The Nature of the Transition Structure for the Oxidation of Alkanes with Dioxiranes

Mikhail N. Glukhovtsev,*,† Carlo Canepa, and Robert D. Bach*,‡

Contribution from the Department of Chemistry and Biochemistry, University of Delaware, Newark, Delaware 19716

Received April 20, 1998. Revised Manuscript Received August 17, 1998

Abstract: A high-level ab initio study on the oxidations of alkanes (methane, propane and isobutane) with dioxirane (DO), dimethyldioxirane (DMDO), difluorodioxirane (DFDO) and methyl(trifluoromethyl)dioxirane (TFDO) has provided a rationale for the formation of products derived from radical intermediates when dioxygen is rigorously excluded and lends strong support to the generally accepted, highly exothermic, concerted oxygen insertion mechanism for the oxidation of alkanes with dioxiranes under typical preparative conditions. At the B3LYP/6-311+G(3df,2p)//B3LYP/6-311+G(3df,2p) level, the barriers for the oxidation of methane with DO, DMDO, DFDO, and TFDO are 36.5, 41.2, 21.2, and 35.0 kcal/mol. The activation barriers for the oxidation of methane, propane, and isobutane with DMDO are 44.2, 30.3, and 22.4 kcal/mol, respectively, at the CCSD-(T)/6-31G*//B3LYP/6-31G* level. These barriers are higher than the barriers for epoxidations of ethylene, propene, and isobutene (17.9, 15.9, and 15.4 kcal/mol, respectively, at the B3LYP/6-31G* level). Calculations at the G2 level have shown that C−H bond homolysis is not thermodynamically favorable in hydrogen abstraction reactions of methane, propane, and isobutane with either DMDO, its parent DO, or DFDO. If the sources of the initiating radical species are hydrogen atoms produced by breaking X−H bonds, the energy of the X−H bond should be less than 83.5 kcal/mol in its reaction with DMDO (89.5 and 87.8 kcal/mol for DO and DFDO) for the reaction to be exothermic.

1. Introduction

The oxyfunctionalization of hydrocarbons by dioxiranes under mild conditions is perhaps one of the most useful synthetic reactions of this type.[1] Dioxiranes are three-membered-ring highly strained peroxides that serve as paradigm examples of electrophilic species. Dimethyldioxirane, in particular, is a powerful oxidant with unusual synthetic utility, that can be produced readily in situ by the reaction of acetone with Caroate ($2KHSO_5 \cdot KHSO_4 \cdot K_2SO_4$).[2c] Recent efforts to isolate dimethyldioxirane (DMDO) have proven successful, and it is sufficiently stable to remain in solution for several days at room temperature.[2d,e] This highly reactive cyclic peroxide can readily epoxidize alkenes, insert oxygen into carbon−hydrogen bonds of alkanes, and oxidize nucleophiles such as amines, phosphines, and sulfides. Methyl(trifluoromethyl)dioxirane (TFDO)[2d] was synthesized a few years later demonstrating that electron withdrawing groups can markedly enhance the oxygen donor propensity of these cyclic peroxides. Indeed TFDO is several hundred times more reactive than DMDO, and it is capable of oxidizing saturated hydrocarbons to their alcohols at relatively low temperatures.[3e] Solutions of TFDO can be stored at −20 °C for 48 h with only minor loss. The sterically encumbered mesityl dioxirane is stable in the solid phase, but in solution it slowly rearranges to its ester.[3f] Difluorodioxirane, F_2CO_2 (DFDO), is the only simple known substituted dioxirane that can be readily isolated as a pure substance and is thermally stable.[4] It exists in the gaseous state at room temperature.

Although many general mechanistic features of the oxidation of saturated hydrocarbons with such commonly employed oxidants as dimethyldioxirane (DMDO) and methyl(trifluoromethyl)dioxirane (TFDO)[2] are known, the transition structure for this unique oxygen insertion reaction remains a matter of debate. Stereochemical selectivities[1e,2] and kinetic evidence[3d] indicate a concerted "oxenoid" mechanism of insertion into C−H bonds, without the intervention of discrete radical or carbenium ion intermediates (Scheme 1).[1−3] The kinetic isotope effect (KIE) for oxygen insertion into a tertiary C−H bond (k_h/k_d ca. 5)[1b] and the selective hydroxylation of (−)-2-phenylbutane by DMDO, which proceeds with complete retention of configuration and no loss of optical activity,[1e] provide ample support

---

[†] E-mail: rbach@Udel.edu. WWW: http://www.Udel.edu/chem/bach.

[‡] E-mail: mng@Udel.edu. WWW: http://Udel.edu/∼mng.

(1) For reviews, see: (a) Adam, W.; Curci, R.; Edwards, J. O. *Acc. Chem. Res.* **1989**, *22*, 205. (b) Murray, R. W. *Chem. Rev.* **1989**, *89*, 1187. (c) Bunnelle, W. H. *Chem. Rev.* **1991**, *91*, 335 and references therein. (d) Adam, W.; Hadjiarapoglou, L. P.; Curci, R.; Mello, R. In *Organic Peroxides*; Ando, W.; Ed., Wiley: New York, 1992; p 195. (e) Curci, R.; Dinoi, A.; Rubino, M. F. *Pure Appl. Chem.* **1995**, *67*, 811.

