Diradical versus Concerted Mechanisms for the Dihydroxylation of Protoanemonin by OsO_4 and $OsO_4{-}NH_3$ − The Effect of the Base in the Reaction

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The dihydroxylation of a set of monosubstituted olefins [ethene (**1**), propene (**2**), styrene (**3**)] and 5-methylene-2(5*H*)-furanone [protoanemonin (**4**)] by osmium tetroxide have been studied by means of DFT (B3LYP) calculations. The effect on the reaction mechanism of the coordination of a base (NH_3) to OsO_4 (**5**) to form OsO_4–NH_3 (**6**) has been investigated. These calculations show that the activation barriers for the [3+2] concerted mechanisms are lowered by the presence of an amine coordinating the osmium tetroxide, in agreement with experiment. For the dihydroxylation of protoanemonin (an olefin having a stepwise diradical mechanism in the Diels–Alder reaction) both the concerted and the diradical mechanisms have been evaluated. These studies indicate that the dihydroxylation of olefins proceeds through a concerted mechanism, although in the dihydroxylation of protoanemonin the diradical mechanism may play a significant role.

Introduction

The dihydroxylation of olefins by osmium tetroxide is one of the most efficient catalytic reactions developed in the laboratory.[1] Its importance is remarkable because of its common use in organic and natural product synthesis.[2] One of the most interesting qualities of this reaction is its power to catalyze the oxidation of hydrocarbons that have no functional groups.[3] In addition, with the use of appropriate ligands the reaction becomes enantioselective.[2,3] Currently, this is a very active field of research.[4,5]

The reaction mechanism of the dihydroxylation of olefins has been a matter of controversy for a long time.[6−9] Two different mechanisms, concerted [3+2] and stepwise [2+2], have mainly been proposed as possible mechanisms for the reaction. After the thorough work of several experimental and theoretical research groups, the scientific consensus is that the [3+2] mechanism is the one operating in the dihydroxylation of olefins by osmium tetroxide.[10−13] In very special cases, however, and using other metal oxides, the activation barrier for the [2+2] mechanism is lower in energy than the activation barrier for the [3+2] mechanism.[14,15]

Experiments show that adding a base to the osmium tetroxide increases the reaction rate.[16,17] The fact that the presence of an amine accelerates the reaction rate has been known for many years.[18] Moreover, depending on the base used, the diol product can be obtained in an enantioselective way. In their pioneering work on asymmetric dihydroxylation, Sharpless and co-workers discovered that chiral bases induce enantioselectivity in the reaction.[19] During their studies they developed several ligands that gave impressive enantiomeric excesses for the reaction, especially the bis-cinchona alkaloids.[20,21] Other research groups discovered their own ligands that also gave excellent results for enantiomeric excess in the dihydroxylation of olefins.[22−25]

The theoretical basis of the enantioselectivity introduced by the amine has been studied in our group[26−28] by means of QM/MM (IMOMM)[29,30] calculations, and by other groups.[31,32] These studies determined the main interactions between the olefin substituents and the different moieties of the ligand that govern the enantioselectivity.

Despite the great efforts carried out to elucidate the reaction mechanism, and to determine the origin of the enantioselectivity introduced by the coordinated amine ligand, only a few of the previous theoretical studies paid any attention to evaluating how the coordination of an amine to the osmium tetroxide itself affects the reaction.[10−13,33] This paper presents a systematic study of the effects introduced by the coordination of NH_3 to OsO_4 in the dihydroxylation of several monosubstituted olefins (ethene, propene and styrene).

Another goal of this work is to study the dihydroxylation of protoanemonin by osmium tetroxide. The reaction between this olefin and osmium tetroxide is electronically quite similar to the well-known Diels−Alder reaction. In the

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Diels−Alder reaction where the dienophile is protoanemonin, it has been experimentally and theoretically shown that the reaction goes through a stepwise mechanism with a diradical intermediate.[34] The olefin substituents are the ones capable of stabilizing the diradical mechanism. This is one of the very few examples[35] in which an olefin clearly shows a diradical mechanism. Given the behavior of protoanemonin in the Diels−Alder reaction, this olefin is an excellent candidate to test whether its dihydroxylation can also go through a stepwise diradical mechanism. Hence, both the concerted [3+2] and the stepwise diradical mechanisms for the dihydroxylation of protoanemonin by osmium tetroxide have been studied by means of DFT calculations. The effect of a base (NH_3) coordinated to OsO_4 has also been investigated for both mechanisms.

Results and Discussion

The results are presented in two sections. In the first section, the role of amine coordinated to osmium tetroxide in the concerted [3+2] addition is studied by means of DFT calculations. The selected olefins are a group of monosubstituted olefins (ethene, propene and styrene) and protoanemonin. In the second section, the concerted and diradical mechanisms for the dihydroxylation of protoanemonin by OsO_4 and OsO_4-NH_3 are discussed.

A) The Effect of a Base (NH_3) Coordinated to OsO_4 in the Dihydroxylation of Olefins

The reactants and transition states for the dihydroxylation of a selected group of monosubstituted olefins by osmium tetroxide have been characterized. The selected olefins are ethene, the simplest olefin, propene, an olefin with an alkane substituent, and styrene, an olefin with an aryl substituent. The dihydroxylation of protoanemonin has also been investigated; this reaction is particularly interesting because of the specific behavior of this olefin in the Diels−Alder reaction.

The monosubstituted olefins selected for this work serve as models for a systematic study of several aspects of the dihydroxylation reaction: the effects that different purely organic substituents of the olefin have on the energetic profiles and the geometries of the transition states and intermediates, and how these species are affected by the presence or absence of NH_3 coordinated to OsO_4. In all cases a concerted [3+2] transition state has been characterized as a transition state for the reaction.

Except in the most simple case of ethene, the dihydroxylation reaction of the studied olefins can yield two different isomers of the osmylated product. One has the substituted carbon atom of the olefin forming a bond to an axial oxygen atom of the osmium tetroxide. In the other, the substituted carbon atom is forming a bond to one of the equatorial oxygen atoms of the osmium tetroxide. The transition states were characterized for all the regioisomers (see Figure 1).

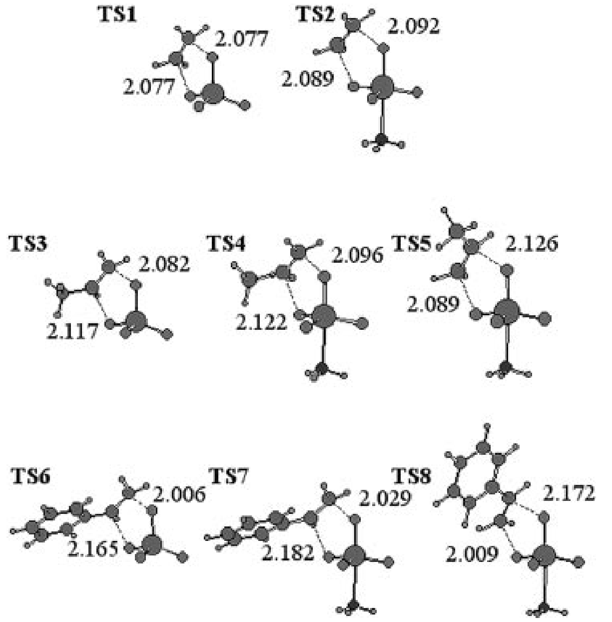

Figure 1. Transition states in the concerted mechanism for the dihydroxylation of ethene, propene and styrene by OsO_4 and OsO_4-NH_3; distances are in Å

The dihydroxylation of ethene by OsO_4 gives a symmetric transition state **TS1**. The forming C−O bond lengths are both 2.077 Å. For the reaction of ethene with OsO_4-NH_3, the forming $C-O_{ax}$ and $C-O_{eq}$ bond lengths in the transition state **TS2** are 2.092 and 2.089 Å, respectively. The transition state **TS3** for the dihydroxylation of propene by OsO_4 is not as symmetric as the transition state for ethene. The forming C−O bond lengths are 2.082 and 2.117 Å, respectively. In the reaction of propene with OsO_4-NH_3, two different regioisomers can be formed. In **TS4**, where the olefin's substituted carbon atom is closer to an equatorial oxygen atom, the lengths of the forming $C-O_{ax}$ and $C-O_{eq}$ bonds are 2.096 and 2.122 Å, respectively. In **TS5**, the other regioisomer, the lengths of the forming $C-O_{ax}$ and $C-O_{eq}$ bonds are 2.126 and 2.089 Å, respectively.

The transition state **TS6** for the dihydroxylation of styrene by OsO_4 has lengths of forming C−O bonds of 2.006 and 2.165 Å, respectively. For the reaction of styrene with OsO_4-NH_3 the lengths for the forming $C-O_{ax}$ and $C-O_{eq}$ bonds in **TS7** are 2.029 and 2.182 Å, respectively, whereas in **TS8** these lengths are 2.172 and 2.009 Å, respectively. The transition states for the dihydroxylation of styrene are more asynchronic than the transition states of either of the previous olefins.

In the dihydroxylation of protoanemonin by OsO_4, the lengths of the forming C−O bonds in the transition state **TS9** are 1.933 and 2.200 Å, respectively. However, when the catalyst is OsO_4-NH_3, there are two regioisomers with their corresponding transition states. When the olefin's substituted carbon atom is forming a bond to an equatorial oxygen atom, as in **TS10**, the lengths of the forming $C-O_{ax}$

and $C-O_{eq}$ bonds are 1.956 and 2.226 Å, respectively. For the other regioisomer, where the substituted carbon atom is forming a bond to an axial oxygen atom, the lengths of the forming $C-O_{ax}$ and $C-O_{eq}$ bonds in the transition state **TS11** are 2.232 and 1.931 Å, respectively (Figure 2).

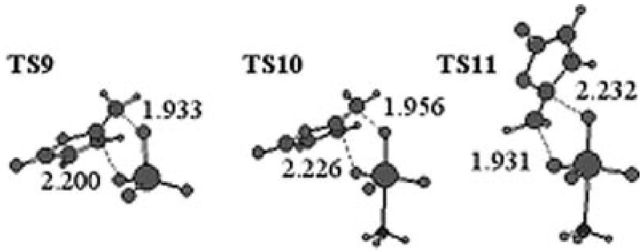

Figure 2. Transition states in the concerted mechanism for the dihydroxylation of protoanemonin by OsO_4 and OsO_4-NH_3; distances are in Å

The degree of asynchronicity depends on the olefin substituents. If the olefin has no substituents (ethene) or an alkyl substituent (propene) the transition states are quite symmetric. In the case of styrene (with an aryl substituent) or protoanemonin (with two substituents) the transition state becomes more asymmetric.

Table 1. Activation energies for the dihydroxylation of the studied olefins by the concerted mechanism (energies in kcal/mol)

		E_a			$\Delta E^{[a]}$		
Basis set		I	II	III	I	II	III
Ethene	TS1	4.8	4.5	8.2			
	TS2	3.9	3.7	7.3	0.9	0.8	.09
Propene	TS3	4.8	5.6	8.9			
	TS4	4.2	4.8	8.9	0.6	0.8	0.0
	TS5	3.9	4.5	8.2	0.9	1.1	0.7
Styrene	TS6	5.1	7.7	12.0			
	TS7	4.1	7.3	10.8	1.0	0.4	1.2
	TS8	4.4	7.7	11.2	0.7	0.0	0.8
Protoanemonin	TS9	9.5	7.9	11.7			
	TS10	6.3	5.3	9.4	3.2	2.6	2.3
	TS11	6.4	5.0	8.6	3.1	2.9	3.1

[a] $\Delta E = E_a(OsO_4) - E_a(OsO_4-NH_3)$.

Table 1 presents the activation energies for all these reactions. Three different basis sets have been used to calculate the activation barriers (see Computational Details). The comments in the text will be made mainly for basis set I, only mentioning the results of basis set II and basis set III when they are markedly different.

The activation energies for the dihydroxylation of ethene by OsO_4 and OsO_4-NH_3 are 4.8 and 3.9 kcal/mol, respectively. These results are in agreement with both our own[10] and other[11-13] previously published results.

The activation energy for propene is 4.8 kcal/mol when the catalyst is OsO_4. The activation energies when the catalyst is OsO_4-NH_3 are 4.2 and 3.9 kcal/mol for **TS4** and **TS5**, respectively. **TS4** is 0.3 kcal/mol higher in energy than **TS5**. Similar energy differences were found for these transition states when basis set II (0.3 kcal/mol) and basis set III (0.7 kcal/mol) were used. The transition state for the regioisomer in which the substituted carbon atom of the olefin is forming a bond to an axial oxygen atom is slightly favored.

The dihydroxylation of styrene by OsO_4 has an activation energy of 5.1 kcal/mol. The energies of the transition states **TS7** and **TS8** for the two regioisomers when the catalyst is OsO_4-NH_3 are 4.1 and 4.4 kcal/mol, respectively. In this case, the regioisomer having the substituted carbon atom forming a bond with an equatorial oxygen atom is slightly favored. Similar results are found for basis set II and III.

For protoanemonin, the activation energy for the dihydroxylation by OsO_4 is 9.5 kcal/mol. When the catalyst is OsO_4-NH_3, the transition states **TS10** and **TS11** for the two regioisomers have energies of 6.3 and 6.4 kcal/mol, respectively. In this case, depending on the basis set, one or other regioisomer is slightly favored.

The addition of NH_3 to OsO_4 lowers the activation energy of the reaction in all the examples studied (Table 1) but the difference in the activation energy is not the same in all cases. The effect on the activation energy of the coordination of a base to the catalyst depends on the olefin to be dihydroxylated. For protoanemonin this effect is significantly larger than for the monosubstituted olefins.

In the dihydroxylation of ethene the activation energy is lowered by 0.9 kcal/mol. When the olefin is propene the activation energy is lowered by 0.6 or 0.9 kcal/mol, depending on the regioisomer. The coordination of an amine to osmium tetroxide has similar effects whether the olefin has a methyl group as substituent or has no substituents. For the styrene reaction (the olefin substituent is an aryl group), the addition of a base to the catalyst reduces the activation energy by 1.0 or 0.7 kcal/mol, depending on the regioisomer. These results are in agreement with experiment, although experimental data show greater decreases in the activation barriers.[16,17]

Of all the olefins studied, protoanemonin shows the greatest reduction in activation energy by the coordination of a base to the catalyst. The activation barriers are reduced by 3.2 or 3.1 kcal/mol depending on the regioisomer. The transition state is also by far the most asymmetric one. From the literature, it is also known that in a Diels−Alder reaction with protoanemonin as dienophile the mechanism is stepwise with a diradical intermediate. These facts together may suggest that the dihydroxylation of protoanemonin by OsO_4, or especially by OsO_4-NH_3, might occur through a stepwise diradical mechanism. In the next section both concerted and diradical mechanisms are evaluated.

B) Diradical versus Concerted Mechanisms in the Dihydroxylation of Protoanemonin

For the dihydroxylation of protoanemonin one can envisage several diradical reaction mechanisms. As far as the protoanemonin is concerned, either of the carbons atoms of the reacting double bond could form a bond with an oxygen atom of osmium tetroxide. Nevertheless, previous work on the diradical Diels−Alder reaction has shown that the carbon atom involved in the first bond formation is the unsubstituted one.[34] Hence, mechanisms involving the substituted carbon atom in the first step are highly improbable, and will be neglected here. For mechanisms in which the first C−O bond forms between the unsubstituted carbon atom and an oxygen atom, if the catalyst is OsO_4 there is only one possible mechanism, but if the catalyst is OsO_4-NH_3 there are two: (a) one in which the first C−O bond is formed between the unsubstituted carbon atom and an axial oxygen atom, and (b) one in which the first C−O bond is formed between the unsubstituted carbon atom and an equatorial oxygen atom. Because of the computational effort required, in this paper we will analyze only mechanism (a). We chose this mechanism because an energetic comparison of the diradical intermediates for the two mechanisms shows that the intermediate of mechanism (a) is lower in energy (1.7 kcal/mol). We also checked the stability of the analogous diradical intermediates for ethene, which also gave a lower energy for mechanism (a) (ca. 2 kcal/mol). In addition, the results on the concerted mechanism show that the activation barriers for both regioisomers are quite similar. These facts suggest that the energy profile for both mechanisms will be quite similar, with mechanism (a) slightly lower in energy.

The reactants, intermediates and transition states for the selected mechanism have been characterized. The first step of the reaction corresponds to the formation of a C−O bond between the unsubstituted carbon atom of the protoanemonin and an oxygen atom of the catalyst. After that, the diradical intermediate is formed. The next step is cyclization to form the five-membered ring osmylated product.

In the first step of the reaction between protoanemonin and OsO_4 (Figure 3), the length of the forming C−O bond in the transition state **TS12** is 1.786 Å. The Os−O bond (of the O atom involved in the C−O bond formation) elongates from 1.718 to 1.809 Å on going from the reactant to the transition state. The dihedral angle between the protoanemonin and the osmium tetroxide, measured by the Os−O−C−C dihedral angle is 120.0°. A C−H bond of the protoanemonin (from the unsubstituted carbon atom) is eclipsing the $Os-O_{bound}$ bond. The $Os-O_{free}$ distances range from 1.712 to 1.751 Å, and the $O_{bound}-Os-O_{free}$ angles range from 95.4 to 111.5°. In the intermediate **7** the C−O bond is formed with a length of 1.491 Å. The protoanemonin rotates slightly giving a dihedral Os−O−C−C angle of 115.4°. The $O_{bound}-Os-O_{free}$ bond angles range from 91.6 to 111.1°. The $Os-O_{bound}$ bond length is 1.882 Å, whereas the $Os-O_{free}$ bond lengths range from 1.710 to 1.762 Å. For the cyclization transition state **TS13**, the length of the new forming C−O bond is 3.116 Å. The Os−O−C−C dihedral angle is substantially reduced on going from the intermediate (115.4°) to the transition state (58.6°). The protoanemonin has rotated to bring the carbon atom close to an oxygen atom. The $O_{bound}-Os-O_{free}$ angles are between 101.9 and 111.6°. The Os−O bond length of the O atom involved in the forming C−O bond is slightly elongated, from 1.710 to 1.730 Å, on going from the intermediate to the second transition state.

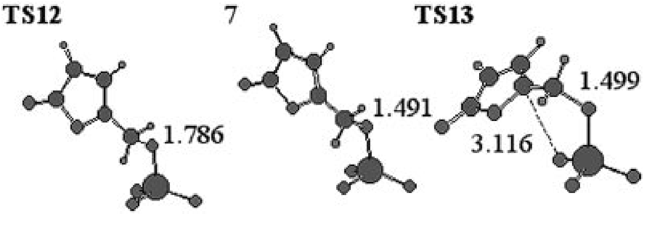

Figure 3. Transition states and intermediate in the diradical mechanism for the dihydroxylation of protoanemonin by OsO_4; distances are in Å

In the reaction between protoanemonin and OsO_4-NH_3 (Figure 4), the length of the forming C−O bond in the transition state **TS14** for the first step is 1.852 Å. The Os−O−C−C dihedral angle is 107.9°. The $O_{ax}-Os-O_{eq}$ angles range from 95.9 to 100.5°. The $Os-O_{eq}$ distances are between 1.729 and 1.758 Å. In the intermediate **8** the length of the formed C−O bond is 1.455 Å. The dihedral Os−O−C−C angle is significantly reduced to 74.7°. The $O_{ax}-Os-O_{eq}$ bonding angles range from 93.1 to 99.1° and the $Os-O_{eq}$ bond lengths range from 1.725 to 1.762 Å. The $Os-O_{ax}$ bond length has elongated from 1.804 Å in **TS14** to 1.915 Å in **8**. For the cyclization transition state **TS15** the length of the forming C−O bond is 2.995 Å. The Os−O−C−C dihedral angle is 81.8°. The $O_{ax}-Os-O_{eq}$ bond angles range from 92.4 to 97.5° and the $Os-O_{eq}$ bond lengths range from 1.732 to 1.767 Å. The Os−O bond length of the oxygen atom involved in the forming C−O bond is 1.743 Å.

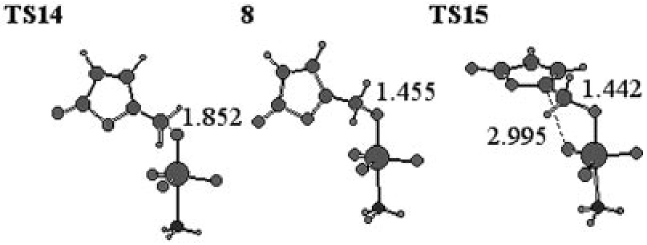

Figure 4. Transition states and intermediate in the diradical mechanism for the dihydroxylation of protoanemonin by OsO_4-NH_3; distances are in Å

Table 2 presents the energies corresponding to the diradical mechanism of the dihydroxylation of protoanemonin by OsO_4 and OsO_4-NH_3. We shall first discuss the case of OsO_4. The activation energy for the initial step (the first C−O bond formation) in the osmium tetroxide catalyzed reaction, corresponding to **TS12**, is 17.8 kcal/mol. The energy of the intermediate **7** (where the C−O bond is fully formed) is 13.5 kcal/mol. The activation energy for the ring-closing step (where a new C−O bond is forming), corresponding to **TS13**, is 18.8 kcal/mol. The energy values for **TS12**, **7** and **TS13** using basis set II are 16.2, 9.8 and 15.4 kcal/mol, and using basis set III are 20.3, 15.5 and 21.1 kcal/mol, respectively. The difference in the activation energies for **TS12** and **TS13** is within 1 kcal/mol. According to

Table 2. Calculated activation energies for the dihydroxylation of protoanemonin by the diradical mechanism

Basis set		ΔE[a]			$\Delta E_{\text{spin-corrected}}$[b]		
		I	II	III	I	II	III
	TS12	17.8	16.2	20.3	14.2	12.6	16.6
OsO_4	**7**	13.5	9.8	15.5	11.2	8.0	13.1
	TS13	18.8	15.4	21.1	6.5	13.4	19.6
OsO_4-NH_3	**TS14**	13.0	12.3	16.0	9.7	7.5	12.7
	8	2.0	−0.9	4.9	1.4	−1.2	4.7
	TS15	2.5	−0.6	5.3	1.7	−1.1	4.9

[a] ΔE = Energy difference compared to reactants. [b] Energy correction calculated using the Yamaguchi et al. approximation (ref.[36]).

these results, both transition states of the diradical pathway have similar energies.

In this mechanism, the intermediate and transition states are not regular closed-shell singlets. The $<S^2>$ values for **TS12**, **7** and **TS13** are 0.49, 0.93 and 0.98, respectively. The approximate method of Yamaguchi et al.[36] was used to calculate the spin-corrected energies. Using this approximate method, the activation energies for **TS12**, **7** and **TS13** were calculated as 14.2, 11.2 and 6.5 kcal/mol, respectively. Using the same method and basis set II, the activation energies are 12.6, 8.0 and 13.4 kcal/mol, respectively; for basis set III the activation energies are 16.6, 13.1 and 19.6 kcal/mol, respectively. The corrected energies give lower activation barriers for the entire reaction. The energies are lowered by ca. 4 and ca. 2 kcal/mol for **TS12** and **7**, respectively. The most significant difference is for **TS13**, where the activation barrier is lowered by 12.3 kcal/mol for basis set I, 2.0 kcal/mol for basis set II, and 0.5 kcal/mol for basis set III. Hence, looking at the spin-corrected energies it is not clear which is the rate-determining step of the reaction.

For the dihydroxylation reaction of protoanemonin by OsO_4-NH_3 a diradical mechanism has also been characterized (Table 2). The transition state **TS14**, corresponding to the initial C−O bond formation, has an activation barrier of 13.0 kcal/mol. The energy of the diradical intermediate **8** is 2.0 kcal/mol compared to the reactants. The activation barrier for the cyclization step (**TS15**) is 2.5 kcal/mol. When basis set II is used, the energies for **TS14**, **8** and **TS15** are 12.3, −0.9 and −0.6 kcal/mol, respectively; for basis set III these energies become 16.0, 4.9 and 5.3 kcal/mol, respectively. The rate-determining step for this system corresponds to the first step. The intermediate is remarkably stable, and the activation barrier for the cyclization step is also quite low. The addition of amine to the osmium tetroxide lowers the energy for the complete reaction, though the intermediate **8** and the transition state **TS15** of the second step are drastically stabilized.

The $<S^2>$ values for **TS14**, **8** and **TS15** are 0.42, 1.03 and 1.02, respectively. The Yamaguchi approximation has also been applied to calculate the spin-corrected energies. These energies are 9.7, 1.4 and 1.7 kcal/mol for **TS14**, **8** and **TS15**, respectively. For basis set II those values become 7.5, −1.2 and −1.1 kcal/mol, respectively, whereas for basis set III those values become 12.7, 4.7 and 4.9 kcal/mol, respectively. The spin-corrected energy values are lower than the uncorrected ones. The rate-determining step is again the first step. The intermediate **8** is remarkably stable, and the transition state for the second step is also quite low in energy.

A comparison of the geometries for the transition states and intermediates in the dihydroxylation reaction of protoanemonin by OsO_4 (**TS12**, **7**, **TS13**) and by OsO_4-NH_3 (**TS14**, **8**, **TS15**), shows that they are quite similar (see Figures 3 and 4). The energetic profile, however, is very different when NH_3 is coordinated to OsO_4. The activation barriers are significantly lower when NH_3 is coordinated. The activation energy for the first transition state (**TS12**) is lowered by ca. 5 kcal/mol when the amine is present (**TS14**). The intermediate is much more stable when NH_3 is coordinated to OsO_4; when comparing **7** and **8**, the energy is reduced by ca. 11 kcal/mol. The ring-closing transition state shows the largest difference in the calculated non-corrected activation energies. When comparing **TS13** and **TS15** the decrease in the activation barrier is ca. 16 kcal/mol. Similar trends are found for the spin-corrected activation barriers. These results show that the coordination of ammonia to osmium tetroxide has a key role in accelerating the reaction rate in the dihydroxylation of protoanemonin by a stepwise mechanism.

When comparing the diradical to the concerted mechanism, the activation energy for the rate-determining step of the diradical mechanism (9.7 kcal/mol) is higher by 3.4 kcal/mol than the activation energy for the concerted [3+2] mechanism (6.3 kcal/mol). The same comparison for basis set II and III again gives the concerted mechanism a lower energy, by 2.2 and 3.3 kcal/mol, respectively. Hence, the concerted mechanism is the preferred one. Nevertheless, in the diradical mechanism the coordination of an amine to osmium tetroxide has a greater effect on lowering the activation energy than in the concerted mechanism, in better agreement with experiment; the activation barrier for the concerted mechanism is lowered by ca. 3 kcal/mol, whereas for the diradical mechanism the activation barrier decreases by ca. 5 kcal/mol. These values suggest that the diradical mechanism may play a significant role in the dihydroxylation of protoanemonin.

The energy difference between the two mechanisms is not large enough to allow us to discount the diradical mechanism completely. Moreover, the concerted mechanism exhibits a very asymmetric transition state, with differences in the lengths of the forming C−O bonds of up to 0.3 Å. For a long time, there was controversy over the concerted [3+2] and the stepwise [2+2] mechanisms. The stepwise [2+2] mechanism was ruled out by theory and experiment. The results in this paper, however, suggest that in the cases for which a stepwise mechanism may be plausible, it will be the diradical mechanism instead of the [2+2] mechanism. Comparable results have been obtained in studies of the cycloreversion of rhenium(V) diolates (an analogous metal oxide system), which reflect a probability that highly asynchronous concerted and diradical mechanisms are involved.[37]

Conclusions

The olefin dihydroxylation of several monosubstituted olefins by osmium tetroxide has been studied by means of DFT calculations. All the transition states correspond to a concerted [3+2] mechanism. The dihydroxylations of ethene and propene show symmetric transition states, whereas the dihydroxylation of styrene shows a more asymmetric transition state. For all the cases studied, the coordination of an amine to osmium tetroxide accelerates the reaction, in agreement with experiment. Nevertheless, the calculated reduction in the activation energy due to the presence of an amine is not as large as that suggested by the experimental results.

For the particular case where the olefin is protoanemonin, the concerted and diradical mechanisms have been studied for both the OsO_4 (**5**) and the OsO_4-NH_3 (**6**) catalysts. This reaction is particularly interesting because it has been theoretically and experimentally shown that when this olefin reacts as dienophile in a Diels−Alder reaction the mechanism is stepwise, with a diradical intermediate. The activation energies of the concerted mechanisms are lower than the activation barriers for the diradical mechanism for both catalysts **5** and **6**. Nevertheless, the energetic profile for the dihydroxylation of protoanemonin when the base is introduced is lowered to a greater extent for the diradical mechanism (5 kcal/mol) than for the concerted mechanism (3 kcal/mol). The concerted transition state is highly asymmetric. Moreover, the energy difference between the concerted and diradical mechanisms is not too large, around 2−3 kcal/mol. These facts together suggest that the reaction pathway goes through a concerted mechanism, though the transition state has a significant diradical character.

The general implication of these results is that the more the activation energy is decreased by the addition of a base to the osmium tetroxide, the greater the role played by the diradical mechanism in the reaction. This is also suggested because the transition state becomes much more asymmetric. Hence, in those cases where a stepwise mechanism may be feasible, it will be a diradical mechanism instead of the [2+2] mechanism.

In the dihydroxylation of protoanemonin by OsO_4 or OsO_4-NH_3 the concerted pathway is lower in energy than the stepwise mechanism. Therefore, it is quite probable that the diradical mechanism would be even more disfavored than the concerted mechanism for the dihydroxylation of the monosubstituted olefins studied.

The results described here indicate that more sophisticated calculations, such as multireference wave functions and the inclusion of dynamic effects, may be necessary to give a better description of the system. Moreover, as has already been shown in previous work, the HF base function is not appropriate to describe osmium tetroxide. Despite this, the DFT (B3LYP) calculations presented here are able to reproduce the major trends of the reaction mechanisms.

Computational Details

All calculations were performed using the Gaussian98 series of programs.[38] The calculations were carried out at the BECKE3LYP[39] level of theory. In basis set I, the inner electrons of the osmium atom are described by the LANL2DZ effective core potential (ECP).[40] The outer electrons are described using the double-ξ base associated to the corresponding ECP, also called LANL2DZ. The oxygen atoms directly bonded to the osmium atom are described by the 6-31G(d) basis set.[41] The oxygen atoms of the protoanemonin, and all the N, C and H atoms are described by the 6-31G basis set.[42] This basis set for osmium tetroxide has been previously shown to appropriately describe the system.[43] In basis set II, the Os atom is also described by the LANL2DZ ECP and its associated basis set, and the O, N C and H atoms are described by the 6-31G(d) basis set.[41] Basis set III is similar to basis set II but adding one set of *f* polarization functions (exponent = 0.886)[44] to the metal center. All geometry optimizations were carried out with basis set I, and basis set II and III were used only for single-point energy calculations.

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[1] K. B. Sharpless, *Angew. Chem. Int. Ed.* **2002**, *41*, 2024−2032.
[2] H. C. Kolb, M. S. VanNieuwenhze, K. B. Sharpless, *Chem. Rev.* **1994**, *94*, 2483−2547.
[3] H. C. Kolb, K. B. Sharpless in *Transition Metals in Organic Synthesis*, vol. 2 (Eds.: M. Beller, C. Bolm), Wiley-VCH, Weinheim, **1998**, pp. 243−260.
[4] M. A. Andersson, R. Epple, V. V. Fokin, K. B. Sharpless, *Angew. Chem. Int. Ed.* **2002**, *41*, 472−475.
[5] B. M. Choudary, N. S. Chowdari, K. Jyothi, M. L. Kantam, *J. Am. Chem. Soc.* **2002**, *124*, 5341−5349.
[6] T. Göbel, K. B. Sharpless, *Angew. Chem. Int. Ed. Engl.* **1993**, *32*, 1329.
[7] E. J. Corey, M. C. Noe, S. Sarshar, *J. Am. Chem. Soc.* **1993**, *115*, 3828.
[8] P.-O. Norrby, H. Becker, K. B. Sharpless, *J. Am. Chem. Soc.* **1996**, *118*, 35.
[9] E. J. Corey, M. C. Noe, *J. Am. Chem. Soc.* **1996**, *118*, 319.
[10] S. Dapprich, G. Ujaque, F. Maseras, A. Lledós, D. G. Musaev, K. Morokuma, *J. Am. Chem. Soc.* **1996**, *118*, 11660−11661.
[11] U. Pidun, C. Boehme, G. Frenking, *Angew. Chem. Int. Ed. Engl.* **1996**, *35*, 2817.
[12] M. Torrent, L. Deng, M. Duran, M. Solà, T. Ziegler, *Organometallics* **1997**, *16*, 13.
[13] A. J. Del Monte, J. Haller, K. N. Houk, K. B. Sharpless, D. A. Singleton, T. Strassner, A. A. Thomas, *J. Am. Chem. Soc.* **1997**, *119*, 9907.
[14] D. V. Deubel, S. Schlecht, G. Frenking, *J. Am. Chem. Soc.* **2001**, *123*, 10085−10094.
[15] D. V. Deubel, *J. Phys. Chem. A* **2002**, *106*, 431−437.

[16] D. J. Berrisford, C. Bolm, K. B. Sharpless, *Angew. Chem. Int. Ed. Engl.* **1996**, *34*, 451−454.
[17] D. W. Nelson, A. Gysper, P. T. Ho, H. C. Kolb, T. Kondo, H.-L. Kwong, D. V. McGrath, A. E. Robin, P.-O. Norrby, D. P. Gable, K. B. Sharpless, *J. Am. Chem. Soc.* **1997**, *119*, 1840.
[18] R. Criegee, *Justius Liebigs Ann. Chem.* **1936**, *522*, 75.
[19] S. G. Hentges, K. B. Sharpless, *J. Am. Chem. Soc.* **1980**, *102*, 4263.
[20] K. B. Sharpless, W. Amberg, Y. L. Bennani, G. A. Crispino, J. Hartung, K.-S. Jeong, H.-L. Kwong, K. Morikawa, Z. -M Wang, D. Xu, X. -L Zhang, *J. Org. Chem.* **1992**, *57*, 2768.
[21] G. A. Crispino, K.-S. Jeong, H. C. Kolb, Z.-M. Wang, D. Xu, K. B. Sharpless, *J. Org. Chem.* **1993**, *58*, 3785.
[22] E. J. Corey, P. D. Jardine, S. Virgil, P.-W. Yuen, R. D. Connell, *J. Am. Chem. Soc.* **1989**, *111*, 9243.
[23] T. Oishi, M. Hirama, *Tetrahedron Lett.* **1992**, *33*, 639.
[24] S. Hanessian, P. Meffre, M. Girard, S. Beaudoin, J.-Y. Sancéau, Y. Bennani, *J. Org. Chem.* **1993**, *58*, 1991.
[25] K. Tomioka, M. Nakajima, K. Koga, *J. Am. Chem. Soc.* **1987**, *109*, 6213.
[26] G. Ujaque, F. Maseras, A. Lledós, *Theor. Chim. Acta* **1996**, *94*, 67−73.
[27] G. Ujaque, F. Maseras, A. Lledós, *J. Am. Chem. Soc.* **1999**, *121*, 1317−1323.
[28] G. Ujaque, F. Maseras, A. Lledós, *J. Org. Chem.* **1997**, *62*, 7892−7894.
[29] F. Maseras, K. Morokuma, *J. Comput. Chem.* **1995**, *16*, 1170.
[30] F. Maseras, *Chem. Commun.* **2000**, 1821−1827.
[31] P.-O. Norrby, T. Rasmussen, J. Haller, T. Strassner, K. N. Houk, *J. Am. Chem. Soc.* **1999**, *121*, 10186−10192.
[32] N. Moitessier, B. Maigret, F. Chretien, Y. Chapleur, *Eur. J. Org. Chem.* **2000**, 995−1005.
[33] A. Veldkamp, G. Frenking, *J. Am. Chem. Soc.* **1994**, *116*, 4937.
[34] V. Branchadell, J. Font, A. G. Moglioni, C. O. