

Establishing the (3 + 2) Mechanism for the Permanganate Oxidation of Alkenes by Theory and Kinetic Isotope Effects

K. N. Houk*[†] and Thomas Strassner*

Department of Chemistry and Biochemistry, University of California, Los Angeles, California 90095-1569, and Department of Inorganic Chemistry, Technical University Munich, Lichtenbergstrasse 4, D-85747 Garching, Germany

Received August 3, 1998

Permanganate hydroxylation follows the (3 + 2) cycloaddition mechanism established earlier for osmium tetroxide. Density functional theory (Becke3LYP/6-31G*) predicts that the concerted (3 + 2) pathway is favored by about 40 kcal/mol relative to a stepwise process involving a (2 + 2) cycloaddition. The activation energy for the (3 + 2) transition state is calculated to be only 9.2 kcal/mol. The energetics are remarkably similar to the results for osmylation, where the activation energies are calculated to be 3.2 kcal/mol for the (3 + 2) and 44.1 kcal/mol for the (2 + 2) transition state. Calculated kinetic isotope effects for a substituted case are in good agreement with experiment.

The mechanism of the oxidation of alkenes by permanganate is believed to be similar to the oxidation of alkenes by OsO₄, even though the reaction rates are influenced differently by donor and acceptor olefins.¹ The concerted (3 + 2) mechanism was generally favored, until the suggestion was made of a stepwise mechanism involving a metallaoxetane intermediate.² Much discussion of osmylations has ensued in the literature in recent years.³ For osmylations, theoretical studies predict that the (3 + 2) mechanism is favored.⁴ A recent study successfully predicted the experimental kinetic isotope effects from calculations of the corresponding transition states by high level density functional theory calculations, providing strong evidence for the (3 + 2) mechanism.^{5,6} Here we apply similar methods to the related permanganate oxidation.

Experimental studies of the oxidative cleavage of cinnamic acid by acidic permanganate⁷ gave secondary kinetic isotope effects, k_H/k_D , of 0.77 (α) and 0.75 (β), whereas a later paper from the same group on the same reaction with quaternary ammonium permanganates⁸ reported very different isotope effects of 1.0 (α) and 0.91–0.94 (β), depending on the counterion. Different mecha-

nisms were discussed in the literature⁹ to explain the variety of experimental results available, but the mechanistic issues are unresolved.

The density functional/Hartree–Fock hybrid model Becke3LYP^{10,11} implemented in GAUSSIAN-94¹² has been used throughout this study. The split valence double- ζ (DZ) basis set 6-31G* has been employed in the DFT calculations together with a triple- ζ (TZ)¹³ valence basis set for manganese. The wave functions were all stable with respect to unrestricted (UB3LYP) calculations.

The same reaction pathways are possible for permanganate as are available for osmium tetroxide. The reaction can proceed as a one-step (3 + 2) reaction or a stepwise (2 + 2) mechanism involving a rearrangement of the manganooxetane to the five-membered intermediate, as shown in Scheme 1. Electron-transfer processes have also been proposed for reactions of other manganese oxo species.

We calculated the products and transition states for both pathways. The structures and relative energies are shown in Figure 1.

The (3 + 2) pathway is favored by about 40 kcal/mol! The activation energy for the (3 + 2) transition state is calculated to be only 9.2 kcal/mol. The energetics are remarkably similar to the results for osmylation, where the activation energies are calculated to be 3.2 kcal/mol for (3 + 2) and 44.1 kcal/mol for the (2 + 2) transition state.

[†] University of California.

(1) (a) Waters, W. A. *Quart. Rev.* **1958**, *12*, 29. (b) Henbest, H. B.; Jackson, W. R.; Robb, B. C. G. *J. Chem. Soc. B* **1966**, 803.

(2) Sharpless, K. B.; Teranishi, A. Y.; Bäckvall, J. E. *J. Am. Chem. Soc.* **1977**, *99*, 3120.