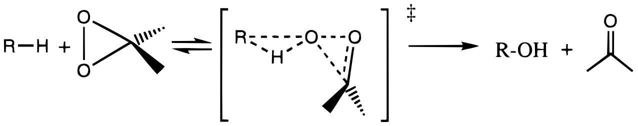
(2) (a) Adam, W.; Asensio, G.; Curci, R.; González-Núriez, M. E.; Mello, R. *J. Org. Chem.* **1992**, *57*, 953. (b) Mello, R.; Cassidei, L.; Fiorentino, M.; Fusco, C.; Hümmer, W.; Jäger, V.; Curci, R. *J. Am. Chem. Soc.* **1991**, *113*, 2205. (c) Curci, R.; Fiorentino, M.; Tvoisa, L.; Edwards, J. O.; Pater, R. H. *J. Org. Chem.* **1980**, *45*, 4758. (d) Mello, R.; Fiorentino, M.; Sciacovelli, O.; Curci, R. *J. Org. Chem.* **1988**, *53*, 3890. (e) Adam, W.; Chan, Y.-Y.; Cremer, D.; Gauss, J.; Scheutzow, D.; Schindler, M. *J. Org. Chem.* **1987**, *52*, 2800.

(3) (a) Curci, R.; Dinoi, A.; Fusco, C.; Lillo, M. A. *Tetrahedron Lett.* **1996**, *37*, 249. (b) Adam, W.; Curci, R.; D'Accolti, L.; Dinoi, A.; Fusco, C.; Gasparrini, F.; Kluge, R.; Paredes, R.; Schulz, M.; Smerz, A. K.; Veloza, L. A.; Weinkötz, S.; Winde, R. *Chem. Eur. J.* **1997**, *3*, 105. (c) Adam, W.; Paredes, R.; Smerz, A. K.; Veloza, L. A. *Liebigs Ann.* **1997**, 547. (d) Asensio, G.; Mello, R.; Gonzalez-Nunez, M. E.; Boix, C.; Royo, J. *Tetrahedron Lett.* **1997**, *38*, 2373. (e) Curci, R.; Dinoi, A.; Rubino, M. F. *Pure Appl. Chem.* **1995**,*67*, 811. (f) Kirschfeld, M.; Muthusamy, A. S.; Sander, W. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 2212.

(4) (a) Rahman, M.; McKee, M. L.; Shevlin, P. B.; Sztyrbicka, R. *J. Am. Chem. Soc.* **1988**, *110*, 4002. (b) Russo, A.; DesMarteau, D. D. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 905. (c) Kraka, E.; Konkoli, Z.; Cremer, D.; Fowler, J.; Schaefer, H. F. *J. Am. Chem. Soc.* **1996**, *118*, 10595.

S0002-7863(98)01315-8 CCC: $15.00

Scheme 1



for such a concerted insertion process. No indication of freely diffusing alkyl radicals was reported in this series of mechanistic studies. However, some controversy has arisen recently as to whether this is a concerted electrophilic insertion or if radical intermediates are involved.[3,5]

Radical-derived side products have been observed in oxidations with DMDO and TFDO accompanied by radical-chain decompositions of the dioxiranes.[3a,d,5,6] Recently, Minisci et al.[5] have reported the observation that the rigorous exclusion of dioxygen and radical inhibitors can have a dramatic influence upon the reaction pathway, which prompted the suggestion that oxidations of alkanes with DMDO proceed via a "molecule-induced homolysis" or "radical-oxygen rebound" mechanism (Scheme 2). The transition structure for this reaction pathway should exhibit considerable radical character with some charge separation.

While these general suggestions for the transition structure geometry based upon experimental data are controversial,[3,5] no computational studies on the direct functionalization of C−H bonds have appeared to date. Well-studied examples of alkane oxyfunctionalizations with dioxiranes are represented by the conversion of cyclohexanes into cyclohexanones and the selective bridgehead hydroxylation of adamantanes.[1] The thermodynamics of these reactions cannot differ significantly from the oxidations of such prototypical alkanes as methane, propane, and isobutane considered in the present study. For example, the C−H bond energy in adamantane was estimated[7a] to be 99 kcal/mol, a value that is only 3.8 kcal/mol greater than the *tert*-C−H bond energy in isobutane.[7b,8]

We have described a frontier molecular orbital (FMO) model for electrophilic oxygen insertion that also included a rationale for the regioselective hydroxylation of the side chain of steroids with DMDO.[9a] Subsequently, we reported on the orientation of the reactants and the origin of the barrier for divalent carbon insertion into C−H bonds.[9b] We have also shown earlier[9] that oxygen atom transfer from dioxiranes to a typical nucleophilic two-electron σ- or π-donor (e.g., :Nuc = alkene, amine, phosphine, sulfide) proceeds via an S_N2-like displacement along the O−O σ bond axis with concomitant breaking of the O−O bond and formation of an O$\leftarrow$:Nuc bond. In contrast to the S_N2-like pathway, insertion into a C−H bond cannot proceed via a similar mechanism because in addition to the breaking of the O−O bond and formation of an O−C bond, it also involves C−H bond cleavage in the hydrocarbon fragment. We now report a high-level ab initio study on the oxidations of alkanes (methane, propane, and isobutane) with DMDO, DFDO, TFDO, and the parent dioxirane (DO).

