11660 *J. Am. Chem. Soc.* **1996,** *118,* 11660−11661

Theory Does Not Support an Osmaoxetane Intermediate in the Osmium-Catalyzed Dihydroxylation of Olefins

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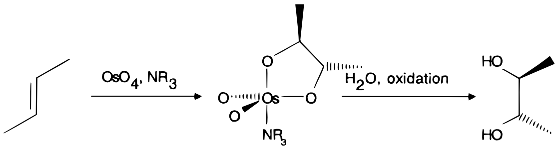
Received July 29, 1996

The osmium-catalyzed asymmetric dihydroxylation of olefins (Scheme 1) is a highly efficient and experimentally well-studied example of the application of transition metal complexes for practical syntheses of biologically important compounds.[1] Its outstanding selectivity and broad scope is unique for an organic reaction. However, despite the large number of experimental studies a conclusive determination of the reaction mechanism has not yet been achieved.[1−4] On the contrary, a certain controversy on the subject can be found in recent chemical literature.[4,5] At this point, two major pathways for the formation of the cyclic ether intermediate are supported by different experimental data provided by different research groups.

One pathway postulates an initial [2 + 2] cycloaddition leading to an osmaoxetane intermediate, followed by a rearrangement to a five-membered ring, the osmium(VI) glycolate product.[2,6] Kinetic studies have shown a nonlinear temperature−enantioselectivity relationship, strongly supporting the presence of an intermediate on the reaction pathway and at least two selectivity-determining steps.[7] The other suggested pathway is a concerted [2 + 3] cycloaddition, leading directly to the formation of the primary product.[3,8−10] In cases where monodentate chiral bases were used, a rapid, reversible formation of an olefin−Os(VIII) *π*−*d* complex prior to the [2 + 3] cycloaddition step should appear.[5] This enzyme−substrate-like complexation has been shown to follow Michaelis−Menten kinetics.[5] However, none of the mechanisms have been proven directly, though a number of indirect evidence is accumulated in favor of each of them.

Scheme 1



Theoretical calculations have not yet been able to solve this controversy.[11−14] An *ab initio* study based on Hartree−Fock (HF) geometry optimizations could not locate the transition states (TS) because of the large effect of correlation energy.[12] Molecular mechanics have been able to explain experimental stereoselectivity in a satisfactory way.[4] Remarkably, the same qualitative results have been obtained through the assumption of each of the two possible mechanisms mentioned above.[13,14]

In this paper, we present the theoretically determined structures and energetics for the transition states and products for the [2 + 2] and [2 + 3] cycloaddition steps without base and with one and two NH_3 ligands as model bases. Figure 1 shows the calculated geometries and energies without base, and Figure 2 shows those with one and two NH_3 ligands. Experimental structures for some related cyclic ether intermediates are in very good agreement with our theoretical values. For example, the experimental Os−N distance (2.243 Å) for structure **8** (with a cinchona alkaloid ligand instead of NH_3) is in excellent agreement with our calculated value of 2.238 Å.[15] In complex **9** with pyridine as a coligand, the X-ray determined bond lengths are 1.72 Å for Os═O (1.781 Å calc.), 1.95 Å for Os−O (1.957 Å calc.), and 2.21−2.24 Å for Os−N (2.234 Å calc.).[16,17]

Without base, the formation of a four-membered ring **2** via [2 + 2] cycloaddition is calculated to be endothermic by 17.1 kcal/mol. The [2 + 3] cycloaddition leading to structure **4** is an exothermic process (−15.8 kcal/mol). The QCISD(T)//HF results by Veldkamp and Frenking[12] (+13.6 kcal/mol for the reaction $OsO_4 + C_2H_4 \rightarrow$ **2** and −16.7 kcal/mol for $OsO_4 + C_2H_4 \rightarrow$ **4**) are qualitatively in agreement with the present accurate energies at the CCSD(T) level. On the basis of the energies of the reaction, these authors concluded that the [2 + 2] addition intermediate was at least energetically accessible on the potential energy surface.

The optimized transition states **1** and **3** for the reaction pathways leading from the reactants to the intermediates **2** and **4** are also shown in Figure 1. Arrows indicate the eigenvectors of the imaginary frequency, showing the approach of each olefinic carbon center to its respective oxygen or osmium atom.

The activation barrier of 43.3 kcal/mol for the [2 + 2] pathway is very high. This result makes a [2 + 2] cyclization as an inital step of the osmium-catalyzed dihydroxylation highly unfavorable. In contrast, the activation barrier for the [2 + 3] addition is only 1.9 kcal/mol, which is even much lower than the energy of the [2 + 2] intermediate **2** (17.1 kcal/mol). The TS is very reactant-like with a carbon−oxygen distance of 2.365 Å. The carbon−carbon bond (1.374 Å) is slightly elongated in comparison with free ethene (1.348 Å). Our calculations strongly suggest that the osmium-catalyzed dihydroxylation involving a [2 + 2] cycloaddition step is practically impossible under base-free conditions. It was discovered very recently that similar results are obtained by Frenking and co-workers.[18]

