution revealed the formation of 1-adamantanol (27%), traces of 2-adamantanol (<1%), 1-acetoxyadamantane (18.8%), 2-acetoxyadamantane (4.2%), and acetoxyacetone (7.2%).

Deuterated acetone (0.2 mL) was added to 0.8 mL of the reaction solution and the resulting solution was analyzed by NMR. The deuterated solvent was used to provide a deuterium signal for the instrument lock. For cost reasons the reaction was carried out in nondeuterated acetone, so the NMR spectrum is dominated by the solvent signal. Such a very intense peak precludes the detection of weak signals and thus it was suppressed using the presaturation technique: a long soft RF pulse (55−60 dB attenuation) was applied at the frequency of acetone (2.05 ppm) during the recycle delay followed by the acquisition of the spectrum. To avoid any saturation of the signals the spectra were acquired with a long recycle delay (10−15 s) between pulses. Due to the presaturation RF field, the signals near the region of 2 ppm are distorted and partially suppressed; thus, in this region they are difficult to assign and cannot be integrated.

We observe clean singlets due to the presence of methane (0.15 ppm, CH_4), methanol (3.29 ppm, CH_3), methyl acetate (3.58 ppm, OCH_3) and acetoxyacetone (4.70 ppm, $-OCH_2-$). All these products have been unequivocally identified by addition to the solution of traces of the authentic samples. The signals have been carefully integrated to determine the relative quantities of the products in solution. The integration was done after a very careful baseline correction of the spectrum and phase adjustment of the signals to minimize errors. The evaluation of methane, in that it is a gas, can be only qualitative. In this way we have determined, for methyl acetate, methanol, and acetoxyacetone, a ratio 3.2:0.8:1 and, considering that the yield of acetoxyacetone, determined by GC, was 7.2%, the yields of methanol and methyl acetate were 5.8% and 23.1%, respectively.

Oxidation of Diethyl Ether and THF by DMD in the Presence of Protonated Quinaldine. Diethyl ether (10 mmol), quinaldine (1 mmol), and CF_3COOH (1 mmol) were dissolved at 0 °C in a solution of 1 mmol of DMD in 11.2 mL of acetone. After 8 h the solution was analyzed by GC and GC−MS: quinaldine *N*-oxide was formed in 12% yield, 2,4-dimethylquinoline in 1.2% yield, and 2-methyl-4-ethylquinoline in 3.2% yield. Authentic samples were used for the identification and the quantitative analysis. Iodometric titration revealed that 79% of DMD had reacted, leading mainly to ethanol, acetaldehyde, and acetic acid (a quantitative evaluation was not carried out) as previously reported.[30]

Similarly, THF gave 23% of quinaldine *N*-oxide, 3.2% of 2,4-dimethylquinoline, and 2.8% of 4-(a-tetrahydrofuranyl)-2-methylquinoline.

Induced Homolysis of DMD by Diisopropyl Ether under Argon. A solution of 1 mmol of DMD and 4 mmol of diisopropyl ether in 11 mL of acetone was purged with argon for 10 min and then kept under argon for 6 h at 22 °C. Iodometric titration revealed that 83% of DMD had reacted; NMR analysis of the acetone solution, carried out as above-described, has shown the presence of CH_4, CH_3COOCH_3 (38.4% based on DMD), CH_3OH (12.1%), and acetoxyacetone (11.8%). The same experiment, carried out in the presence of diethyl ketone (2 mL), gave 9.6% of α-acetoxydiethyl ketone and 2.1% of acetoxyacetone.

In the absence of diisopropyl ether under the same conditions, no substantial decomposition of DMD occurred.

Oxidation of Cyclohexanol by DMD under Argon and under Oxygen. **Method A.** The reaction was carried out under argon as for diisopropyl ether. GC and NMR analyses revealed the formation of cyclohexanone (45% based on DMD), $CH_3CO-OCH_3$ (27.2%), CH_3OH (13.5%), acetoxyacetone (12.1%), and CH_4.

Method B. As in method A under oxygen, cyclohexanone was obtained in 87% yield.

Oxidation of Acetaldehyde and Pivalaldehyde by DMD in the Presence of Protonated Quinaldine or Lepidine. Method A. A 10 mmol portion of acetaldehyde, 1 mmol of quinaldine, and 1 mmol of CF_3COOH were dissolved at 0 °C in a solution of 1 mmol of DMD in 10.8 mL of acetone. After 8 h the solution was analyzed by GC and GC−MS: acetic acid was obtained in 77% yield, quinaldine *N*-oxide in 7% yield, 2,4-dimethylquinoline in 4.1% yield, and 2-methyl-4-acetylquinoline in 4.2% yield.