2. Computational Methods

Ab initio molecular orbital calculations[10] were performed with the GAUSSIAN 94 system of programs.[11] The Becke three-parameter hybrid functional[12a,13a] combined with the Lee, Yang, and Parr (LYP) correlation functional,[12b] denoted B3LYP,[13b] was employed in the calculations with use of density functional theory (DFT). Both singlet and triplet stabilities of the RHF and RB3LYP solutions have been checked.[14] Geometries were optimized[15] at the B3LYP and QCISD levels by using the 6-31G* and 6-311+G(3df,2p) basis sets (the latter was used only for the B3LYP optimizations). The B3LYP level of theory has been shown to give adequate geometries for a series of reactions with peracids.[16] The reaction enthalpies were calculated with G2 theory.[17] The activation energies were refined by single-point calculations at the CCSD(T) level[18] of theory with use of the 6-31G* and 6-311G** basis sets. Activation barriers for some reactions were calculated by using the G2(QCI/MP2CC) scheme. The G2(QCI/MP2/CC) level is the G2(B3LYP/MP2/CC) method[19a] modified with QCISD/6-31G* geometries and ZPE(B3LYP/6-31G*) corrections. The G2-(B3LYP/MP2/CC) method[19a] is a modification of the G2(MP2) scheme[19b] with geometry optimization and calculation of vibrational frequencies at the B3LYP/6-31G* level and with use of CCSD(T)/6-311G**, MP2/6-311+G(3df,2p), and MP2/6-311G** energies. The stationary points on the potential energy surfaces were characterized by calculations of vibrational frequencies at the B3LYP/6-31G* level. Zero-point energies (ZPE) computed at the B3LYP/6-31G* level were scaled by 0.9806 according to Scott and Radom.[20] Throughout the text, bond lengths are in angstroms and bond angles are in degrees.

3. Results and Discussion

Thermochemistry of Molecule-Induced Homolysis of Dioxiranes with Alkanes. The recent controversy concerning the

---

(5) (a) Bravo A.; Fontana, G.; Minisci, F. *Tetrahedron Lett.* **1995**, *38*, 6945. (b) Minisci, F.; Zhao, L.; Fontana, F.; Bravo, A. *Tetrahedron Lett.* **1995**, *36*, 1697. (c) Bravo A.; Fontana, G.; Fronza, G.; Minisci, F. *J. Chem. Soc. Chem., Commun.* **1995**, 1573. (d) Bravo, A.; Fontana, F.; Fronza, G.; Minisci, F.; Zhao, L. *J. Org. Chem.* **1998**, *63*, 254 and references therein.

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

(7) (a) Kruppa, G. H.; Beauchamp, J. L. *J. Am. Chem. Soc.* **1986**, *108*, 2162. (b) The *tert*-C−H bond energy in isobutane is 95.2 ± 0.7 kcal/mol (298 K).[8] The C−H and *sec*-C−H bond energies in methane and propane are 103.2 ± 0.3 and 99.4 ± 0.3 kcal/mol (298 K), respectively.[8.]

(8) Lias, S. G.; Bartmess, J. E.; Liebman, J. F.; Holmes, J. L.; Levin, R. D.; Mallard, W. G. *J. Phys. Chem. Ref. Data* **1988**, *17*, Suppl. 1.

(9) (a) Bach, R. D.; Owensby, A. L.; Andrés, J. L.; Su, M.-D.; McDouall, J. J. W. *J. Am. Chem. Soc.* **1993**, *115*, 5768. (b) Bach, R. D.; Su, M.-D.; Aldabbagh, E.; Andrés, J. L.; Schlegel, H. B. *J. Am. Chem. Soc.* **1993**, *115*, 10237. (c) Baboul, A. G.; Schlegel, H. B.; Glukhovtsev, M. N.; Bach R. D. *J. Comput. Chem.* **1998**, *19*, 1353.

(10) Hehre, W. J.; Radom, L.; Schleyer, P. v. R.; Pople, J. A. *Ab Initio Molecular Orbital Theory*; Wiley: New York, 1986.

(11) Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Gill, P. M. W.; Johnson, B. G.; Robb, M. A.; Cheeseman, J. R.; Keith, T. A.; Peterson, G. A.; Montgomery, J. A.; Raghavachari, K.; Al-laham, M. A.; Zakrzewski, V. G.; Ortiz, J. V.; Foresman, J. B.; Cioslowski, J.; Stefanov, B. B.; Nanayakkara, A.; Challacombe, M.; Peng, C. Y.; Ayala, P. Y.; Wong, M. W.; Replogle, E. S.; Gomperts, R.; Andres, J. L.; Martin, R. L.; Fox, D. J.; Binkley, J. S.; DeFrees, D. J.; Baker, J.; Stewart, J. J. P.; Head-Gordon, M.; Gonzalez, C.; Pople, J. A. GAUSSIAN-94, Gaussian Inc.: Pittsburgh, PA, 1995.

(12) (a) Becke, A. D. *Phys. Rev. A* **1988**, *37*, 785. (b) Lee, C.; Yang, W.; Parr, R. G. *Phys. Rev.* **1988**, *B41*, 785.

(13) (a) Becke, A. D. *J. Chem. Phys.* **1993**, *98*, 5648. (b) Stevens, P. J.; Devlin, F. J.; Chablowski, C. F.; Frisch, M. J. *J. Phys. Chem.* **1994**, *98*, 11623.

(14) For the HF instabilities, see, for example: (a) Seeger, R. R.; Pople, J. A. *J. Chem. Phys.* **1976**, *65*, 265. (b) Chambaud, G.; Levy, B.; Millie, P. *Theor. Chim. Acta* **1978**, *48*, 103. (c) Glukhovtsev, M. N.; Mestechkin, M. M.; Minkin, V. I.; Simkin, B. Ya. *Zh. Strukt. Khim.* (*USSR*) **1982**, *23*, 14. (d) Glukhovtsev, M. N.; Simkin, B. Ya.; Yudilevich, I. A. *Theor. Eksper. Khim.* (*USSR*) **1982**, *18*, 726. (e) Schlegel, H. B.; McDouall, J. J. W. In *Computational Advances in Organic Chemistry*: *Molecular Structure and Reactivity*; Ögretir, C., Csizmadia, I. G., Eds.; Kluwer: Dordrecht, 1991; p 167. (f) Chen, W.; Schlegel, H. B. *J. Chem. Phys.* **1994**, *101*, 5957.