Is this conclusion valid if bases are included? Figure 2 shows, in comparison with Figure 1, that the energetical changes of

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(1) Kolb, H. C.; VanNieuwenhze, M. S.; Sharpless, K. B. *Chem. Rev.* **1994**, *94*, 2483.
(2) Norrby, P.-O.; Kolb, H. C.; Sharpless, K. B. *Organometallics* **1994**, *13*, 344.
(3) Corey, E. J.; Noe, M. C.; Sarshar, S. *J. Am. Chem. Soc.* **1993**, *115*, 3828.
(4) Norrby, P.-O.; Becker, H.; Sharpless, K. B. *J. Am. Chem. Soc.* **1996**, *118*, 35.
(5) Corey, E. J.; Noe, M. C. *J. Am. Chem. Soc.* **1996**, *118*, 319.
(6) Sharpless, K. B.; Teranishi, A. Y.; Bäckvall, J.-E. *J. Am. Chem. Soc.* **1977**, *99*, 3120.
(7) Göbel, T.; Sharpless, K. B. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 1329.
(8) Criegee, R. *Justus Liebigs Ann. Chem.* **1936**, *75*, 522.
(9) Criegee, R.; Marchand, B.; Wannowius, H. *Justus Liebigs Ann. Chem.* **1942**, *550*, 99.
(10) Corey, E. J.; Jardine, P. D.; Virgil, S.; Yuen, P.-W.; Connell, R. D. *J. Am. Chem. Soc.* **1989**, *111*, 9243.
(11) Jørgensen, K. A.; Hoffmann, R. *J. Am. Chem. Soc.* **1986**, *108*, 1867.
(12) Veldkamp, A.; Frenking, G. *J. Am. Chem. Soc.* **1994**, *116*, 4937.
(13) Norrby, P.-O.; Kolb, H. C.; Sharpless, K. B. *J. Am. Chem. Soc.* **1994**, *116*, 8470.
(14) Wu, Y.-D.; Wang, Y.; Houk, K. N. *J. Org. Chem.* **1992**, *57*, 1362.
(15) Pearlstein, R. M.; Blackburn, B. K.; Davis, W. M.; Sharpless, K. B. *Angew. Chem., Int. Ed. Engl.* **1990**, *29*, 639.
(16) Hermann, W. A.; Eder, S. J.; Scherer, W. *Angew. Chem., Int. Ed. Engl.* **1992**, *31*, 1345.
(17) Cartwright, B. A.; Griffith, W. P.; Schröder, M.; Skapski, A. C. *Inorg. Chim. Acta* **1981**, *53*, L129.
(18) Pidun, U.; Boehme, C.; Frenking, G. *Angew. Chem.* **1996** In press.

S0002-7863(96)02599-1 CCC: $12.00

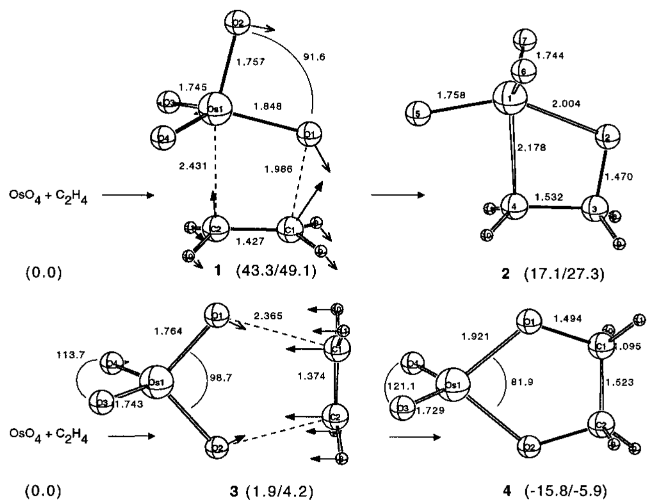

Figure 1. Optimized structures (in Å and deg) of the transition states and intermediates for the base-free osmylation reaction calculated at the B3LYP level of theory. Relative energies (in kcal/mol) and Gibbs free energies at 298 K (after a slash) at the CCSD(T)//B3LYP level are given in parentheses. The arrows at the transition states **1** and **3** are the reaction coordinate vectors.