Method B. As in method A but using pivalaldehyde and lepidine instead of acetaldehyde and quinaldine, lepidine *N*-oxide (60%) and pivalic acid (26%) were the main reaction products, but small amounts of 4-methyl-2-*tert*-butylquinoline (0.4%) and 2-pivaloyl-4-methylquinoline (1.1%) were also determined.

Oxidation of Phenylacetaldehyde by DMD under Oxygen and under Argon. **Method A.** A 1 mmol sample of phenylacetaldehyde was dissolved at 20 °C in a solution of 1 mmol of DMD in 11.4 mL of acetone under an oxygen atmosphere. After 6 h, 76% conversion of phenylacetaldehyde was observed, with formation of phenylacetic acid in 98% selectivity.

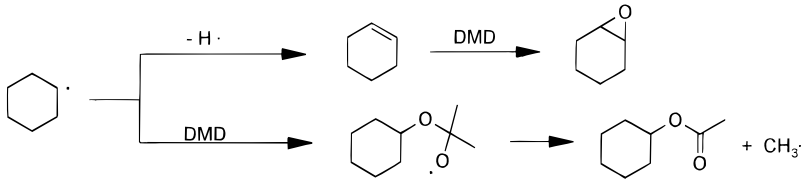
Method B. The reaction was carried out under argon as in method A. Only 6% of phenylacetaldehyde was converted, with 67% selectivity in benzyl acetate and 33% in phenylacetic acid; CH_3COOCH_3 was the main reaction product (42%), with minor amounts of CH_3OH (9.1%), acetoxyacetone (8.4%), and CH_4. At 60 °C the conversion of phenylacetaldehyde increases to 16% with 87% selectivity in benzyl acetate and 13% in phenylacetic acid.

Competitive Oxidation of Cyclohexene and Quinoline by DMD and *m*-CPBA. **By DMD**. A 4 mmol portion of cyclohexene and 4 mmol of quinoline were dissolved in a solution of DMD (1 mmol) in 10.5 mL of acetone at 18 °C. After 4 h, GC analysis only revealed the formation of cyclohexene epoxide, without traces of quinoline *N*-oxide.

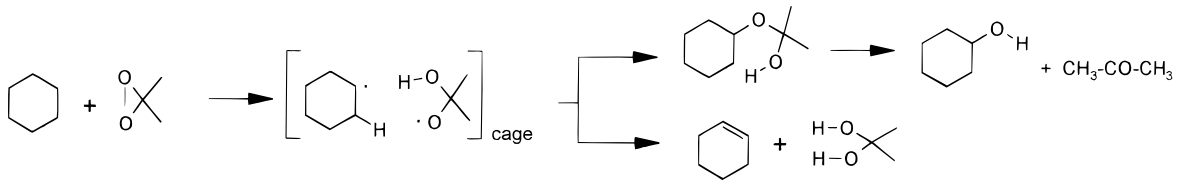
By *m*-CPBA. A 4 mmol portion of cyclohexene and 4 mmol of quinoline were dissolved in a solution of DMD (1 mmol) in 10.5 mL of acetone at 18 °C. After 4 h, GC analysis revealed the formation of 13% of cyclohexene epoxide and 87% of quinoline *N*-oxide.

Oxidation of α- and *β*-Methylstyrene by DMD. α-Methylstyrene. A 2 mmol sample of α-methylstyrene was dis-

Scheme 5



Scheme 6



solved at 20 °C in a solution of DMD (1 mmol) in 11 mL of acetone under nitrogen. After 6 h the GC analysis revealed the presence of 86% of the epoxide and minor amounts of byproducts. Careful GC−MS analysis revealed the presence of small amounts of 2-phenylpropenol (6%) and 2-phenylpropenal (5%); the compounds were identified by comparison with MS of authentic samples. During the GC−MS analysis, 51% of the epoxide rearranges to α-phenylpropionaldehyde. The analyses were performed on a GLC−MS Finnigan TSQ70 instrument, using a Varian 3700 gas chromatograph, equipped with a SBP-1 fused silica column (30 m × 0.2 mm i.d., 0.2 mm film thickness) and helium as carrier gas. An analytical experiment with pure α-methylstyrene epoxide has verified its partial rearrangement to α-phenylpropionaldehyde.

***β*-Methylstyrene.** Under the same conditions, *β*-methylstyrene substantially gave only the epoxide, with a selectivity >98%.