(15) (a) Schlegel, H. B. *J. Comput. Chem.* **1982**, *3*, 214. (b) Schlegel, H. B. *Adv. Chem. Phys.* **1987**, *67*, 249. (c) Schlegel, H. B. In *Modern Electronic Structure Theory*; Yarkony, D. R., Ed.; World Scientific: Singapore, 1995; p 459.

(16) Bach, R. D.; Glukhovtsev, M. N.; Gonzalez, C.; Marquez, M.; Estévez, C. M.; Baboul, A. G.; Schlegel, H. B. *J. Phys. Chem. A* **1997**, *101*, 6092 and references therein.

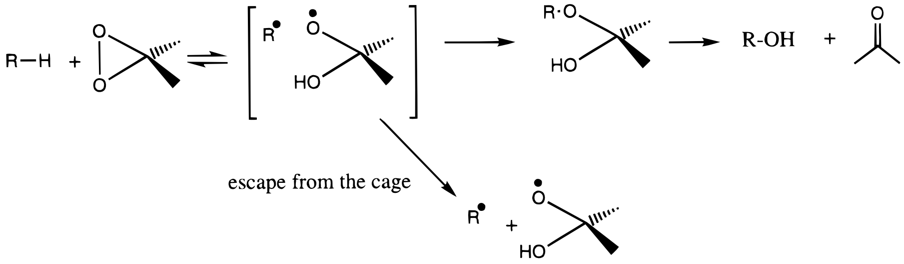
(17) (a) Curtiss, L. A.; Raghavachari, K.; Trucks, G. W.; Pople, J. A. *J. Chem. Phys.* **1991**, *94*, 7221. (b) Curtiss, L. A.; Raghavachari, K.; Pople, J. A. *J. Chem. Phys.* **1997**, *106*, 1063.

(18) (a) Bartlett, R. J.; Purvis, G. D. *Int. J. Quantum Chem.* **1978**, *14*, 516. (b) Bartlett, R. J. *Annu. Rev. Phys. Chem.* **1981**, *32*, 359.

(19) (a) Bauschlicher, C. W.; Partridge, H. *J. Chem. Phys.* **1995**, *103*, 1788. (b) Curtiss, L. A.; Raghavachari, K.; Pople, J. A. *J. Chem. Phys.* **1993**, *98*, 1293.

(20) Scott, A. P.; Radom, L. *J. Phys. Chem.* **1996**, *100*, 16502.

Scheme 2



mechanism of the oxyfunctionalization of saturated hydrocarbons with dioxiranes stems mainly from the observation that the rigorous exclusion of dioxygen from the reaction mixture results in the formation of products derived from a free radical chain process. The radical pathway is suppressed by the presence of dioxygen that appears to function as a radical scavenger. This has raised the question as to whether such an induced radical chain process constitutes the principal reaction pathway for the oxidation of hydrocarbons under typical laboratory conditions or is the intervention of radical species simply a side reaction. Minisci et al. suggested[5] that "the molecule-induced homolysis of dioxirane with alkanes would be almost thermoneutral for tertiary C—H bonds", although no estimates on the thermochemistry of these reactions were given.[5d] To test this idea, we examined initially the thermochemistry of the formation of the oxygen radical intermediate described in Scheme 2 at the G2 level of theory. The cleavage of the O—O bond in several dioxiranes, induced by the attack of a hydrogen atom to effect ring opening, results in the formation of the proposed oxyradical intermediate:

$$C_nH_{n+2} + R_2CO_2 \rightarrow C_nH_{n+1}^{\bullet} + HOR_2C{-}O^{\bullet}$$

The formation of the corresponding oxygen radical by the addition of hydrogen atom to DMDO is highly exothermic ($\Delta H = -83.5$ kcal/mol), reflecting the balance between the cleavage of a relatively weak O—O bond and the formation of an O—H bond and the relief of ring strain. The exothermicity of O—O bond cleavage is even more exothermic for DFDO ($\Delta H = -87.8$ kcal/mol) and DO ($\Delta H = -89.5$ kcal/mol). Similar energetics would be observed for carbon radical (e.g. CH_3) induced homolysis of the O—O bond in DMDO for the radical process as suggested by Minisci.[5] To complete the overall thermochemical balance for the proposed induced O—O bond homolysis by a hydrocarbon,[5] we included the energetics of C—H bond cleavage for several model hydrocarbons, including isobutane. The G2 C—H BDE values for methane, propane, and isobutane are 104.0, 98.5, and 96.9 kcal/mol, respectively. Unfortunately, the O—H BDE values for the oxygen radicals are not readily available because of the problems associated with the calculation of the various excited-state diradicals formed from O—O bond cleavage in dioxiranes.[9,21] However, the G2 calculations do readily show that the overall C—H bond homolysis is not thermodynamically favorable in hydrogen abstraction reactions of methane, propane, and isobutane with either DMDO ($R = CH_3$), its parent DO ($R = H$), DFDO ($R = F$), or TFDO ($R = CH_3$, $R = CF_3$) (eqs 1—3, Table 1). Indeed, hydrogen abstraction from isobutane by DMDO (eq 3) is endothermic by 13.4 kcal/mol. The abstraction of a tertiary C—H by DMDO represents a fairly realistic experimental model for this type of O—O bond homolysis, and the level of theory employed should put this result well within a range of credibility that strongly argues against the exothermic hydrogen abstraction from an alkane (Scheme 2).

Table 1. Reaction Enthalpy Changes (kcal/mol) for the Molecule-Induced Homolysis of Substituted Dioxiranes with Alkanes Calculated with G2 Theory[a]

	reaction	ΔH R = H	 R = CH_3	 R = F
(1)	$CH_4 + R_2CO_2 \rightarrow CH_3^{\bullet} + HOR_2C{-}O^{\bullet}$	14.5	20.5	16.2
(2)	$C_3H_8 + R_2CO_2 \rightarrow C_3H_7^{\bullet} + HOR_2C{-}O^{\bullet}$	9.0	15.0	10.7
(3)	i-$C_4H_{10} + R_2CO_2 \rightarrow t$-$C_4H_9^{\bullet} + HOR_2C{-}O^{\bullet}$	7.4	13.4	9.1

[a] The ΔH values were calculated at 0 K.

These thermochemical data, as exemplified by the H atom induced O—O bond homolysis, do suggest that spurious radicals present in the reaction mixture could result in O—O bond homolysis to afford oxygen radicals and that the exothermicity attending the dioxirane ring-opening process could induce further homolytic fragmentation[22] of these oxygen radicals, thereby propagating the ensuing free radical chain reaction.[3d,5d,6] If the source of the initiation of radical species is a hydrogen atom produced by breaking an X—H bond in a molecule that induces radical decomposition of the dioxirane, the energy of that X—H bond should be less than 83.5 kcal/mol in its reactions with DMDO (89.5 and 87.8 kcal/mol for DO and DFDO) to make these processes thermodynamically favorable. For methane, propane, and isobutane, these energetic requirements suggest that the hydrocarbon-induced homolysis of DO, DMDO, DFDO, and TFDO is thermodynamically unfavorable even for tertiary C—H bonds.[23] In marked contrast, the overall oxyfunctionalizations of alkanes affording alcohols are highly exothermic (Table 2). For example, the oxidation of isobutane to *tert*-butyl alcohol by DMDO is attended by the liberation of 69.0 kcal/mol providing one rationale for how such typically unreactive substrates as saturated hydrocarbons can be oxidized even at low temperature.

Since no apparent effort is made to exclude dioxygen under typical laboratory conditions, it is quite ironic that the interdic-

---

(21) Anglada, J. M.; Bofill, J. M.; Olivella, S.; Sole, A. *J. Phys. Chem. A* **1998**, *102*, 3398.

(22) It is also noted that the abstraction of a hydrogen atom from isobutane by the oxygen radical, $HOMe_2C{-}O^{\bullet}$, is exothermic (−5.9 kcal/mol at the G2 level), affording acetone (by the loss of water: i-$C_4H_{10} + HOMe_2C{-}O^{\bullet} \rightarrow C_4H_9^{\bullet} + Me_2C{=}O + H_2O$) and also contributing to the chain reaction producing additional "free radical" products.

(23) (a) The molecule induced homolysis of DMDO with the formation of a radical pair can be thermodynamically favorable in its reactions with allylic hydrogens in alkenes such as 1-butene (the $H{-}CH(CH_3)CH{=}CH_2$ bond enthalpy is 82.3 kcal/mol (experimental value[8] corrected to 0 K.; the G2(MP2) calculations[23b] give 84.8 kcal/mol) and in reactions of DO with such aldehydes[5d] as formaldehyde (the C—H bond enthalpy is 87.8 kcal/mol, G2). Experimental data[5c,23c] indicate that radical chain processes also can occur when radical species are produced by cleavage of such relatively weak bonds as the C—O bonds in ethers (the $C_2H_5O{-}CH_3$ bond energy is 85.1 kcal/mol at the G2 level, calculated by using G2 energies reported in ref 17b). Furthermore, radical reactivity of DMDO can be triggered by the presence of such species as CCl_3Br.[3a,5b,d] (b) Bauschlicher, C. W. *Chem. Phys. Lett*. **1995**, *239*, 252. (c) Ferrer, M.; Sanchez-Baeza, F.; Casas, J.; Messeguer, A. *Tetrahedron Lett*. **1994**, *35*, 2981.