(3) (a) Corey, E. J.; Noe, M. C. *J. Am. Chem. Soc.* **1993**, *115*, 5, 12579. (b) Göbel, T.; Sharpless, K. B. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 1329. (c) Becker, H.; Ho, P. T.; Kolb, H. C.; Loren, S.; Norrby, P.-O.; Sharpless, K. B. *Tetrahedron Lett.* **1994**, *35*, 7315. (d) Corey, E. J.; Noe, M. C.; Grogan, M. J. *Tetrahedron Lett.* **1996**, *37*, 4899. (e) Vanhessche, K. P. M.; Sharpless, K. B. *J. Org. Chem.* **1996**, *61*, 7978. (f) Corey, E. J.; Sarshar, S.; Azimioara, M. D.; Newbold, R. C.; Noe, M. C. *J. Am. Chem. Soc.* **1996**, *118*, 7851.

(4) (a) Pidun, U.; Boehme, C.; Frenking, G. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 2817. (b) Dapprich, S.; Ujaque, G.; Maseram, F.; Lledos, A.; Musaev, D. G.; Morokuma, K. *J. Am. Chem. Soc.* **1996**, *118*, 11660. (c) Torrent, M.; Dend, L.; Duran, M.; Sola, M.; Ziegler, T. *Organometallics* **1997**, *16*, 13.

(5) DelMonte, A. J.; Haller, J.; Houk, K. N.; Sharpless, K. B.; Singleton, D. A.; Strassner, Th.; Thomas, A. A. *J. Am. Chem. Soc.* **1997**, *119*, 9907.

(6) The mechanistic debate and its resolution were recently reported: Rouhi, M. *Chem. Eng. News* **1997**, *75*, 23.

(7) Lee, D. G.; Brownridge, J. R. *J. Am. Chem. Soc.* **1974**, *96*, 5517.

(8) Lee, D. G.; Brown, K. C. *J. Am. Chem. Soc.* **1982**, *104*, 5076.

(9) (a) Wolfe, S.; Ingold, C. F.; Lemieux, R. U. *J. Am. Chem. Soc.* **1981**, *103*, 938. (b) Simandi, L. I.; Jáky, M. *J. Am. Chem. Soc.* **1976**, *98*, 1995.

(10) Lee, C.; Yang, W.; Parr, R. G. *Phys. Rev. B* **1988**, *37*, 785.

(11) Becke, A. D. *J. Chem. Phys.* **1992**, *97*, 9173. (b) Becke, A. D. *J. Chem. Phys.* **1993**, *98*, 1372. (c) Becke, A. D. *J. Chem. Phys.* **1993**, *98*, 5648.

(12) Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Gill, P. M. W.; Johnson, B. G.; Robb, M. A.; Cheeseman, J. R.; Keith, T.; Petersson, 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.; Chen, W.; Wong, M. W.; Andres, J. L.; Replogle, E. S.; Gomperts, R.; Martin, R. L.; Fox, D. J.; Binkley, J. S.; Defrees, D. J.; Baker, J.; Stewart, J. P.; Head-Gordon, M.; Gonzalez, C.; Pople, J. A. *Gaussian 94, Revision B.2*; Gaussian, Inc.: Pittsburgh, PA, 1995.

(13) Schäfer, A.; Huber, C.; Ahlrichs, R. *J. Chem. Phys.* **1994**, *100*, 5829.

