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Transition structures for the stepwise insertion of oxygen into alkane tertiary C–H bonds by dimethyldioxirane

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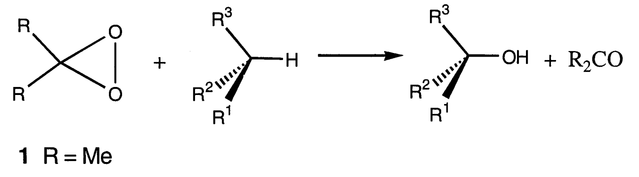
Abstract—Oxygen insertion into the isobutane C–H bond by dimethyldioxirane **1** was computationally studied at the R(U)B3LYP level to address the mechanistic concerted-stepwise problem. We located genuine TSs, diradicaloid in nature, that can lead to final products via radical pair intermediates. These TSs have lower energies than their concerted counterpart. Thus, calculations support the viability of radical pair formation in the reaction of dioxiranes with alkanes. © 2001 Elsevier Science Ltd. All rights reserved.

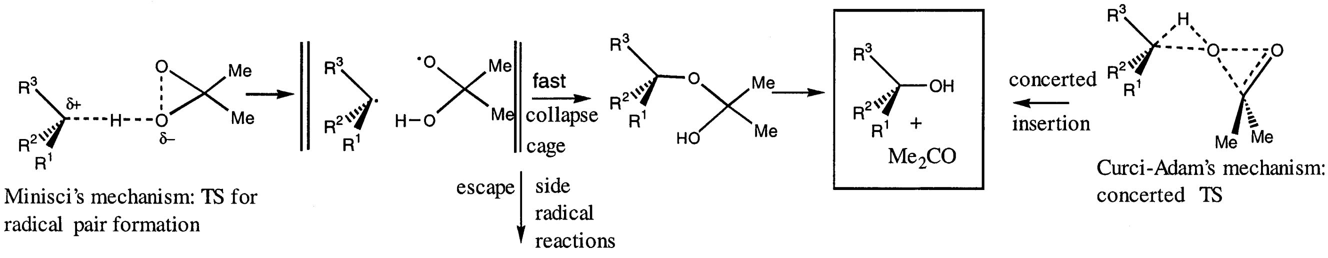
The synthetically interesting oxygen insertion into unactivated C–H bonds of alkanes by dioxiranes is one of the most recent additions to the armory of oxidation reactions (Scheme 1).[1] The hypothesis of a concerted process advanced by Curci and Adam[2] was challenged by Minisci[3] who suggested a stepwise mechanism (Scheme 2).

Recently, the feasibility of a concerted process was supported by the RB3LYP/6-31G* transition structures (e.g. **conc-3** in Scheme 3) located in three computational studies.[4–6] Actually, these TSs exhibit considerable diradical character and are highly polarized. At the TS the oxygen being transferred not only interacts strongly with the H atom (the O_1–H is almost completely formed) but also, even if much more weakly, with the C_4 atom. Moreover, IRC calculations starting from **conc-3** produce on one side a dioxirane+alkane and on the other side lead directly to an alcohol+carbonyl compound.[4–6] However, TSs of type **conc-3** exhibit an RHF→UHF instability[7] (for example, 5.3 kcal/mol for **conc-3**) that casts some doubt on their nature.

In the context of our systematic theoretical search on oxidation reactions with dioxiranes[8] and peroxy acids,[9] we report here that the stepwise process is also a viable route, as demonstrated by the 'genuine' diradicaloid TSs (**rad-4** and **rad-5**, Scheme 3 and Fig. 1) located by



Scheme 1.



Scheme 2.

Keywords: dioxiranes; hydroxylation; transition states.