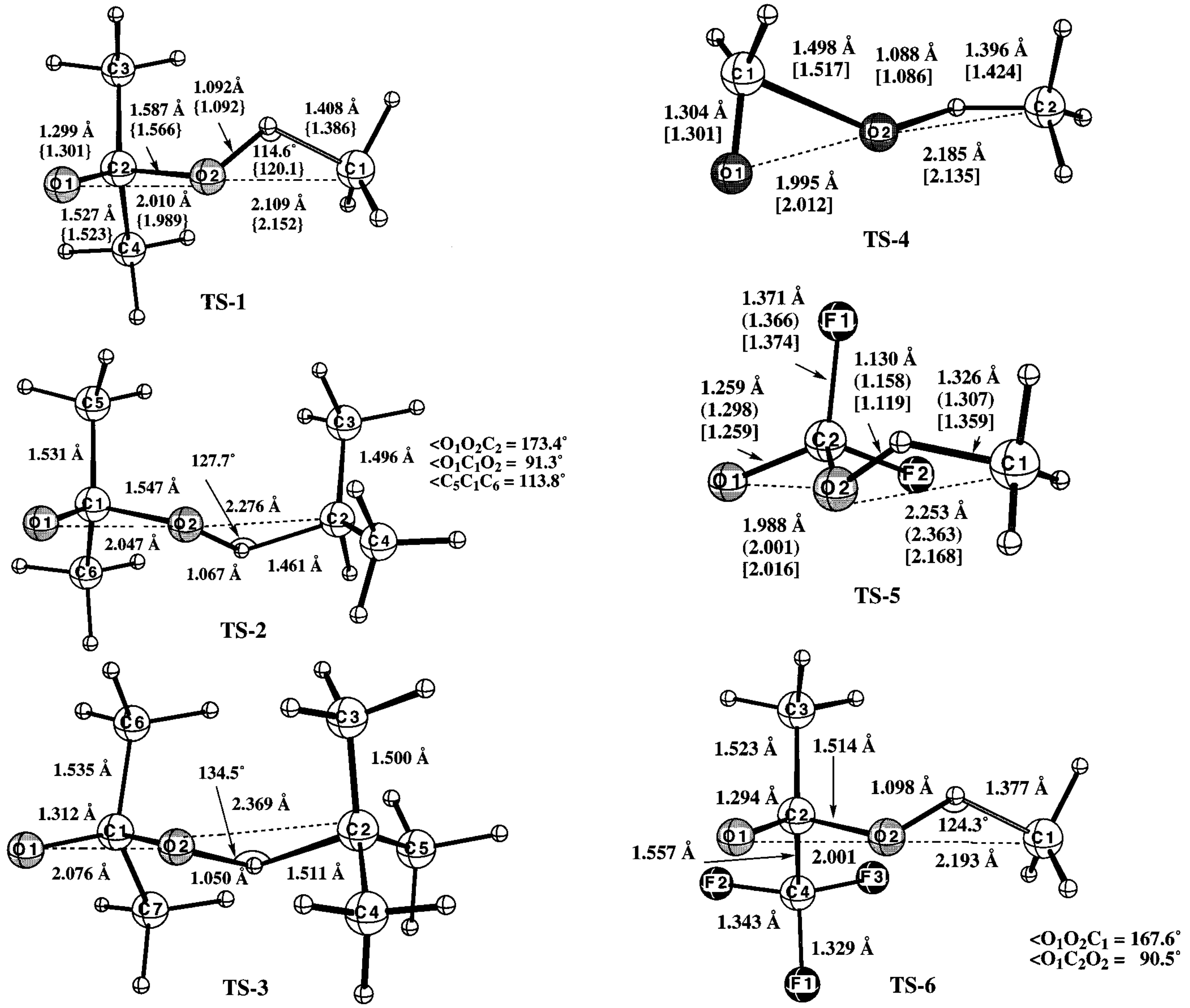


Figure 1. Transition structures for oxygen atom insertion into the C−H bonds of methane (**TS-1**), propane (**TS-2**), and isobutane (**TS-3**) in reactions with dimethyldioxirane optimized at the B3LYP/6-31G* level, as well as transition structures of oxygen atom insertion into the C−H bonds of methane in its reactions with substituted dioxiranes (**TS-4**, **TS-5**, and **TS-6**) optimized at the B3LYP/6-311+G(3df,2p) level. Geometrical parameters of **TS-5** optimized at the QCISD/6-31G* and B3LYP/6-31G* levels are given in parentheses and square brackets, respectively. Geometrical parameters of **TS-1** optimized at the B3LYP/6-311+G(3df,2p) level are given in curly brackets.

tion of spurious dioxygen promotes the formation of radicals whereas its presence serves to scavenge the relatively low concentration of adventitious free radicals present, allowing a concerted oxygen atom insertion to ensue. While the G2 thermochemical estimates for reactions of simple alkanes (eqs 1−3, Table 1) contradict the suggestion that the molecule-induced homolysis of DMDO is thermodynamically driven,[5] they do not answer directly the more subtle question about the nature of the transition structure for alkane oxidations and still leave open the possibility for both a stepwise reaction and a concerted oxygen insertion into the C−H bond. Location of the transition structures (TS) for alkane oxidations with dioxiranes can provide additional mechanistic insight into this rather unusual oxidative process.

Transition Structures and Activation Barriers for Alkane Oxidations with Dioxiranes. Transition structures for the oxidations of methane, propane, and isobutane with DMDO (**TS-1**−**TS-3**) are shown in Figure 1. The corresponding activation barriers are given in Table 3. We have also carried out calculations on oxidations of methane with the parent dioxirane DO, DFDO, and TFDO (**TS-4**, **TS-5**, and **TS-6**, Figure 1). The geometries of **TS-5** optimized at the B3LYP/6-31G* and B3LYP/6-311+G(3df,2p) levels are in good agreement with the geometry found at the QCISD/6-31G* level. Furthermore, the B3LYP activation barriers calculated with these two basis sets for the oxidation of methane with DFDO are close to the barriers calculated at the CCSD(T)/6-311G** and G2(QCI/MP2/CC) levels. The B3LYP calculated activation barriers[24] for oxidations of methane and propane with DMDO are slightly higher than the CCSD(T)/6-31G*//B3LYP/6-31G* values although the

Table 2. G2 Calculated Reaction Enthalpy Changes (kcal/mol)[a] for the Oxidation of Methane, Propane, and Isobutane into Alcohols with Substituted Dioxiranes[b]

	DO	DMDO	DFDO	TFDO[c]
methane	−56.9	−55.8	−64.6	−55.2
propane	−67.4	−66.2	−75.0	−65.5
isobutane	−70.1	−69.0	−77.8	−68.3

