Density Functional Study of the [2+2]- and [2+3]-Cycloaddition Mechanisms for the Osmium-Catalyzed Dihydroxylation of Olefins

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The postulated intermediates in the base-free and base-assisted addition of OsO₄ to olefins have been optimized using density functional theory (DFT). Ammonia was chosen as the base and ethylene as the olefin. The corresponding transition states have been characterized fully. Further, the activation barriers have been computed at the nonlocal level, and special attention has been given to the two different mechanistic hypothesis proposed for this reaction. In particular, the hypothesis by Sharpless of a [2+2]-cycloaddition pathway involving the formation of a four-member ring as an intermediate has been ruled out since the corresponding activation barrier was calculated to be as high as 39 kcal mol⁻¹. The addition of a NH₃ ligand to the osmium catalyst does not reduce significantly the [2+2] energy barrier. By contrast, it seems perfectly feasible that the dihydroxylation reaction proceeds through a [2+3] mechanism leading to the formation of a five-member ring intermediate as claimed by Corey. Such a process is found to be clearly exothermic and to involve a very small activation barrier of less than 2 kcal mol⁻¹. A detailed analysis of the sequence describing exactly how the cycloaddition proceeds along the reaction path has also been performed by means of intrinsic reaction coordinate (IRC) calculations for the two studied mechanisms.

Introduction

Certain oxo-metal compounds play a key role in organic synthesis because of their ability to selectively attach oxygen atoms to olefinic bonds. Among the high oxidation state transition metal oxides, osmium tetroxide is one of the most effective reagents for cis-dihydroxylation of alkenes to give the corresponding vicinal diols, Scheme 1.

It has long been recognized that the rate of reaction of OsO₄ with olefins is greatly increased in the presence of tertiary amines. Thus, OsO₄ reacts with monodentate tertiary amines under nonreducing conditions to give the adducts LOsO₄ (L = pyridine, isoquinoline, phthalazine, ammonia, or dihydroquinidine derivatives).

The key to the high selectivity and great scope found in osmium tetroxide's reaction with olefin resides of course in the mechanism and specifically in the sequence by which the two oxygen atoms are transferred from osmium to olefin. Several mechanistic proposals have been advanced for the dihydroxylation process. Initially, the mechanism was thought to proceed via a concerted [2+3] cycloaddition of two oxygen atoms to the olefin bond, Scheme 2.

Later, Sharpless et al. suggested a stepwise mechanism involving a [2+2]-like addition of the olefin

Scheme 1

Scheme 2

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\begin{align*}
\text{Scheme 1} & \\
\text{Scheme 2} & \end{align*}
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to an Os–O bond, leading to a four-membered osmaoxetane intermediate. This intermediate is then considered to rearrange in a subsequent rate-determining step to a five-membered cyclic ester complex, Scheme 3. According to recent work by Sharpless,7 experimental facts based on the relationship between temperature and enantioselectivity do not support a concerted [2+3] mechanism.

Corey and Noe,8 by contrast, have argued against the [2+2]-cycloaddition pathway claimed by Sharpless. These authors have recently reported kinetic, structural and stereochemical data which strongly support a different mechanism involving: (a) rapid, reversible formation of an olefin–Os(VIII) π–d complex and (b) slow rearrangement to a [2+3]-cycloaddition transition state, Scheme 4. Additional evidence against a metallooxetane-like transition state has also been obtained from a 12C/13C kinetic isotop effects study.15

From the theoretical point of view,14,16–19 several studies have dealt with the cis-dihydroxylation of alkenes by OsO4. Perhaps the most extensive investigation is that of Veldkamp and Frenking,18 who thoroughly analyzed the thermochromy corresponding to the osmylation reaction in the presence of bases, using quantum mechanical ab initio methods. These authors, however, were not able to report any transition state structure for the processes under study, and consequently, they did not manage to rule out any of the suggested mechanisms. A similar work was performed by Norrby14 et al., who calculated the structure of several ruthenium complexes using DFT. Again, Norrby14 et al. did not provide any transition state structures.

Our goal in the present study is then to provide a critical analysis of the [2+2] and [2+3] mechanisms on the basis of calculated transition state structures, activation barriers, and reaction paths. The present calculations are based on approximate density functional theory,20 which over the past decade has been employed successfully to solve many problems previously covered exclusively by ab initio Hartree–Fock (HF), and post-HF methods. The recently acquired popularity of approximate DFT stems in large measure from its computational expenditure which makes it amenable even to large-size molecules at a fraction of the time required for post-HF calculations. This is in particular the case for systems involving transition metals.21 The ability of DFT to predict transition state structures and activation energies has been studied for both transition metal complexes22a,b and main group compounds.22c–h

**Computational Methods**

The reported calculations were carried out by using the Amsterdam density functional (ADF) package developed by Baerends23 et al. and vectorized by Ravenek.24 The numerical integration procedure applied for the calculations is that of te Velde and Baerends.25 An uncontracted triple–STO basis set was used for describing the 5s, 5p, 5d, 6s, and 6p orbitals of osmium. For carbon (2s, 2p), oxygen (2s, 2p), nitrogen (2s, 2p), and hydrogen (1s), double–ζ basis sets were employed and augmented by an extra polarization function.26,27 Electrons in lower shells were treated within the frozen core approximation.28 A set of auxiliary s, p, d, f, and g functions, centered in all nuclei, was introduced in order to fit the molecular density and Coulomb potential accurately in each SCF cycle.28 All the geometries and frequencies were calculated at the local density approximation (LDA) level29 with the parametrization of Vosko30 et al. The relative energies were evaluated by including Becke’s nonlocal exchange23 and Perdew’s nonlocal correlation corrections31 as perturbations based on the LDA density. This approach is denoted NL–P, and its validity has been discussed elsewhere.32 The geometry optimization procedure was based on an analytical gradient scheme developed

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**Scheme 3**

**Scheme 4**
Results and Discussion

In the first part of this section, we present results from our calculations on the [2+2] and [2+3] addition of olefin to OsO₄ without the presence of a base. The influence of the base upon the reaction pathway is investigated in the second part. Ammonia and ethylene were chosen as model compounds for the base and olefin, respectively.

**Base-Free [2+2] Addition of Ethylene to Osmium Tetraoxide.** Figure 1 displays the optimized geometries for the stationary points on the reaction path corresponding to the [2+2]-cycloaddition potential energy surface. All structures were optimized without symmetry constraints.

Structure 1a corresponds to the tetrahedrally symmetric osmium catalyst. The TS structure, 1b, has a single imaginary frequency of 764\,\text{cm}^{-1}, with the next three lower frequencies at 61, 115, and 228\,\text{cm}^{-1}, respectively. The normal mode corresponding to the imaginary frequency represents a displacement along the emerging C–O bond. The ring closure finishes up in the metallacycle, 1c, which is the product for the [2+2] cycloaddition. In 1c, the C–O distance has decreased to a typical bond length for a C–O single bond (1.43\,\text{Å}), and the two carbon centers have undergone an sp² to sp³ hybridization.

The energy profile for the base-free [2+2] cycloaddition, Figure 2, reveals that the reaction is endothermic. The osmaoxetane, 1c, lies about 3.7 kcal mol⁻¹ above the two reacting species, 1a + C₂H₄. It can also be seen from the asymmetric profile that 1b is a productlike TS. Even more significant is the fact that the reaction has a large activation barrier of 39.7 kcal mol⁻¹. The formation of the osmaoxetane intermediate, 1c, is, therefore, unlikely to take place under the experimentally mild conditions usually employed in the osmium-catalyzed dihydroxylation of olefins. At room temperature such a barrier is unsurmountable.

A further detailed description of the reaction is given in Figure 3. Here, we display changes in key internal coordinates along the IRC. The IRC was constructed in Figure 3. Here, we display changes in key internal coordinates along the IRC. The length of the IRC is given by s (amu⁻¹/² bohr). Definitions: ΔE, energies relative to free OsO₄ and C₂H₄; s = 0.0, the transition state; s ≈ 8.5, the cycloaddition product; s → −∞, OsO₄ + C₂H₄.

![Figure 1. Optimized geometries for the stationary points along the base-free [2+2]-cycloaddition reaction path: Reactant, 1a; transition state, 1b; the osmaoxetane product, 1c. Bond lengths are in Å, and bond angles are in degrees.](image)

![Figure 2. Energy profile for the [2+2]-cycloaddition reaction along the IRC path. The length of the IRC is given by s (amu⁻¹/² bohr). Definitions: ΔE, energies relative to free OsO₄ and C₂H₄; s = 0.0, the transition state; s ≈ 8.5, the cycloaddition product; s → −∞, OsO₄ + C₂H₄.](image)
It is worthwhile to notice that one of the crucial chemical changes of this reaction, which is the conversion from an olefinic bond to a C–C single bond, occurs around as well as immediately after the TS in the case of the [2+2] mechanism. Thus, as displayed by g in Figure 3, it is not until \( s \approx 0.0 \) that the olefin starts losing its double-bond character. Notice that, as soon as the R(C–C) bond length becomes stable (at \( s \approx 3.0 \)), the R(C–O) distance also becomes constant (1.43 Å). At this point in the path (\( s = 3.0 \)) the four atoms involved in the ring practically occupy the same positions as in the final intermediate, 1c. However, the energy still decreases due to the favorable change occurring in the ab angle. This bond angle experiences a steady decrease starting precisely at \( s \approx 3.0 \) (94°) and finishing close to the product around \( s = 7.2 \) (78°).

Aside from the stretching of the olefinic C–C bond, the other main process responsible for the large activation barrier seems to be the Os–O bond stretch. As can be seen from Figure 3, the R(Os–O) bond distance depicted by b begins to stretch at \( s = -3.1 \) (1.74 Å), and once the TS has been reached, it continues increasing smoothly until 1c (1.97 Å). The remaining three Os–O bonds (a/c/d) are nearly constant along the reaction path.

Let us turn now our attention to the sequence of the reaction. There has been some debate as to whether the [2+2] cycloaddition would proceed initially as an electrophilic or nucleophilic attack of OsO₄ on olefin. Veldkamp and Frenking investigated the orbital energies of the frontier orbitals in OsO₄, and in light of their results, they suggested that the [2+2] reaction should be considered as an initial nucleophilic attack of the osmium complex on olefin. More specifically, they predicted that first one oxygen atom attacks nucleophilically an olefinic carbon, and then, the other carbon attacks electrophilically the oxygen atom, yielding the postulated four-member intermediate. However, it has been shown that electron-withdrawing groups on the olefin retard its reactivity toward OsO₄, which is evidence against the rate-determining nucleophilic reaction step proposed by Veldkamp and Frenking. At least if the [2+2] addition is involved in osmium-catalyzed dihydroxylation of olefins.

Our calculations suggest, on the other hand, an initial nucleophilic attack of the olefinic carbon on the metal center before and around the TS, followed by a nucleophilic attack of an oxygen atom on the other olefinic carbon after the TS has been reached, Figure 3. In effect, from the initial stages of the process up to the TS, 1b, both the R(Os–C) and the R(C–Os) distances have been decreased by roughly the same amount, as shown by the parallel lines for e and f in the region \(-10.8 < s < -1.0 \), Figure 3. By contrast, on the product side of the pathway up to the final metallacycle, 1c, the R(Os–C) distance shortens only 0.2 Å whereas the length of the C–O bond decreases by more than 0.5 Å. In particular, the main difference between e and f (Figure 3) occurs in the region \( 0.0 < s < 3.0 \), where the curvature for e tends to flatten, whereas the slope for f becomes more negative. It is thus clear from the changes in the R(Os–C) and R(C–Os) distances along the IRC, Figure 3, that Os–C bond making is ahead of C–O bond formation in the [2+2] cycloaddition. Folga et al. have recently reported an analogous conclusion for the formation of a four-center metallacycle from ethylene and molybdenum carbene.

**Base-Free [2+3] Addition of Ethylene to Osmium Tetraoxide.** Figure 4 displays the optimized

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**Figure 3.** Change of internal coordinates for the [2+2]-cycloaddition reaction along the IRC path. The length of the IRC is given by \( s \) (amu\(^{1/2}\) bohr). Definitions: \( s = 0.0 \), the transition state, 1b; \( s \approx 8.5 \), the product, 1c; \( s = \infty \), the reactants, 1a + C₂H₄.

**Figure 4.** Optimized geometries for the stationary points along the base-free [2+3]-cycloaddition reaction path: Adduct, 2a; transition state, 2b; five-membered ring product, 2c. Bond lengths are in Å, and bond angles are in degrees.
molecular structures for the species involved in a [2+3]-cyclodaddition reaction. In the early stages of the process, a symmetrical adduct, 2a, is formed. At this point, the interaction between C₂H₄ and OsO₄ is expected to be very weak since 2a is only 0.2 kcal mol⁻¹ more stable than the separated reactant species. The bond angle between the two oxygen atoms pointing toward the C=C double bond in 2a is only 3.8° smaller than in the free reactant 1a (109.5°). The transition state, 2b, does not differ remarkably from the adduct. In comparison to 2a, the transition state, 2b, exhibits further shortening of the C–O distances and closing of the O–Os–O bond angle in the emerging five-membered ring. At the same time an opening takes place of the O–Os–O bond angle in the plane perpendicular to the ring. Further, in the TS the two carbon centers still retain their initial sp² hybridization, and the whole structure can still be considered to have a C₅v symmetry. As in 2a, the five atoms of the incipient ring in 2b are still coplanar. Thus, 2b can be considered a reactant-like TS. This is in good agreement to the energy profile displayed in Figure 5. The reactant side of this process has a very flat energy profile, as confirmed by the four lower frequencies of the TS 2b (−85, 96, 118, and 195 cm⁻¹). If we come back to Figure 4, the reaction finally leads to the five-membered ring labeled as 2c. In this species, not only do the carbon atoms display sp³ hybridization but also the O–C–C–O fragment exhibits the typical shape and distances of a diol skeleton.

As far as energy considerations are concerned, Figure 5 reveals that the path for the [2+3] cyclodaddition is clearly exothermic, since the five-membered intermediate 2c is 20.6 kcal mol⁻¹ more stable than the two reacting species. A similar qualitative conclusion was also found by Veldkamp³⁸ and Frenking. In their study, the osmium ester complex was reported to be 12.2 kcal mol⁻¹ lower in energy than the reactants. However, if we come back to Figure 5, more important is the fact that only a very small activation barrier of 1.8 kcal mol⁻¹ must be surmounted in order for the reaction to proceed through a [2+3]-addition mechanism. Unlike the [2+2] mechanism discussed in the previous section (Figure 2), the [2+3] pathway seems to be perfectly feasible.

Figure 6 contains all information concerning the way in which the [2+3] reaction proceeds. It represents the change in the internal coordinates as a function of the IRC length s, from −2.0 to 4.5. The IRC was constructed from a total of 80 steps. The natural reaction coordinate for the [2+3] cyclodaddition is the R(C–O) distance (e or f) which varies linearly with s from 2.28 Å at s = −2.0 to 1.48 Å in the region close to 2c. Another highlighted change is the closing of the bc bond angle (which could alternatively describe the reaction). However, this change is not as linear as in the case of the R(C–O) distance, especially in the second half of the reaction path. As also expected from Figures 2 and 5, not many structural changes occur in the path from the reactants to 2b (s = 0.0). By contrast, significant structural changes occur on the product side of the reaction leading to the ester complex 2c. Thus, the stretching of the two Os–O bonds (bc) becomes more pronounced once the TS has been reached (s > 0.0). Even clearer is the case of the C–C bond elongation (g), where the conversion from an olefinic to a single bond can be considered to take place after the TS. The variation of the bond angle hi, which is related to the rehybridization of the carbon atoms from sp² to sp³, also supports the previous statement since no important changes on hi are detected for s < 1.0. With regard to the bond angle between Os and the terminal oxygens (ad), it smoothly opens along the reaction path until a maximum of 121.3° is reached in 2c. A similar trend is observed for the bond angle ab, the only exception being a slight decrease near the final ring (4.1 < s < 4.5). Notice that the olefinic carbons and the two oxygen atoms bonded to them remain coplanar along the entire reaction path, as indicated by the nearly constant value of the dihedral angle efg around 0°. The bond distances depicted by a and d also remain constant.

**Base-Assisted Cycloaddition.** The starting point for the study of the base-catalyzed dihydroxylation reaction is chosen here to be the adduct of stoichiometry OsO₄·NH₃, since kinetic studies suggest that only a single ligand molecule is involved in the rate-determining step.⁴⁰

Figures 7 and 8 display the optimized molecular structures of the stationary points for the [2+2]- and
[2+3]-cycloaddition reaction paths, respectively. A comparison between these two figures and their corresponding analogs without NH₃ (Figures 1 and 4, respectively) reveals that the addition of a base does not affect significatively the way in which the reaction proceeds. However, a few points must be mentioned.

With regards to the [2+2]-cycloaddition reaction (Figure 1 vs Figure 7), the main difference is a slight delay of the base-free TS, 1b, with respect to the base-assisted TS, 3b, along the reaction path. For instance, the R(Os–C) distance in 3b is 2.450 Å, whereas in 1b it is closer to the final distance in the ring (2.379 Å). Also notice that the curvature of the energy profile around the TS 3b is slightly less pronounced than around 1b: the four lower frequencies of 3b (−568, 31, 85, and 140 cm⁻¹) are numerically smaller than those of 1b (see above). Another point of interest concerns the extent of interaction between olefin and the osmium complex. As can be seen from a comparison between 1c and 3c, a stronger interaction between the olefin and the catalyst is found in the final intermediate when the cycloaddition is base assisted. Thus, not only R(Os–C) and R(C–O) distances are shorter in 3c than in 1c, but also R(Os–O) and R(C–C) distances in the ammonia-free 1c structure are not as long as in 3c.

Regarding the [2+3]-cycloaddition reactions (Figure 4 vs Figure 8), similar conclusions can be drawn. Thus, here again the interaction between C₂H₄ and the osmium complex in the final intermediate has progressed further when ammonia is present (4b) than when the reaction is non-base assisted (2c). Notice that, since the four lower frequencies of the TS 4a (−36, 67, 99, and 107 cm⁻¹) are even smaller than in the case of the TS 2b, the reaction side of the base-assisted cycloaddition is expected to have an energy profile even flatter than in the case of the base-free cycloaddition. This partially explains why no adduct for the ammonia-assisted reaction has been found. Further, as already mentioned for the [2+2] cycloadditions, the base-free TS, 2b, is also found to be remarkably later than the base-assisted TS, 4a, along the reaction path. This is shown, for instance, by a shorter R(C–O) average distance in 2b (2.04 Å) than in 4a (2.28 Å).

At this point it is worthwhile mentioning that the calculations presented here can provide theoretical support to some structural assumptions made by Corey et al. in terms of molecular structures. Thus, conclusions drawn by these authors on a ¹²C/¹³C kinetic isotope effects investigation were established by assuming that the postulated [2+2]-like transition state would resemble the metallaoxetane structure. As seen from Figures 1 and 7 in this paper, such assumptions can now be established as valid because of the similarity found between the structure of the product-like TS involved in the [2+2] mechanism and the structure of the final osmaoxetane (1b vs 1c in Figure 1 and also 3b vs 3c in Figure 7).

On the other hand, the present results are in disagreement with an early remark by Sharpless and co-workers about the relative stabilities of the [2+2] and [2+3] intermediates, based on structural considerations. According to these authors’ hypothesis, a five-membered intermediate such as 2c is not likely to be formed because of severe angle strain due to the long Os–O bonds. By contrast, it was claimed that a four-membered intermediate such as 1c should be substantially less strained since the long Os–C and Os–O bonds would have the effect of relieving the angle strain. It was also said that these objections to the [2+3] mechanism are only removed when prior coordination of a nucleophile to OsO₄ is invoked. From our investigation, it is in the four-membered intermediate (1c or 3c) where there seems to be considerable strain, since one of the carbons is forced to get out of the plane, and the other three oxygen atoms suffer large distortion to make room for the first entering carbon atom. On the contrary, atoms manage to be accommodated well in the five-membered ring (2c), without losing so much the tetrahedral integrity of the OsO₄ fragment.

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From the present investigation, there is enough evidence to rule out the [2+2] mechanism proposed by Sharpless and co-workers for the osmium-catalyzed dihydroxylation reaction of olefins. Our calculations indicate that such a [2+2] pathway has an activation barrier too high for the whole process to be feasible under the experimental reaction conditions (more than 39 kcal mol\(^{-1}\)). On the other hand, the present results are not in contradiction with a two-step pathway involving a [2+3] transition state as suggested by Corey. In fact, such a mechanism seems to be very plausible from the calculations presented in this study, since only a low energy barrier of less than 2 kcal mol\(^{-1}\) is involved in the formation of the predicted five-membered species.

Although our results favor the mechanism proposed by Corey et al., we have been unable to optimize any weak olefin–Os(VIII) \(\pi\)-d complex, whose existence is postulated to precede the formation of the [2+3] TS. At this point several considerations must be taken into account. Since the binding energy between OsO\(_4\) and NH\(_3\) is theoretically predicted\(^{18}\) to be about only 7–8 kcal mol\(^{-1}\), a complex between OsO\(_4\) and C\(_2\)H\(_4\) (which is a weaker base than NH\(_3\)) should have an even smaller complexation energy. However, under experimental conditions, such a complex is not unlikely to exist because bulky substrates can easily bring the olefinic double bond close to the osmium-catalyst fragment in an appropriate geometry for further conversion to the TS. Our simple model, where the chain of the substrate has been substituted by a free C\(_2\)H\(_4\) molecule, cannot reproduce these conditions. Therefore, despite our efforts to force the olefin to enter in a facial approach, we have not been able to report any \(\pi\)-d complex.

A comparison between the base-free and the base-assisted systems reveals that the addition of a ligand molecule is not crucial regarding the feasibility of one reaction path or another. The presence of a base enhances slightly the rate of formation of the five-membered ring while increasing its stability. On the whole, mechanistic conclusions drawn from the investigation of the base-free system are also suitable when the reaction is assisted with a base molecule.

Since further work is still required for a full understanding of these mechanisms, a more detailed investigation based on the results presented here will appear in a forthcoming paper. As a whole, the hypothesis suggested by Corey et al. seems to be more plausible to us and encourages us to continue studying the gradually sequence by which oxygen atoms are transferred to olefin in the metal-promoted dihydroxylation reaction of alkenes.

After the completion of this work two other groups\(^{42}\) have independently reached the same conclusion as to the preference of the [2+3] addition over the [2+2] addition.

Concluding Remarks

From the present investigation, there is enough evidence to rule out the [2+2] mechanism proposed by Sharpless and co-workers for the osmium-catalyzed dihydroxylation reaction of olefins. Our calculations indicate that such a [2+2] pathway has an activation barrier too high for the whole process to be feasible under the experimental reaction conditions (more than 39 kcal mol\(^{-1}\)).

Figure 9. Schematic representation of the energetics involved in the [2+2]- and [2+3]-cycloaddition reactions, with and without ammonia. Energies are in kcal mol\(^{-1}\).

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