

Transition States for Alkane Oxidations by Dioxiranes

Xiaohui Du and K. N. Houk*

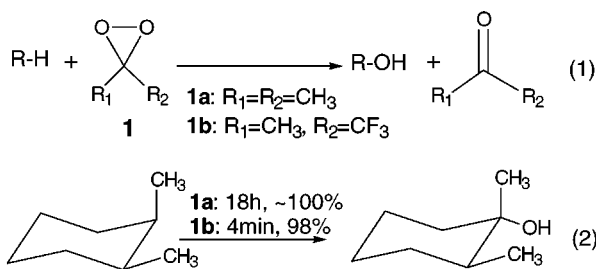
Department of Chemistry and Biochemistry, University of California, Los Angeles, California 90095-1569

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The mechanism of the oxygen insertion by dioxiranes into alkane C–H bonds has been investigated theoretically. Becke3LYP hybrid DFT calculations with the 6-31G* basis set on the reactions of dioxirane and cyanodioxirane with methane and on the reactions of cyanodioxirane with ethane, propane, and isobutane predict that the reactions are concerted with highly asynchronous transition states. The transition states have considerable diradical character, but are polarized as well. Substituent effects, stereoselectivity, and the possibility of the formation of radical pairs are discussed.

Introduction

Dioxiranes are powerful oxidants which react with a variety of functionalities under mild conditions.¹ Among these transformations, the oxygen insertions into unactivated alkane C–H bonds by dimethyl dioxirane, **1a**, and methyl(trifluoromethyl)dioxirane, **1b**, are especially remarkable (eq 1).² Methyl(trifluoromethyl)dioxirane reacts as much as 700 times faster than dimethyl dioxirane (eq 2).^{2c–e}



Controversy has surrounded mechanisms proposed to account for the formation of alcohols. One of the mechanisms proposed is a concerted electrophilic oxygen insertion process which involves an “oxenoid” transition state (Scheme 1).^{2c,d} An alternate radical mechanism involves hydrogen abstraction from the alkane by the ring-opened dioxymethane biradical and collapse of the radical pair in the solvent cage.³

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Recently, Minisci et al. proposed a “molecule-induced homolysis” mechanism, where a radical pair intermediate is formed in a single step, with no prior homolysis of the O–O bond.^{3e} It was proposed that the lifetime of the radical pair might be too short to allow detection.

The concerted mechanism is supported by the high regioselectivity^{2a,c,e} (tertiary over secondary and secondary over primary C–H bonds), stereoselectivity^{2d,4} (100% retention of configuration), kinetics^{2a–c,5} (second-order kinetics, first-order each in dioxirane and in alkane), solvent effects^{2b} (reaction rate is solvent-dependent), and primary isotope effects.^{2a,c,6} The radical mechanism is supported by the formation of some radical-derived products in these reactions, such as the formation of alkyl bromides^{3a} after adding CBrCl₃ to the normal reaction medium. The formation of radical-derived products is inhibited when the reactions are carried out in the presence of oxygen or other radical traps.^{3c}

In 1993, Bach et al. proposed a unifying mechanism for electrophilic oxygen atom insertion into hydrocarbons with a FMO approach supported by ab initio molecular orbital calculations.⁷ Water oxide was used as a model for the oxidizing reagents such as cytochrome P-450, dimethyldioxirane, and methyl(trifluoromethyl)dioxirane. However, for this type of reaction, water oxide is a somewhat remote model, and competing diradical mechanisms could not be studied with the method used.

In this paper, we report our study of the mechanism of oxidation of alkanes by dioxiranes using dioxirane and cyanodioxirane as models. A concerted transition state with OH abstraction much more advanced than OC bond formation (Figure 1) has been found.