[a] At 0 K. [b] R−H + R′R″CO$_2$ → R−OH + R′R″C=O. We did not consider the possible further oxidation of alcohols into aldehydes or ketones. [c] At the G2(MP2) level.[19b]

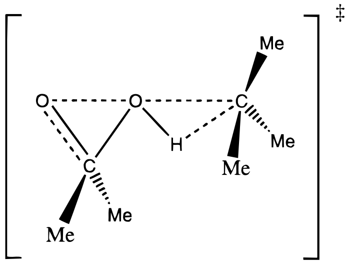
Table 3. Activation Barriers (kcal/mol) for the Oxidation of the Methane, Propane, and Isobutane with Dimethyldioxirane[a]

computational level	methane **TS-1**	propane **TS-2**	isobutane **TS-3**
B3LYP/6-31G*//B3LYP/6-31G*	45.8 (41.2)[b]	36.1 [31.1][d]	32.0[e]
CCSD(T)/6-31G*//B3LYP/6-31G*	44.2[c]	30.3 [27.5][d]	22.4

[a] Barrier heights are relative to isolated reactants. [b] The B3LYP/6-311+G(3df,2p)//B3LYP/6-311+G(3df,2p) barrier is shown in parentheses. [c] The barriers for oxidations of methane with DMDO and DO calculated at the MP2//6-311+G(2df,2p)//B3LYP/6-31G* level of theory are 44.8 and 41.9 kcal/mol, respectively. The barrier for methane oxidation with DO is 44.2 kcal/mol at the CCSD(T)/6-31G*//B3LYP/6-31G* level. [d] The barrier for the oxidation of propane with dioxirane is given in square brackets. [e] 24.2 kcal/mol at the B3LYP/6-311+G**//B3LYP/6-31G* level.

B3LYP barrier height for the oxidation of isobutane is somewhat more sensitive to the basis set used. Calculations at the B3LYP/6-311+G**//B3LYP/6-31G* level lead to a barrier of 24.2 kcal/mol that is close to the CCSD(T)/6-31G* value of 22.4 kcal/mol (Table 3). These combined data show that B3LYP calculations are capable of providing reliable estimates for the transition structures and activation barriers for alkane oxidations with dioxiranes.

Calculations following the intrinsic reaction coordinate (IRC)[25] for **TS-1**−**TS-3** have shown a monotonic decrease in energy and resulted in the formation of the suggested products and reactants (in reverse following). No distinct radical intermediates or second transition structures were found. The oxidation of isobutane by DMDO (**TS-3**) exhibits extensive C−H bond elongation ($R_{C-H} = 1.51$ Å) consistent with the kinetic isotope effect for oxygen insertion into a tertiary C−H bond (k_H/k_D ca. 5).[1a] The approximate orientation of the migrating hydrogen is above the plane of the dioxirane ring. However, with an increasing degree of alkyl substitution the TS becomes more planar ("butterfly") with $O_1-C_1-O_2-H$ dihedral angles in **TS-1**, **TS-2**, and **TS-3** of 144, 150, and 167°. Further support for a concerted reaction comes from examination of the vector of the single negative eigenvalue of the Hessian for **TS-3**. Animation of the vector shows largely migration of the hydrogen due to its lower mass, but clearly exhibits a discernible movement of the oxygen (O_2) toward the tertiary carbon center after the O−H bond is nearly completely formed ($R_{O-H} = 1.05$ Å). The C_1-O_1 and C_1-O_2 bond distances (1.312 and 1.524 Å) also reflect a developing carbonyl group and a departing hydroxyl group. Such a TS represented by what is essentially an O−H group flanked by a tertiary carbon radical center and an oxygen radical should indeed exhibit biradicaloid character as depicted below:



Consistent with this suggestion, the total atomic spin density on O_1 is −0.63 while that on the carbon center (C_2) is 0.58. The electron spin density on the O−H oxygen (O_2) is −0.03. The NBO charges on O_1, C_2 atoms and on the O_2−H group (−0.538, 0.282, and 0.123) also suggest a TS with considerable charge separation. In the absence of a discrete radical intermediate such a TS by definition represents a concerted oxygen insertion process.

Table 4. Activation Barriers (kcal/mol) for the Oxidation of Prototypical Alkanes versus Alkenes with Dimethyldioxirane

computational level	alkanes CCSD(T)/B3LYP/6-31G*	alkenes B3LYP/6-31G*
methane/ethylene	44.2 (45.8)[a]	17.9[b]
propane/propene	30.3 (36.1)[a]	15.9
isobutane/isobutene	22.4 (32.0)[a]	15.4

[a] The barrier values calculated at the B3LYP/6-31G*//B3LYP/6-31G* level are shown in parentheses. [b] The barrier is 19.4 kcal/mol at the QCISD(T)/6-31G*//QCISD(full)/6-31G* level.

Table 5. Calculated Activation Barriers (kcal/mol) for the Oxidation of Methane with Substituted Dioxiranes

computational level	DO	DMDO	difluoro-dioxirane	TFDO
B3LYP/6-311+G(3df,2p)//B3LYP/6-311+G(3df,2p)	36.5[a]	41.2	21.2	35.0
G2(B3LYP/MP2/CC)	33.8		25.8[b]	

[a] 37.4 kcal/mol at the CCSD(T)/6-311G**//B3LYP/6-31G* level. [b] 18.5 kcal/mol at the G2(QCI/MP2/CC) level.[11a] The G2(QCI/MP2/CC) value without ZPE(B3LYP) corrections is 20.0 kcal/mol.