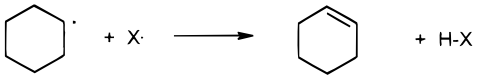
Competitive Oxidation of Iodobenzene and Quinoline by DMD and *m*-CPBA. (A) By DMD. A 4 mmol portion of iodobenzene and 4 mmol of quinoline were dissolved in a solution of DMD (1 mmol) in 10.5 mL of acetone at 22 °C. After 4 h, GC, GC−MS, and NMR analyses only revealed the presence of iodosobenzene, without traces of quinoline *N*-oxide.

(B) By *m*-CPBA. The reaction was carried out as in method A with *m*-CPBA instead of DMD. The analyses revealed only the presence of quinoline *N*-oxide, without traces of iodosobenzene.

Note Added in Proof. An interesting paper[38] concerning the mechanism of the oxidation of alkanes by DMD was published after the submission of this paper.

The oxidation of cyclohexane and perdeuteriocyclohexane was carried out by DMD in the absence of oxygen in order to measure the kinetic isotope effect.[38] In addition to cyclohexanone and cyclohexyl acetate, already reported for the first time in our preliminary paper,[3c] a considerable amount (ca. 10% of the reaction products) of cyclohexene epoxide was obtained. We have verified that a byproduct in the oxidation of cyclohexane, which we had not previously[3c] identified in our experiments, is actually cyclohexene epoxide. To explain their results, Asensio and co-workers[38] suggest two competitive mechanisms: (i) an electrophilic oxygen insertion for the formation of cyclohexanone (Structure 2 in our paper) and (ii) a radical mechanism, in which cyclohexyl radical is formed and then evolves, following two competitive paths, leading to cyclohexyl acetate and cyclohexene epoxide respectively (Scheme 5).

The mechanism for the formation of cyclohexyl acetate is identical with the one previously reported by us[3c] (eq 14), but the mechanism for cyclohexene formation has no kinetic basis: certainly, cyclohexyl radical cannot spontaneously lose a hydrogen atom to yield cyclohexene (we do not believe that this was what the authors[38] meant in reporting Scheme 5), but it could react with another intermediate radical, X•, including the bimolecular self-reaction, to give cyclohexene (eq 30)



(30)

X = Me, cyclohexyl, alkoxyl

Reaction 30, however, cannot take place to a significant extent outside the solvent cage, for obvious kinetic reasons. All the possible X• radicals are transient and the steady-state concentration of cyclohexyl radical can only be very low, due to the high rate constants for the reaction of alkyl radicals with DMD[39] (for Me•, eq 12, we have evaluated a rate constant $>10^6$ M^{-1} s^{-1}) and with acetone, used as solvent (for Me•, eq 15, we have evaluated a rate constant $>10^3$ M^{-1} s^{-1}). The only reasonable explanation for cyclohexene formation is, in our opinion, the competition of the radical pair in the cage between coupling and disproportionation (Scheme 6).

This kind of competition in bimolecular reactions between two radicals is well-known in radical chemistry.

The kinetic isotope effect reported by ref 38 is in full agreement with this explanation: the higher isotopic effect was observed with cyclohexanone (in this case hydrogen abstraction takes place by the slow induced homolysis, Scheme 6), while the lower isotopic effect occurred with cyclohexyl acetate, in which hydrogen abstraction from cyclohexane mainly takes place by the fast eq 13; cyclohexene epoxide formation shows an intermediate value of the isotopic effect, since the first hydrogen abstraction is slow and the second is extremely fast (Scheme 6). This is also in full agreement with the regioselectivity of adamantane oxidation, discussed in this paper: the hydroxylation is highly selective, while the acetoxylation is much less so. In the gas phase the oxidation of cyclohexane by DMD is more complex:[38] only very low conversion (2%) was achieved, cyclohexene epoxide and cyclohexyl acetate were not detected and the isotope effect for cyclohexanone formation is much lower. Moreover, 1,1,3-trimethylcyclohexane, derived from methyl radical, was formed in significant amounts. Clearly the mechanism in the gas phase is quite different.

Supporting Information Available: GC−MS analysis, MS of 2-phenylpropenol and 2-phenylpropenal from the reaction of α-methylstyrene with DMD, and NMR spectra before and after the reaction of adamantane with DMD, acquired by using the presaturation technique (5 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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(38) Asensio, G.; Mello, R.; Gonzalez-Nuñez, M. E.; Boix, C.; Royo, J. *Tetrahedron Lett.* **1997**, *38*, 2373.

(39) A reviewer suggested that the rate of eq 14 could be close to diffusion-controlled limit; we agree and thank the reviewer for this suggestion.