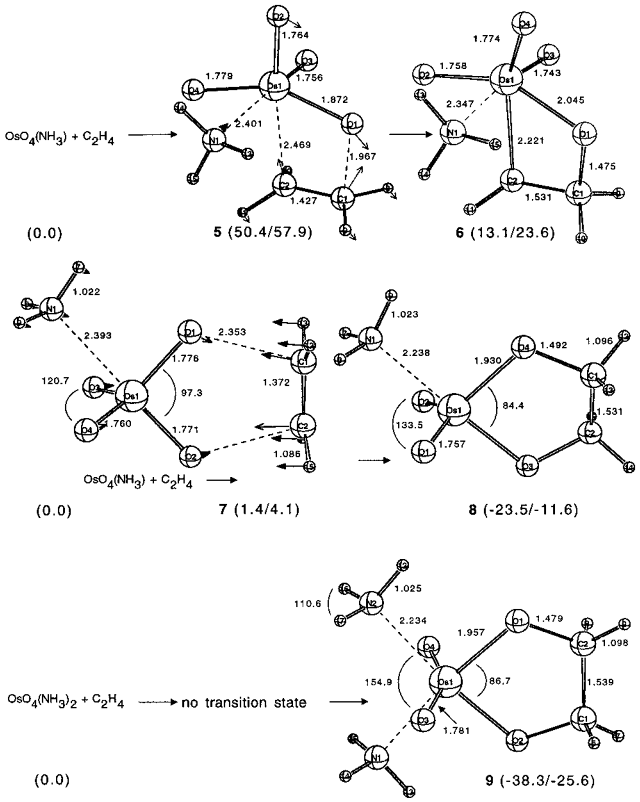

Figure 2. Optimized structures (in Å and deg) of the transition states and intermediates for the osmylation reaction including one and two NH_3 ligands calculated at the B3LYP level of theory. Relative energies (in kcal/mol) and Gibbs free energies at 298 K (after a slash) at the CCSD(T)//B3LYP level are given in parentheses. The arrows at the transition states **5** and **7** are the reaction coordinate vectors.

the reaction profile are minor if NH_3 is used in the theoretical calculations as a model base. Coordination of one NH_3 molecule stabilizes the four-membered ring **6** more with respect to the reactant than without NH_3; the reaction OsO_4 (NH_3) + C_2H_4 → **6** is now endothermic by only 13.1 kcal/mol. The activation barrier of 50.4 kcal/mol is even higher than under base-free conditions. The formation of the osmium(VI) glycolate ester **8** is more exothermic (−23.5 kcal/mol) than without NH_3 (−15.8 kcal/mol). In conjunction with a very low TS, which is only 1.4 kcal/mol higher than the reactants, these facts are compatible with the observation that the reaction is accelerated in the presence of bases.[9]

For the reaction path with two NH_3 ligands coordinated on osmium the formation of the [2 + 3] intermediate **9** is energetically favored by 38.3 kcal/mol. In this case, there is no energy barrier between the reactants and the product, and the reaction is simply downhill. With two NH_3 ligands, the four-membered intermediate would require a seven-coordinated metal atom, and a [2 + 2] mechanism is not possible.

Our calculations have clearly shown that *the reaction mechanism of the osmium-catalyzed dihydroxylation of olefins cannot involve a [2 + 2] intermediate, whether it is base-free or base-assisted.* Even when the Gibbs free energies are used, the conclusion is unchanged. At the present time, we do not have an alternative explanation of the observed nonlinear Eyring relationship, which is attributed to a stepwise process. An explanation might involve either interactions between the olefin and *large* bases used in experiment or important influences of solvent molecules. Work along this line is in progress. The mechanism of the osmylation reaction still remains as a challenge for both experiment and theory.

Computational Details. The geometry optimizations were carried out with the GAUSSIAN94 program[19] at the B3LYP level of density functional theory (DFT)[20,21] in conjunction with the LANL2DZ effective core potential and basis set.[22] Relative energies were obtained by single-point calculations at the CCSD(T)/LANL2DZ level[23] using the B3LYP-optimized geometries including the zero-point energy correction at the B3LYP/LANL2DZ level obtained with our own ECP analytical second-derivative code.[24] Additionally, we calculated Gibbs free energies to account for thermal and entropic contributions (Figures 1 and 2). Geometry optimizations and energy calculations for structures **1**−**8** were repeated using a better basis set with additional polarization functions (6-31G(d) on C, N, O, and H). Since these results are very similar, they are not discussed here.

Acknowledgment. The authors are grateful to Prof. G. Frenking for communication and Prof. E. J. Corey for suggesting calculations. Use of the computational facilities at the National Center for Supercomputing Applications, University of Illinois at Urbana−Champaign, and at the Centre de Supercomputacio de Catalunya (CESCA) is acknowledged. The present research is in part supported by grants (CHE-9409020 and CHE-9627775) from the National Science Foundation. Financial support from the Spanish Dirección General de Investigación Científica y Técnica (DGICYT) under project nos. PB-920621 and PB-950639 is also acknowledged.

JA9625992

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(19) GAUSSIAN94, revision D; 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.; 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. J. P.; Head-Gordon, M.; Gonzalez, C.; Pople, J. A. Gaussian, Inc.: Pittsburgh, PA, 1995.

(20) Labanowski, J.; Andzelm, J. Density Functional Methods in Chemistry; Springer Verlag: Heidelberg, 1991.

(21) Becke, A. D. *J. Chem. Phys.* **1993**, *98*, 5648.

(22) Hay, P. J.; Wadt, W. R. *J. Chem. Phys.* **1985**, *82*, 299.

(23) Bartlett, R. J. *J. Phys. Chem.* **1989**, *93*, 1697.

(24) Cui, Q.; Musaev, D. G.; Svensson, M.; Morokuma, K. *J. Phys. Chem.* **1996**, *100*, 10936.