The oxidation barriers decrease from methane to isobutane similar to the trend in the activation barriers for the oxidations of alkenes (from ethylene to isobutene) with DMDO albeit the alkene oxidation barriers are significantly lower (Table 4). The reactions with DMDO have larger activation barriers than those with DO at the B3LYP level, but the oxidation of methane exhibits comparable barriers derived from the CCSD(T) method with use of B3LYP geometries (Table 5). The alkane oxidations with DFDO have larger exothermicities (Table 2) and lower activation barriers than with DO, DMDO, and TFDO (Tables 3 and 5, Figure 2).

The insertion of oxygen into the tertiary center in isobutane by DMDO proceeded with a barrier of only 22.4 kcal/mol at the CCSD(T)/6-31G*//B3LYP/6-31G* level. A correction for solvation ($CHCl_3$) with the SCIPCM model[26] at the B3LYP/6-311+G(d,p)//6-31G* level reduces the barrier for this reaction from 24.2 kcal/mol in the gas phase to 15.6 kcal/mol, which is as anticipated slightly higher than the $\Delta H^{\ddagger}$ of 11.3 kcal/mol reported for the selective hydroxylation of (−)-2-phenylbutane by TFDO. When this hydroxylation is accomplished with DMDO, it proceeds with complete retention of configuration and no loss of optical activity. At the B3LYP/6-311+G(3df,2p)//B3LYP/6-311+G(3df,2p) level, the barriers for the oxidation of methane with DO, DMDO, DFDO, and TFDO are 36.5, 41.2, 21.2, and 35.0 kcal/mol. The lower barrier for the

---

(24) While the RB3LYP/6-31G* solution for the transition structure for the oxidation of methane with DO exhibits an RHF → UHF wave function instability,[14] calculations with the stable UB3LYP wave function lead to a decrease in energy only of 1.9 kcal/mol. This indicates that the RHF wave function is very close to the stability threshold. Our calculations on oxidation reactions with dioxiranes and peroxyformic and peroxynitrous acids have shown that in cases of an RHF → UHF wave function instability for transition structures when the energy gap between unstable RB3LYP and stable UB3LYP solutions is small, the activation barriers calculated at the QCISD(T)//B3LYP level are close to those computed at the QCISD(T)//QCISD level of theory.

(25) Gonzalez, C.; Schlegel, H. B. *J. Chem. Phys.* **1989**, *90*, 2154.

(26) Foresman, J. B.; Keith, T. A.; Wiberg, K. B.; Snoonian, J.; Frisch, M. J. *J. Phys. Chem.* **1996**, *100*, 16098.

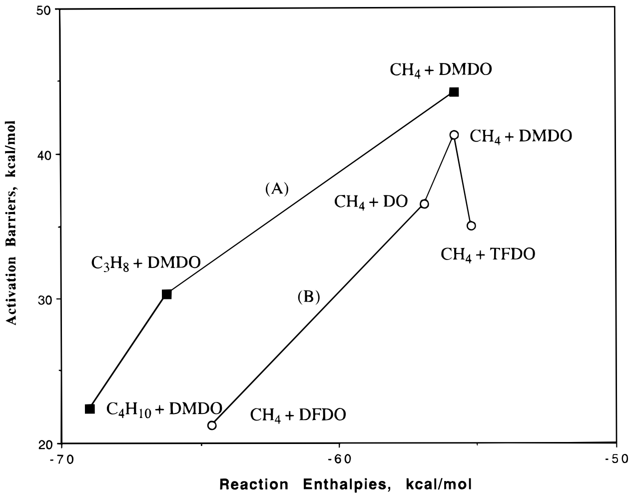


Figure 2. Plot of the activation energies for alkane oxidations versus their reaction enthalpy changes. The activation barriers for oxidations of methane, propane, and isobutane with DMDO (polyline A) were calculated at the CCSD(T)/6-31G*//B3LYP/6-31G* level. The barrier heights for the oxidations of methane with DO, DMDO, DFDO, and TFDO (polyline B) were calculated at the B3LYP/6-311+G(3df,2p)//B3LYP/6-311+G(3df,2p) level. The reaction enthalpy changes (Table 2) were computed with G2 theory (G2(MP2) theory for reactions with TFDO).

oxidation of methane with difluorodioxirane agrees with experimental findings that electron-withdrawing groups on the peroxide moiety result in an increase in its reactivity. The B3LYP/6-311+G(3df,2p)//B3LYP/6-311+G(3df,2p) calculated activation barrier for the oxidation of methane with TFDO, which has a much higher reactivity (up to several thousands times) than DMDO, is 6.2 kcal/mol lower than the barrier for the oxidation with DMDO (Table 5). It is notable that the differences in the activation barriers do not correlate with the enthalpy changes in oxidations with DMDO and TFDO, which are close (Table 1).

4. Summary

Our computational study provides a rationale for the formation of products derived from free radical intermediates in the absence of dioxygen and lends strong support to the generally accepted, highly exothermic, concerted oxygen insertion mechanism for the oxidation of alkanes with dioxiranes under typical preparative conditions.

Acknowledgment. This work was supported by the National Science Foundation (Grant CHE 96-96216). We are also thankful to the National Center for Supercomputing Applications (Urbana, IL) and the Pittsburgh Supercomputing Center for generous amounts of computer time.

Supporting Information Available: G2 and G2(MP2) energies of the species given in eqs 1−3 (Table 1) and products of alkane oxidations with dioxiranes (2 pages, print/PDF). See any current masthead page for ordering information and Web access instructions.

JA9813156