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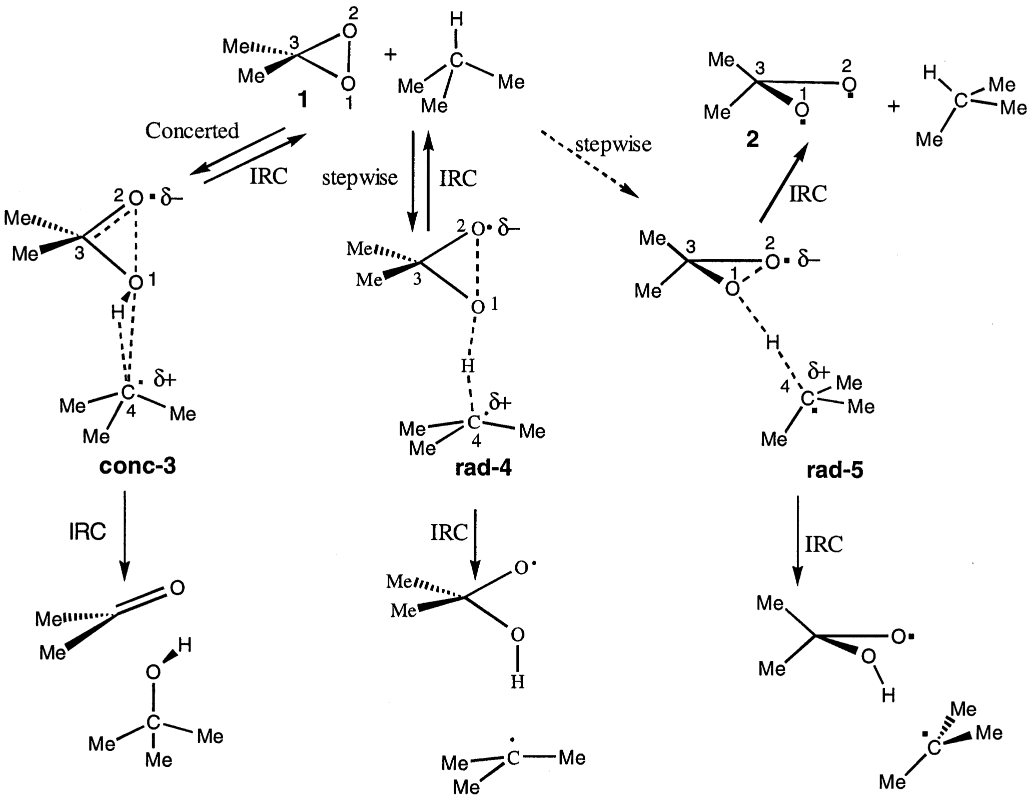

Scheme 3.

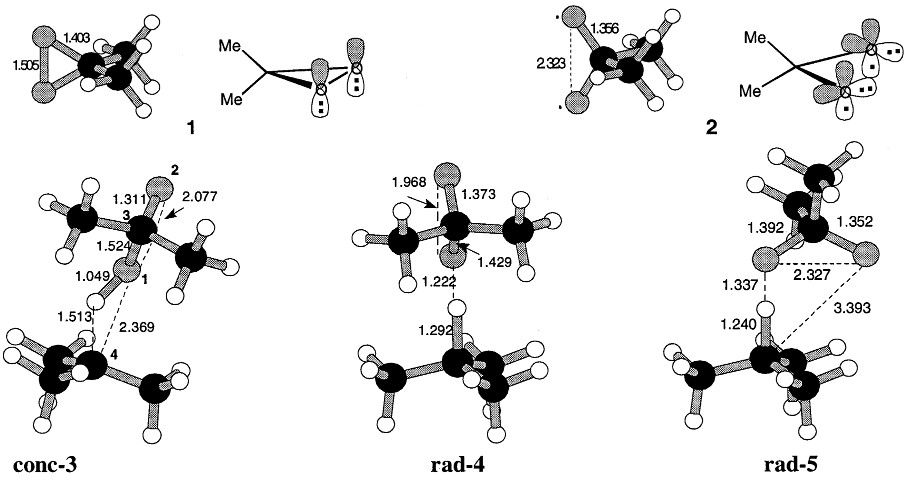

Figure 1. DFT optimized geometries (bond lengths in Å) for isobutane hydroxylation by dimethyldioxirane.

us for the reaction of dimethyldioxirane **1** with isobutane at the UB3LYP/6-31G* level.[10,11]

The two TSs **rad-4** and **rad-5** differ highly from each other as far as the approach trajectory is concerned. In TS **4**, the attacking C–H bond is almost colinear with the breaking O_1–O_2 bond, while in TS **5**, these two bonds are almost perpendicular to each other. However, in both TSs the $<O_1$–H–C_4 angle is not far from 180° (167 and 168°, respectively) and, in contrast with TS **conc-3**, no significant bonding interaction between O_1 and C_4 can be taking place.

The diradicaloid character of these TSs is supported by the considerable spin density at C_4, O_1 and O_2 [atomic spin density for **rad-4** (**rad-5**) on C_4, O_1, and O_2, respectively: −0.41 (−0.41), −0.23 (−0.52), and 0.67 (0.81)]. Both TSs also exhibit considerable polarization that arises from the electron transfer from isobutane to dioxirane. The net positive charge (CHelpG) on the *t*-Bu moiety is 0.37, 0.26 and 0.21 e, respectively, for **3**, **4** and **5**.

The geometry of TS **rad-4** resembles that of TS **conc-3** and the most noticeable difference is in the position of

Table 1. Activation parameters for TSs **3**–**5** in the gas phase[a] and in acetone ($\Delta G^{\neq}_{\text{sol}}$)[b] at the B3LYP/6-31G* and B3LYP/6-311+G**//B3LYP/6-31G* levels[c]

	B3LYP/6-31G*						B3LYP/6-311+G**//B3LYP/6-31G*		
TS	μ (D)	$\Delta E^{\neq}$	$\Delta H^{\neq}$	$\Delta S^{\neq}$	$\Delta G^{\neq}$	$\Delta G^{\neq}_{\text{sol}}$	$\Delta E^{\neq}$	$\Delta G^{\neq}$	$\Delta G^{\neq}_{\text{sol}}$
Conc-3	5.30	31.97	29.81	−22.01	36.39	32.59	24.21	28.63	24.83
Rad-4	4.73	24.52	21.32	−22.12	27.93	28.23	20.00	23.41	23.71
Rad-5	1.25	19.18	15.71	−23.42	22.71	25.24	15.81	19.34	21.87

[a] Barrier heights are relative to **1** and isobutane. Energies in kcal/mol, entropy in cal/mol K; standard state (298.15 K) of the molar concentration scale (gas in ideal mixture at 1 mol/L, $P=1$ atm).[16]

[b] Solvent (acetone) effect according to COSMO model at the B3LYP/6-31G* level.

[c] Barrier values evaluated from B3LYP/6-311+G**//B3LYP/6-31G* calculations. For evaluation of the thermodynamic properties the B3LYP/6-31G* computed kinetic contributions are used.

the H atom. This atom in **3** is almost completely transferred while in **4** its transfer is less advanced and the $<O_1–H–C_4$ angle (134°) in the former TS is smaller by 33° than that in the latter one. Important geometry differences between **5** as compared to **3** and **4** are represented by the higher values of the breaking $O_1\cdots O_2$ bond length (2.33 Å in **5** versus 2.08 and 1.97 Å in **3** and **4**, respectively) and of the $<O_1–C_3–O_2$ angle (116° in **5** versus 94 and 89° in **3** and **4**, respectively). In fact, the geometry of the dioxirane moiety in **5** looks very like that of the dioxymethane diradical **2** ($<O_1–C_3–O_2=118°$ and $O_1\cdots O_2=2.32$ Å) that is formed on ground state ring opening of **1**.[12]

The wave function of both TS **4** and **5** is stable, and vibrational analysis led to only one imaginary frequency that corresponds to the transfer of H from C_4 to O_1. *These TSs are genuine first order saddle points.*

IRC calculations starting from **rad-4** on the reactant side led to **1**+isobutane while on the opposite side produced a radical pair (Scheme 3). Thus, formation of **rad-4** and its successive transformation into a radical pair provides a 'molecule induced homolysis'[13] path for the reaction of **1** with isobutane in alternative to the concerted route.

In the case of **rad-5** IRC analysis of the path toward products gives rise to a radical pair but the descent on the reactant side terminated with isobutane and the open dioxirane, i.e. the dioxymethane diradical **2**. This finding demonstrates that TS **rad-5** can derive from the reaction of **2** with isobutane but it does not definitely exclude the possibility that it is also formed by a direct collision between **1** and isobutane.[14] The radical pair formed from TS **rad-5** can easily collapse to hemiketal (2-*t*-butoxy-2-propanol) without any significant reorientation, while the radicals derived from TS **rad-4**, aside from reacting with each other,[15] have more chance to escape from the cage and trigger radical reactions.

As far as the energy (potential and Gibbs free)[16] is considered TS **rad-5** is definitely more stable than TS **conc-3**, while TS **rad-4** shows intermediate stability (Table 1). These energy gaps are considerably reduced after potential energy refinement by both higher level single point calculations (i.e. B3LYP/6-311+G** calculations on the fully optimized B3LYP/6-31G* geometries) and introduction of solvent effects (acetone solution) by the COSMO model.[17] *However, we are faced with the truly noteworthy observation that both diradicaloid TSs remain favored over their concerted counterpart.*

As a conclusion, it is important to realize that these calculations support the feasibility of radical pair formation in the reaction of dioxiranes with alkanes. Nevertheless, the potential energy surface of oxygen insertion into unactivated C–H bonds by dioxiranes is quite intricate and delicate and, thus, definitive conclusions about competition among the concerted and stepwise mechanisms require further computational data.[18]

Acknowledgements

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7. This behavior has also been observed in two of the three previous studies.[4,5]

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14. A stepwise mechanism starting from **1** and passing through the open form **2** seems highly improbable. It has been theoretically demonstrated that compound **2** once formed rearranges or decomposes so easily (Ref. 11 and Aplicourt, P.; Ruiz-Lopez, M. F. *J. Am. Chem. Soc.* **2000**, *122*, 8990) that it cannot be intercepted by other reactants.
15. Aside from collapsing to a hemiketal (apparently this reaction cannot be very fast since it requires substantial reorientation of the two radicals), the radical pair can undergo a S_H2 reaction to directly afford the final products (alcohol+carbonyl compound) according to a suggestion advanced by Curci and Adam.[2]
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