Pergamon

Tetrahedron Letters, Vol. 37, No. 2, pp. 249-252, 1996
Copyright © 1995 Elsevier Science Ltd
Printed in Great Britain. All rights reserved
0040-4039/96 $15.00 + 0.00

0040-4039(95)02140-X

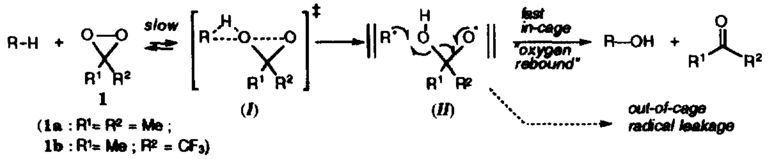
On the Triggering of Free Radical Reactivity of Dimethyldioxirane

Ruggero Curci,* Anna Dinoi,† Caterina Fusco, Maria A. Lillo

Centro CNR "M.I.S.O.", Dipartimento di Chimica, Università di Bari, via Amendola 173, I-70126 Bari, Italy

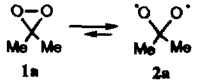
Abstract: Performing the reaction in the presence of CCl_3Br, and/or in inert gas atmosphere, dramatically changes the reaction kinetics, rate-law and product distribution of adamantane oxyfunctionalization by dimethyldioxirane (**1a**). The kinetics of decomposition of the dioxirane is also markedly influenced by the addition of CCl_3Br and by depletion of O_2 gas. The data suggest that these conditions can trigger dioxirane radical reactions; these are widely different from the straightforward, highly selective concerted *O*-insertion into C-H bonds which would take place in the absence of CCl_3Br and of conditions inducing radical reactivity.

The efficient oxyfunctionalization of "unactivated" C-H bonds of alkanes under extremely mild conditions[1,2] undoubtedly counts to date among the highlights of the chemistry of dioxiranes (**1**).[3] In these reactions methyl(trifluoromethyl)dioxirane (**1b**)[1] appears better suited than dimethyldioxirane (**1a**), leading to higher yields and much faster conversions with no loss of selectivity.[3]

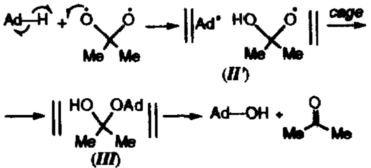


(1)

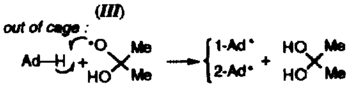
For the oxyfunctionalization of alkanes by the powerful dioxirane (**1b**), we have reported kinetics, H/D isotope effects, selectivity, and stereochemical evidence,[1] which strongly suggest an essentially concerted "oxenoid" mechanism of insertion; in the rate determining step, this should present no *distinct* radical, nor carbenium ion character (eq 1). A t.s. involving electrophilic attack by the dioxirane at the carbon of the hydrocarbon C-H bond has received support by theoretical calculations.[3] However, we pointed out the likelihood that *after the t.s. of the slow step* (I) — alternative to direct collapse into products — some radical character develops.[1a,c] Actually, pursuing an attractive analogy between dioxirane oxidation and metalloporphyrin hydrocarbon oxygenations,[4] we envisaged that the formation of the initial alcohol product could be mediated by caged radical-pairs (II);[1a,d] then, in-cage oxidation ("oxygen rebound")[4] would lead to products (eq 1).



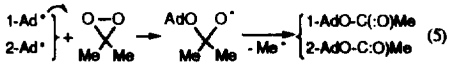
(2)



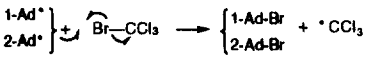
(3)



(4)



(5)



(6)

Quite recently, Minisci *et al.* have studied the oxidation of adamantane by dimethyldioxirane (**1a**) in the presence of CCl_3Br, and concluded that free radicals are involved.[5] The essential features of their mechanism are shown in eq.s 2 and 3-6.

Of course, similar to eq 5, radical attack at the dioxirane (giving rise to radical chain decomposition) had been previously well documented by us,[6a] and by Murray and Singh.[6b] One piece of evidence produced by the Minisci's group concerned the use of added CCl_3Br for trapping adamantyl radicals that are freely diffusing from radical-pair (II'), or else are formed in distinct out-of-cage processes (e.g., eq 4 and 6). This led Minisci to rule out[5b] the mechanism in eq 1.

Faced with this dilemma, we undertook a kinetic study of adamantane oxidation by dimethyldioxirane (**1a**), both in the presence and in the absence of added CCl_3Br.[7a] Kinetic experiments were performed following by iodometry the decay of dioxirane concentration c_D (i.e., [DMDO], in Table 1) with time according to a technique already described.[1]

---

† In partial fulfillment of the requirements for the Ph.D. Degree.

Table 1. Representative kinetic constants for adamantane (AdH) oxidation by dimethyldioxirane and for dioxirane decomposition, both in the absence and in the presence of bromotrichloromethane in acetone at 20.0 °C. [a]

Entry #	10^2 [DMDO]$_0$ (M)	10^2 [AdH]$_0$ (M)	10^2 [CCl$_3$Br]$_0$ (M)	Atmo-sphere	$10^6 R_0$ [b] (M s^{-1})	$10^4 k_1$ (s^{-1})	$10^2 k_2$ (M^{-1}s^{-1})
1	4.80	5.77	—	air	7.95	—	0.309
2	0.601	0.698	—	air	0.144	—	0.283
3	0.601	0.698	—	air	0.145	—	0.288
4	0.508	10.9	—	air	1.30	3.21	0.294 [c]
5	0.504	10.9	—	air	1.28	3.23	0.296 [c]
6	0.504	10.9	—	N_2	1.30	3.59	0.330 [c]
7	4.70	6.01	—	N_2	9.20	—	—
8	5.00	6.00	6.00	air	20.3	—	—
9	0.520	0.600	1.95	air	0.260	—	—
10	0.500	0.602	0.600	air	0.288	—	—
11	0.504	0.600	0.600	N_2	0.456	—	—
12	2.13	—	—	air	0.122	0.062	—
13	2.06	—	1.00	air	0.567	—	—
14	1.98	—	1.02	N_2	0.744	—	—

[a] Most data are averages (± 5%) from duplicate runs. [b] Initial rates, estimated as slopes in plots of dioxirane concentration vs. time, based on the initial 5-15% reaction. [c] Estimated as $k_2 = (k_1/[\mathrm{AdH}]_0$; k_1 values were obtained from pseudo-first order kinetic plots.

Reaction conditions and representative data are given in Table 1 and Figure 1. These show that, in the absence of added CCl_3Br, the kinetics obey a clean overall second-order rate-law (order one each in dioxirane and adamantane); integrated second-order rate law plots were found to be linear to over 80% reaction (Figure 1), yielding reproducible k_2 values (Table 1, entry 1-3). In runs performed under pseudo-first order conditions, plots of ln c_D vs. time (also linear to over 80% reaction) allowed to estimate k_1, and from these consistent k_2 values (entry 4 and 5).

Product studies (Table 2) showed that under "normal" conditions (i.e., under air, protection from light,[1a,6] exclusion of trace metal ions,[1a] etc.) formation of 1-AdOAc (eq 5) is just trifling (ca. 1.5%); it is likely that this reflects the tiny amount of Ad• radicals escaping out of cage *II* (eq 1 and 4). It should also be noted that in our hands reaction times are apparently much faster than those monitored by Minisci; for instance, we find that 52% substrate is consumed during 2 h and 72% in ca. 7.6 h (Table 2, entry 2), while Minisci *et al.* — under practically identical conditions — report[5b] 47% AdH conversion only after 72 h! This is inexplicable unless in the latter case factors that trigger competitive dioxirane decomposition (see below) were not rigorously excluded.