Methods

All calculations were performed with Gaussian 94.⁸ Stationary points (energy minimum, all positive eigenvalues of the Hessian matrix, and transition state, one negative eigenvalue of the Hessian matrix) on the potential energy surface

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Scheme 1. Proposed Mechanisms for Alkane Oxidations by Dioxiranes

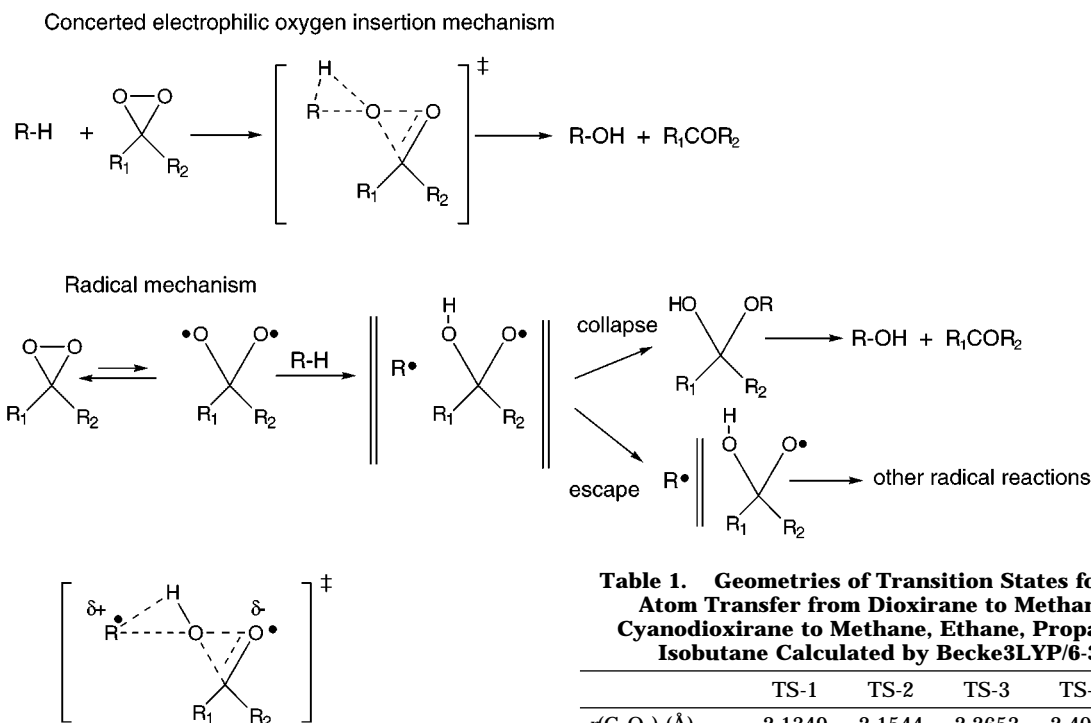


Figure 1. Representation of the asynchronous transition state found by our calculations.

were fully optimized using the Becke3LYP⁹ DFT¹⁰ method. The 6-31G* basis set was used throughout. The value⁵ of the activation energies calculated by this method were checked for the transition state of dioxirane with methane and cyanodioxirane with methane by quadratic configuration interaction with perturbative corrections for triple excitation single point energy calculations on the Becke3LYP geometry (QCISD(T)/6-31G*/Becke3LYP/6-31G*).

All the stationary points were examined with vibrational analyses. The transition states were characterized by a single imaginary frequency.

Results and Discussion

High levels of theory, such as multiconfigurational SCF, configuration interaction, and coupled cluster methods, usually coupled with large basis sets, are frequently employed for studies of dioxirane and isomers such as dioxymethane and carbonyl oxide.¹¹ Such expensive levels of theory are still impractical for large molecular systems such as the transition structures studied here, but MP2 and Becke3LYP methods coupled with moder-

Table 1. Geometries of Transition States for Oxygen Atom Transfer from Dioxirane to Methane and Cyanodioxirane to Methane, Ethane, Propane, and Isobutane Calculated by Becke3LYP/6-31G*

	TS-1	TS-2	TS-3	TS-4	TS-5
$r(\text{C}_1\text{O}_2)$ (Å)	2.1349	2.1544	2.2653	2.4070	2.4732
$r(\text{C}_1\text{H}_9)$ (Å)	1.4243	1.3883	1.4078	1.4409	1.3243
$r(\text{O}_2\text{H}_9)$ (Å)	1.0858	1.1022	1.0922	1.0745	1.1654
$r(\text{O}_2\text{O}_3)$ (Å)	2.0122	2.1080	2.0347	2.0613	1.9665
$r(\text{O}_2\text{C}_4)$ (Å)	1.5165	1.5058	1.4844	1.4638	1.4325
$r(\text{O}_3\text{C}_4)$ (Å)	1.3006	1.2955	1.3009	1.3046	1.3206
$\angle\text{C}_1\text{O}_2\text{O}_3$ (deg)	163.1	162.2	161.7	158.2	161.7
$\angle\text{C}_1\text{H}_9\text{O}_2$ (deg)	115.9	119.3	129.7	145.9	166.8
$\angle\text{O}_2\text{C}_4\text{O}_3$ (deg)	90.8	91.9	93.6	96.1	91.1