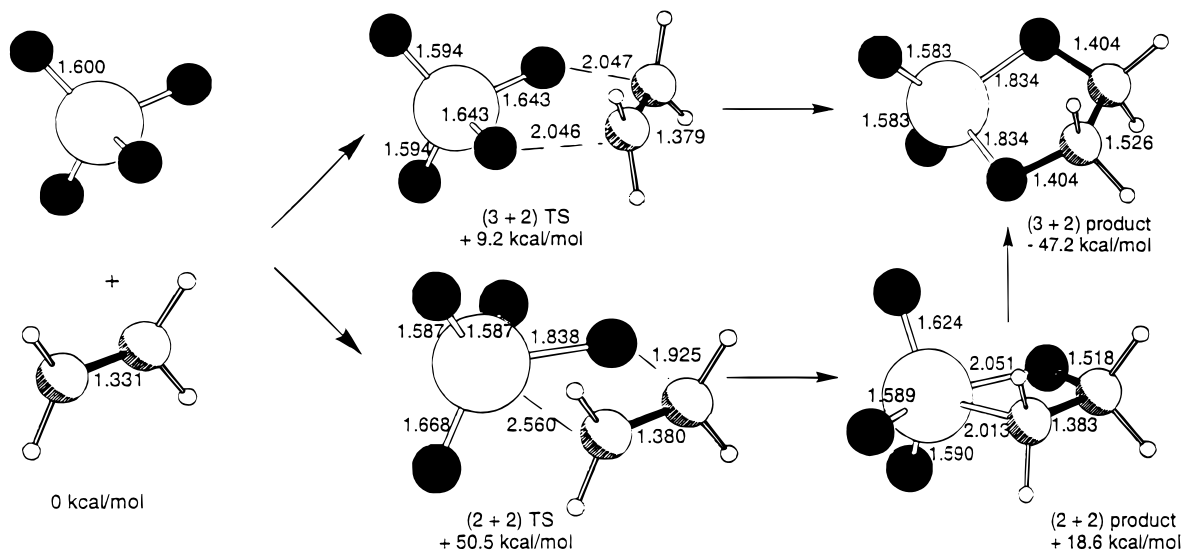
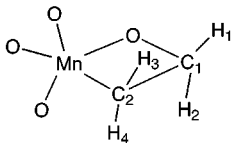
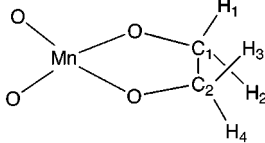
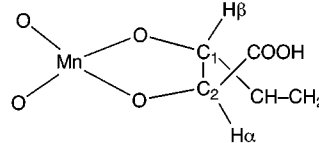
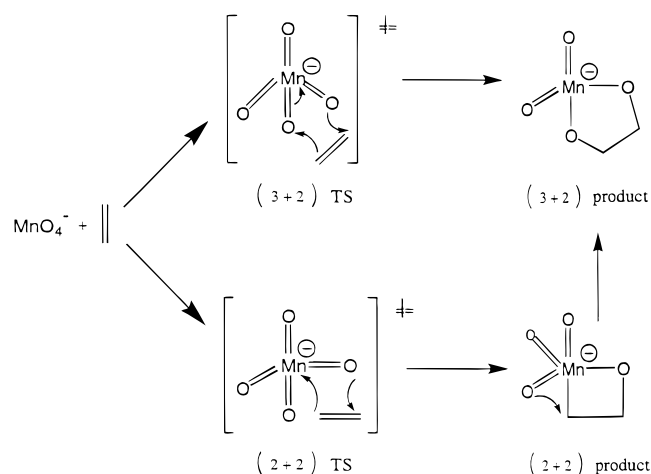


Figure 1. Calculated results for both pathways. Relative energies are shown below the structures.

Table 1. Theoretical $^{12}\text{C}/^{13}\text{C}$ and $^1\text{H}/^2\text{H}$ Kinetic Isotope Effects (298.15 K)¹⁶

					
(2 + 2) TS	KIE	(3 + 2) TS	KIE	(3 + 2) product	KIE
C ₁	1.021	C ₁	1.024	C ₁	1.033
C ₂	1.014	C ₂	1.024	C ₂	1.016
H ₁	0.964	H ₁	0.963	H _α	0.971
H ₂	0.964	H ₂	0.964	H _β	0.923
H ₃	1.009	H ₃	0.966		
H ₄	1.009	H ₄	0.965		

Scheme 1: Possible Reaction Pathways



Because the (2 + 2) adduct will not be formed, we did not explore the rearrangement surface. DFT is capable of predicting a (2 + 2) mechanism when it is favored; the (2 + 2) transition state for the reaction of SO_3 with ethylene is predicted by B3LYP calculations to be lower in energy than the (3 + 2) transition state,¹⁴ in accord with experiment.¹⁵

We also calculated the (3 + 2) transition state of a substituted model system to compare computed with

experimental kinetic isotope effect data for *trans*-cinnamic acid. To model this reaction we chose *trans*-2,4-pentadienoic acid as the alkene. The activation energy for that reaction is calculated to be 3.1 kcal/mol. This is in excellent agreement with the published experimental value of 4.2 kcal/mol for *trans*-cinnamic acid.⁷

The calculated transition state shown in Figure 2 is very asynchronous. One CO-forming bond is 0.23 Å longer than the other. The anionic species acts as a nucleophile, with the shorter bond β to the carbonyl group. The reaction is still concerted, with the average bond length equal to the bond length of the synchronous reaction of permanganate with ethylene.

Kinetic isotope effects were calculated for the reaction of permanganate with ethene and *trans*-2,4-pentadienoic acid to compare them to published kinetic isotope effects. The methodology used has been described elsewhere.^{5,16} On the basis of the transition states shown in Figures 1 and 2, the theoretical isotope effects were calculated. The results are shown in Table 1.

The deuterium and carbon isotope effects for the (3 + 2) reaction of ethylene are similar to those found earlier⁵ for the OsO_4NH_3 reaction, 2.4% normal KIE for C and

(15) Groves, J. J.; Kruper, W. J., Jr.; Haushalter, R. C. *J. Am. Chem. Soc.* **1980**, *102*, 6375. Finney, N. S.; Pospisil, P. J.; Chang, S.; Palucki, M.; Konsler, R. G.; Hansen, K. B.; Jacobsen, E. N. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 1720.

(16) Calculated with the program QUIVER (Saunders, M.; Laidig, K. E.; Wolfsberg, M. *J. Am. Chem. Soc.* **1989**, *111*, 8989) with frequencies scaled by 0.9614 (Scott, A. P.; Radom, L. *J. Phys. Chem.* **1996**, *100*, 16502).

(14) Haller, J.; Beno, B. R.; Houk, K. N. *J. Am. Chem. Soc.* **1998**, *120*, 6468.

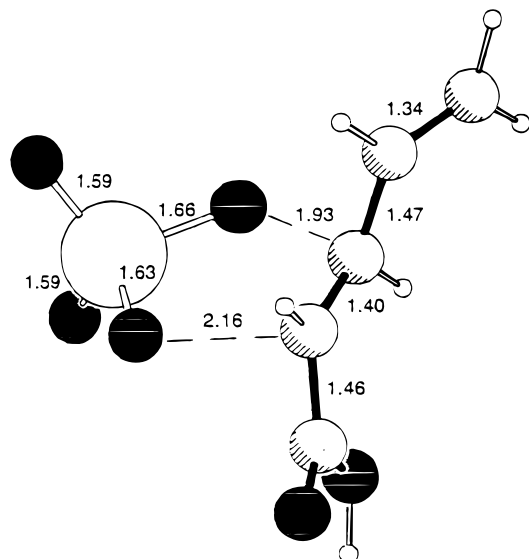


Figure 2. Transition state geometry for the (3 + 2) addition to *trans*-2,4-pentadienoic acid.

4% inverse KIE for D. For the substituted case, the asynchronicity causes the carbon isotope effect to be larger at C₁, where much more hybridization change occurs, and somewhat smaller at C₂. This explains why an inverse secondary isotope effect was observed in the β-position but not in the α-position of the vinylic system.

The experimental kinetic isotope effects, k_H/k_D (295.15 K), are dependent on the counterion and were measured to be 1.0 for C_α and 0.91 (tetra-*n*-butylammonium permanganate) or 0.94 (*p*-fluorobenzyl)triethylammonium permanganate) for C_β.⁸

The kinetic isotope effects reported earlier⁷ were measured for oxidation in acidic solution, where the five-membered intermediate manganate ester decomposes rapidly to give manganese(III) plus cleavage products. Other reactions ensue, but these have not been studied here.

Density functional calculations strongly favor the (3 + 2) pathway for permanganate oxidations under basic conditions. No direct interaction of the transition metal with the alkene is necessary to explain the different kinetic isotope effects for the C_α and C_β atoms. The permanganate transition structure with ethene is nearly the same as that for OsO₄, and differences in substituent effects may be attributed to charge differences between the reagents.

Acknowledgment. We are grateful to the Deutsche Forschungsgemeinschaft for a fellowship to T.S., to the National Institute of General Medical Sciences, National Institutes of Health, for financial support of this research, and to Professors Seth Brown and Daniel Singleton for helpful discussions.

JO981548F