The much lower rate apart, the regular kinetic behavior above parallels that already recorded for the oxyfunctionalization of several hydrocarbons (including adamantane) by the more powerful dioxirane **1b**.[1a,7b] Actually, for the reaction of simple alkanes and cycloalkanes with dioxiranes, the kinetics were found to obey a clean overall second-order rate-law (order one each in dioxirane and substrate) in almost every case that they were studied.[1,2] The observed second-order rate law suggests that the t.s. of the rate-determining step must contain both reagents. Therefore, *any mechanism involving ring-opening of the dioxirane to a dioxyl biradical* **2** *as the rate-determining step (eq 2)* [5] *is untenable*. Indeed, if this were the case, the kinetic order in adamantane substrate would have been zero. Notice that, if the preliminary equilibrium formation of biradical **2** (eq 2) is not rate-determining, the process represented by eq.s 2 and 3 becomes identical with that sketched in eq 1. Then, Occam's razor would demand that one stays with the latter simpler mechanism until discrete evidence is found for the intermediacy of the bisoxyl diradical **2**. Thus, it is unlikely that the chain mechanism in eq.s 2-6 applies to alkane oxidation by dioxiranes under air blanket and *in the absence* of bromotrichloromethane.

We find that a more complex kinetic behavior obtains when the reaction of dioxirane **1a** with AdH is run in the presence of CCl_3Br; indeed, the smooth decay of dioxirane concentration with time is changed into a stepwise c_D loss characterized by an abrupt increase in slope (Figure 1, curve B). Also, there is a significant change in R_0 depending on CCl_3Br concentration (e.g., compare entry 1 with 8, and entry 2 with 9 and 10). A similar c_D vs. time profile is observed when the reaction is run in the absence of the bromide but in solvent purged with N_2 (entry 7), except that the sudden increase in slope occurs much earlier (3-4 min).

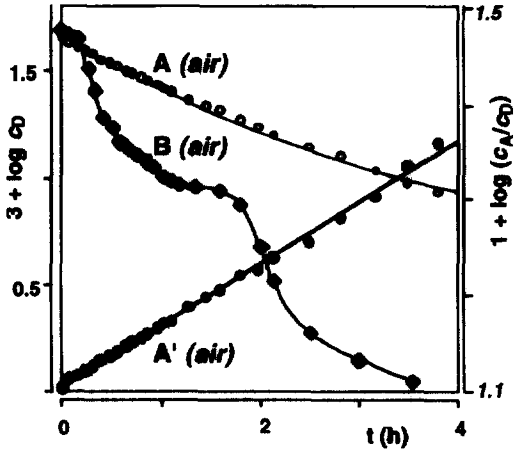


Figure 1. Decay of dioxirane **1a** concentration (c_D) with time in the absence and in the presence of CCl_3Br (curve **A** and **B**, respectively, left axis), and integrated second-order rate law plot for the reaction of dioxirane with adamantane (concentration c_A)(line **A'**, right axis), in acetone at 20.0 °C.

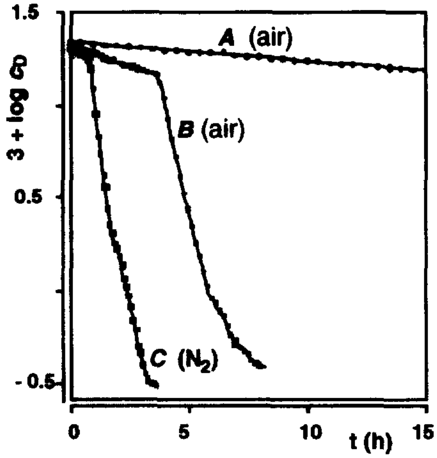
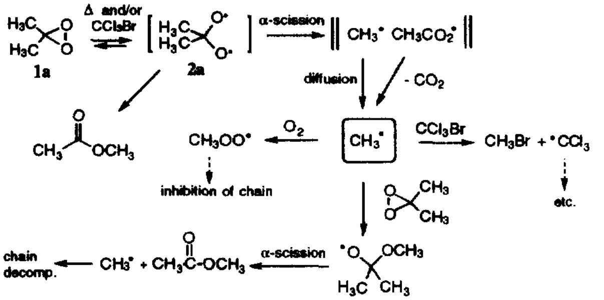


Figure 2. Dioxirane **1a** decomposition in acetone at 20.0 °C. **A**: in the absence of CCl_3Br; **B**: in the presence of equimolar CCl_3Br; **C**: in the presence of equimolar CCl_3Br, solvent purged with dry N_2. Refer to entries 12-14, Table 1.

As a whole, the kinetic data are indicative of a composite rate law of the kind $R = k_2[\mathrm{AdH}][\mathrm{DMDO}] + k_{\mathrm{rad}}[\mathrm{AdH}]^m[\mathrm{DMDO}]^n[\mathrm{CCl_3Br}]^x$,[8] or $R = k_2[\mathrm{AdH}][\mathrm{DMDO}] + k_{\mathrm{rad}}[\mathrm{AdH}]^y[\mathrm{DMDO}]^z$ (under N_2, in the absence of the bromide). In both cases, the second term would soon prevail over the first with O_2 depletion and/or with sizable CCl_3Br concentration. This suggests that the side-reaction represented by the second term is radical in character; this notion is reinforced by the remarkable change in the nature and distribution of products occurring in the presence of CCl_3Br (Table 2). It is worthy of notice that, when CCl_3Br was present, products that witness the dioxirane radical decomposition[6] were also detected. The possibility exists that added CCl_3Br serves not only in trapping freely diffusing radicals (cf., eq 6), but it also participates to the primary process by inducing the radical reactivity of the dioxirane.

Scheme 1



This notion is supported by preliminary kinetic data concerning DMDO decomposition. These were taken according to a spectrophotometric technique; the decay of dioxirane absorbance at 334 nm (ε 11.5) with time was monitored. Representative data are shown in Table 1 and Figure 2. In agreement with literature,[1,6] we find that — in the *absence* of CCl_3Br — dioxirane decomposition can be quite slow.[9,10] Under the conditions adopted, typically In c_D or $\ln(A_t - A_\infty)$ vs. time plots are linear to over 50% dioxirane decomposition, yielding a first-order constant of $6.2 \times 10^{-6}\ s^{-1}$ (Table 1, entry 12).[9] Inspection of data in Table 1 and Figure 1 reveals that addition of CCl_3Br (and depletion of dissolved oxygen) dramatically enhances dioxirane decomposition. Then, the profile of peroxide decay (Figure 2) becomes reminiscent of other oxygen-consuming radical reactions.[11] The GC/MS analysis of reaction products showed, besides the ester $CH_3CO_2CH_3$ in large amount, and along with small amounts of CH_3CO_2H and acetoxy acetone $CH_3C(:O)\text{-}OCH_2C(:O)CH_3$ (the expected products of dioxirane thermal decomposition),[6b] also detectable amounts of CH_3Br, $CHCl_3$, CH_3OH, as well as $ClCH_2C(:O)CH_3$.

To account for these facts, a suitable modification of the process established[6] for the thermal chain-decomposition of dioxiranes is sketched in Scheme 1. Of course, here a key point consists in unraveling the exact nature of the primary interaction between the dioxirane and the bromide that triggers formation of the biradical **2a**. Experiments still in progress are aimed to shed light into this aspect. As a working hypothesis, one might envisage that the bromide (similar to other more effective donors)[12] becomes involved in equilibrium one-electron transfer with the dioxirane, yielding pairs such as $|(CCl_3Br)^{\dot{+}}\ (^-O\text{-}CMe_2\text{-}O^\cdot)|$; from this, back electron transfer[13] would give rise to biradical **2a**.

Table 2. Typical product distributions for adamantane oxidation by dioxirane **1a** in the absence and in the presence of bromotrichlorometane in acetone a 20.0 °C.

Entry #	$[DMDO]_o$ (M)	$[AdH]_o$ (M)	$[CCl_3Br]_o$ (M)	AdH Conversion (%)[a]	Product Distribution (%) [b]
1	0.051	0.060	0.060	38.[c]	1-Ad-OH*(33)*; 1-AdBr *(42.3)*; 1-AdCl *(9.2)*; 2-AdBr *(10.5)*; 2-AdCl *(2.5)*; 2-AdOH *(2.0)*; Ad=O *(< 0.5)* [d]
2	0.051	0.060	—	72.[e]	1-AdOH *(91.5)*; 1,3-Ad$(OH)_2$ *(4.5)* [f]

[a] Reactions run in stoppered flasks under air blanket; adamantane conversion is referred to stoicheiometric amount of dioxirane (limiting reagent); it was determined (± 2%) by GC (VOCOL, 60m × 0.53mm ID, 3.0 mm film thickness) by using HT70 (a perfluoro polyether) as internal standard. [b] Products were identified by GS/MS (Hewlett-Packard mod. 5970, EI 70 eV, and mod. 5890 gas chromatograph; HP1 cross-linked methyl silicone, 25m × 0.2mm ID, 0.33mm film thickness column) upon comparison of *m/z* of M^+ and fingerprint fragmentation pattern with that of authentic samples. [c] Reaction time ca.3.5 h; during this time dioxirane concentration decay was ca. 58% and CCl_3Br ca. 22%. [d] By using GC/MS (GC column cf.note *a*; FISONS AutoSpecE, EI 70 eV) along with methyl acetate, sizable amounts of CH_3OH, $ClCH_2$-CO-CH_3, CH_3Br, and $CHCl_3$ could also be revealed. [e] Reaction time 7.6 h. [f] The diol likely derives from further selective bridgehead oxidation of product 1-AdOH (ref. 1b). Also detected were small amounts of 2-AdOH (1%), Ad=O (1.5%), and of 1-AdOAc (1.5%). The latter likely arise from minor leakage of Ad• out of cage (*II*) (eq 1).

However, subsequent or parallel with the formation of the said caged radical pairs, one might even envisage that some CCl_3Br oxidation to CCl_3BrO occurs; this would quickly generate $CCl_3^•$ and $BrO^•$ radicals, which could then partecipate to the radical-chain decomposition of the dioxirane.

In summary, we believe that existing literature and data presented herein corroborate the conclusion that alkane oxyfunctionalization by dioxiranes — *in the absence of conditions and/or reaction partners which promote radical reactivity* — is still best represented by the process in eq 1. While some radical character (and products thereof) might develop *after* the rate determining step, the latter should have mainly the characteristics of a rather concerted "oxenoid" *O*-insertion.

It should be noted that there is nothing *magical*[5a] in the term "oxenoid"; in fact, in its original formulation,[14] this simply refers to the net stoicheiometry (*not to mechanism*) of a reaction in which an electrophilic oxygen donor yields *O*-atom insertion into a given substrate. Rather, oblivious of reaction kinetics, one might find amazing that the simple addition of CCl_3Br does the *magic*[5a] of turning a remarkably selective and synthetically useful reaction (such as the alkane oxyfunctionalization by dioxiranes) into a Pandora's box, letting out a variety of products (Table 2).

Acknowledgment. This work was supported in part by CNR - P. S. "Tecnologie Chimiche Innovative" (Rome, Italy), and the Italian Ministry of Research (MURST 40). Thanks are due to Dr. R. Mello (University of Valencia, Spain) for performing some of the GC/MS analyses.

References and Notes

1. (a) Mello, R.; Fiorentino, M.; Fusco, C.; Curci, R. *J. Am. Chem. Soc.* **1989**, *111*, 6749. (b) Mello, R.; Cassidei, L.; Fiorentino, M.; Fusco, C.; Curci, R. *Tetrahedron Lett.* **1990**, *31*, 3067. (c) Adam, W.; Asensio, G.; Curci, R.; Gonzalès-Nuñez, M. E.; Mello, R. *J. Org. Chem.* **1992**, *57*, 953. (d) Mello, R.; Cassidei, L.; Fiorentino, M.; Fusco, C.; Hümmer, W.; Jäger, V.; Curci, R. *J. Am. Chem. Soc.* **1991**, *113*, 2205. See also references therein.
2. (a) Murray, R. W.; Jeyaraman, R.; Mohan, L. *J. Am. Chem. Soc.* **1986**, *108*, 2470. (b) Murray, R. W.; Gu, D. Q. *J. Chem. Soc., Perkin Trans. 2* **1994**, 451.
3. For a recent review on dioxirane reactivity, see: Curci, R.; Dinoi, A.; Rubino, M. F. *Pure Appl. Chem.* **1995**, *67* , 811. See references to the pertinent articles quoted therein.
4. For instance, see: C. L. Hill, in *Advances in Oxygenated Processes*; A. L. Baumstark, Ed.; JAI: Greenwich, CT, 1988; Vol. 1, Chapter 1, pp 1-30 and references therein.
5. (a) Minisci, F.; Zhao, L.; Fontana, F.; Bravo, A. *Tetrahedron Lett.* **1995**, *36*, 1697. (b) Bravo, A.; Fontana, F.; Fronza, G.; Mele, A.; Minisci, F. *J. Chem. Soc., Chem. Comm.* **1995**, 1573.
6. (a) Adam. W.; Curci, R.; Gonzalès-Nuñez, M. E.; Mello, R. *J. Am. Chem. Soc.* **1991**, *113*, 7654. (b) Singh, M; Murray, R. W. *J. Org. Chem.* **1992**, *57*, 4263.
7. (a) In order to exclude trace amounts of HBr impurity, bromotrichloromethane was carefully purified by washing with 5% aqueous $NaHCO_3$, drying ($MgSO_4$), and distillation (bp 101-103 °C) just prior to use. (b) Our preliminary data confirm (ref 1a) that, in the reaction of AdH with dioxirane (**1b**) under air at 10 °C, no AdOAc or AdO(CO)CF_3 are formed in detectable amounts.
8. The kinetic order in bromotricloromethane (x), appears to be fractional. A $\log[R_o/([AdH]_o[DMDO]_o)]$ vs. $\log[CCl_3Br]_o$ plot (data from entries 8-10) yields $x = 1.5$, as a preliminary rough estimate.
9. By extrapolation of data taken at higher temperatures, $k_1 = 1.5 \times 10^{-6}\ s^{-1}$ has been estimated for DMDO decomposition at 25 °C: Hull, L. A.; Budhai, L. *Tetrahedron Lett.* **1993**, *34*, 5039.
10. However, precautions should be taken as to avoid any trace of contaminants (e.g., trace amounts of transition-metal ions), as well as to employing freshly prepared and carefully dried ($MgSO_4$, Molecular Sieves 5Å) dioxirane solutions.
11. For instance, see: (a) Edwards, J. O.; Gallopo, A. R.; McIsaac, J. E., Jr. *J. Am. Chem. Soc.* **1966**, *88*, 3891. (b) Curci, R.; Delano, G.; Di Furia, F.; Edwards, J. O.; Gallopo, A. R. *J. Org. Chem.* **1974**, *39*, 3020, and references therein.
12. Adam, W.; Asensio, G.; Curci, R.; Gonzalès-Nuñez, M. E.; Mello, R. , *J. Am. Chem. Soc.* **1992**, *114*, 7654.
13. Mello, R.; Ciminale, F.; Fiorentino, M.; Fusco, C.; Prencipe, T.; Curci, R. *Tetrahedron Lett.* **1990**, *31*, 6097.
14. Hamilton, G. A. in *Molecular Mechanisms of Oxygen Activation*; Hayashi, O., Ed.; Academic: New York, 1974; Chapter 10.

(*Received in UK* 5 *October* 1995; *revised* 8 *November* 1995; *accepted* 10 *November* 1995)