ately sized basis sets have been successfully applied for the study of oxidation of sulfides,¹² primary amines,¹³ and alkenes,^{11b,14} by dioxiranes. For alkene epoxidations, Becke3LYP and QCISD are in good agreement, whereas MP2 optimizations^{11b} overemphasize diradical stabilities. We apply Becke3LYP DFT method in our calculations on CH insertion. Studies of some of the same, and related, systems with MP2/6-31G*, QCISD(T)/6-31G*/MP2/6-31G*, and MP2/6-311+G* calculations showed good agreement with our DFT calculations.¹⁵

We first studied the reaction of dioxirane with methane. In the transition state **TS-1** of the reaction of dioxirane with methane calculated by Becke3LYP/6-31G* (Figure 2 and Table 1), the $\text{O}_2\text{-H}_9$ bond is almost completely formed at 1.09 Å, the $\text{C}_1\text{-H}_9$ bond is substantially broken (1.42 Å), and the $\text{O}_2\text{-C}_1$ interaction (2.13 Å) is very weak. There is little cleavage of the dioxirane CO bond in the transition structure, and the two three-membered rings adopt a spiro arrangement.

To model more reactive, electron-deficient species such as fluorinated dioxiranes, we studied the reaction of

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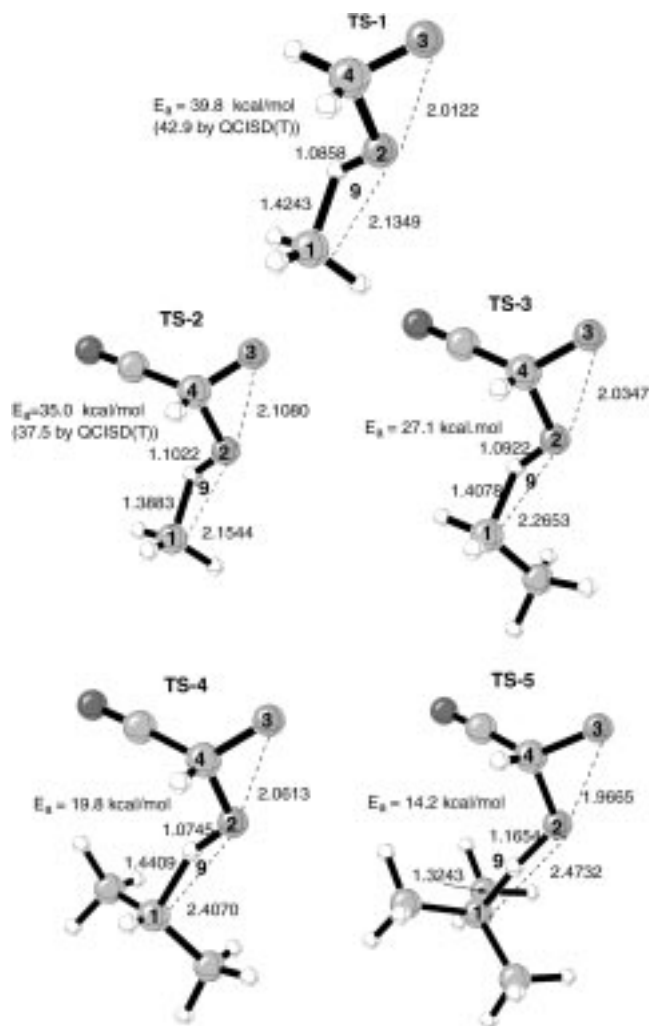


Figure 2. Transition states and activation energies (zero point energies correction included) for reactions of dioxirane with methane and cyanodioxirane with methane, ethane, propane, and isobutane at Becke3LYP/6-31G*. Activation energies in parentheses represent QCISD(T)/6-31G*//Becke3LYP/6-31G* values.

cyanodioxirane. The insertion reactions of cyanodioxirane with methane, ethane, propane, and isobutane were examined with Becke3LYP/6-31G* calculations. All the transition states have similar geometries to the parent reaction with more O₂-H₉ than O₂-C₁ bond formation (Figure 2 and Table 1). All of the geometries are "spiro", with the plane of the dioxirane nearly orthogonal to that defined by the breaking CH bond and the transferring O.

From the transition state **TS-2** of the reaction of cyanodioxirane and methane, an intrinsic reaction coordinate verifies the concerted nature of the reaction. Following the reaction path toward reactants produces complex **A** (Figure 3), while the reaction coordinate in the product direction leads directly to product complex **B**. The concerted insertion of an oxygen atom explains why these reactions are stereospecific with retention of configuration.

There is reasonably good agreement between the activation energies calculated on **TS-1** and **TS-2** by Becke3LYP/6-31G* and QCISD(T)/6-31G*//Becke3LYP/6-31G*. The values by Becke3LYP/6-31G* are consistently lower by about 3 kcal/mol (Figure 2).

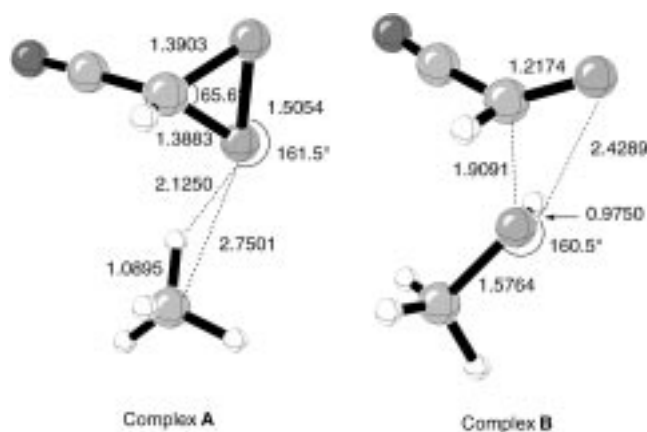


Figure 3. End geometries of intrinsic reaction coordinate search for reactions of cyanodioxirane with methane.

There is a 4.8 kcal/mol decrease in activation energy (Becke3LYP) upon cyano substitution on dioxirane in the reaction with methane. The electron-withdrawing cyano group renders the dioxirane molecule more electrophilic. The activation energy also decreases considerably with increased alkyl substitution on the alkane. The activation energies are 35.0, 27.1, 19.8, and 14.2 kcal/mol for the reaction with methane, ethane, propane, and isobutane, respectively. The experimental activation energy found for conversion of cyclohexane to cyclohexanone^{2c} with methyl(trifluoromethyl)dioxirane **1b** is 14.3 kcal/mol in CH₂Cl₂/CF₃COCH₃ and 11.3 kcal/mol for oxidation of (*R*)-2-phenylbutane with **1b** in CF₃COCH₃.^{2d} The relative stabilities of methyl, ethyl, isopropyl, and *tert*-butyl radicals are 0, -6, -9, and -12 kcal/mol while those of carbocations are 0, -35.8, -54.8, and -69.0 kcal/mol.¹⁶ The differences between the energies of the oxidation transition states with the corresponding alkanes (0, -7.9, -15.2, and -20.8 kcal/mol) are closer to those of radicals than those of carbocations, but are intermediate between the radical and cation stabilities. Thus, the transition states have some diradical character, but are polarized considerably. The charges on the alkane fragments in the transition states are +0.06, +0.12, +0.18, +0.26, and +0.21, indicating that the transition states have partial ionic character which increases as the carbocation is stabilized. The charge separation decreases some for the last example, because the transition state becomes earlier.

With the increase of alkyl substitution, the C₁-H₉-O₂ angle changes from 119° in the reaction of cyanodioxirane with methane to 167° with isobutane. The C-H-O angle for hydrogen abstraction by the hydroxy radical from methane is 171° by Becke3LYP/6-31G(2d,2p) methods.¹⁷ The dioxirane oxygen is more electrophilic than the hydroxyl radical oxygen, and the corresponding C₁-H₉-O₂ angle is less than 171° in the transition state. The increase in the C₁-H₉-O₂ angle with the increase of carbon substitution and the principal interaction of O with H, not C, are consistent with the diradical character of the transition state.

Single point energy calculations on the transition states using unrestricted Becke3LYP/6-31G* calculations give slightly lower energies than those obtained by

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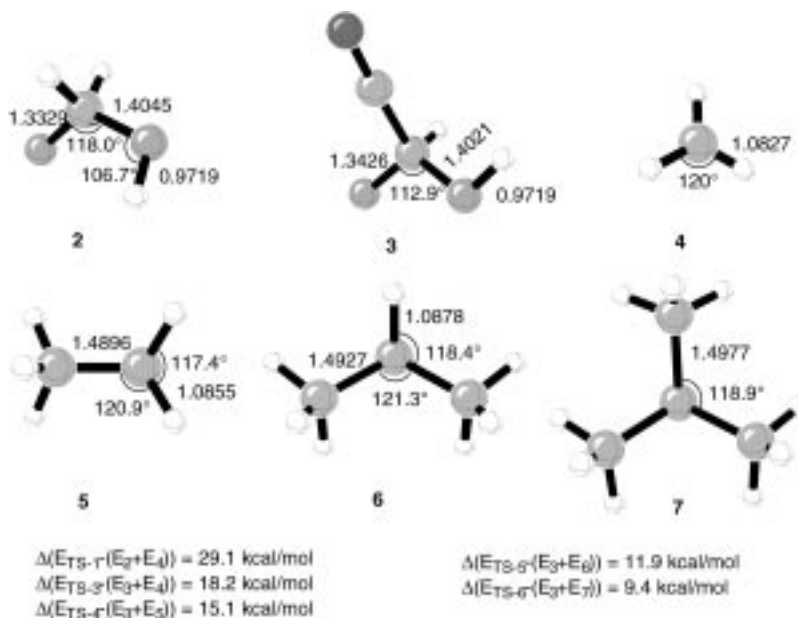


Figure 4. Geometries of possible intermediate radical pairs and their energy difference (zero point energies correction included) with the corresponding transition states.

restricted Becke3LYP/6-31G* calculations. This is another reflection of the diradical character of the transition states. The difference is 1.9 for the reaction of dioxirane with methane and becomes 1.5, 3.0, 4.9, and 3.1 kcal/mol for the reactions of cyanodioxirane with methane, ethane, propane, and isobutane, respectively. However, MP2 and QCI calculations for the parent reaction allow little variation in geometry,¹⁵ so the geometries were not optimized in the substituted cases.

Radical pair energies were obtained by summing the energies of separate radical components calculated by Becke3LYP/6-31G* (Figure 4). They are lower than the energies of the corresponding transition states. Therefore it is energetically feasible for radical pairs to form after the transition state, but direct collapse to the alcohol product occurs instead. The transition state indeed resembles that proposed by Minisci,^{3e} but no discrete radical pairs are predicted by these calculations.

Previous calculations indicate that dioxirane ring opening into the π,π -dioxymethane biradical (the ground state for dioxymethane biradical) is endothermic by about 12 kcal/mol.^{11b,d} The activation barrier for such ring opening is 23.2 kcal/mol^{11b} by QCISD(T)/6-31G*/MP2/6-31G* or 25.4 kcal/mol^{11d} by CASSCF/CASPT2.¹⁸ This barrier is higher than the activation energies to form the oxidation transition states of secondary and tertiary alkanes (19.8 kcal/mol for cyanodioxirane with propane and 14.2 kcal/mol for cyanodioxirane with isobutane). Therefore, the oxygen insertions into secondary and tertiary alkanes are concerted processes, and the higher activation energy reaction of methyl and primary CH

bonds can be a stepwise process involving the methyl-enedioxy intermediate.

In summary, our calculations support the concerted electrophilic oxygen insertion mechanism shown in Scheme 1. An asynchronous transition state (represented by the structure shown in Figure 1) having diradical character has been found for the oxygen insertion of dioxirane into alkane C–H bonds. A total of six bonds are either being broken or being formed at the transition state. Although qualitatively like the models proposed of Curci^{2c} and Bach,⁷ the transition states have much more OH than CO bonding, in contrast to previous models. This, and the polarized nature of the transition state, cause the concerted oxygen insertions into tertiary CH bonds to be highly favored.¹⁹

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Supporting Information Available: Table of total energies, zero-point correction energies (Becke3LYP and QCISD(T)) for reactants, transition states, and radicals (1 page). 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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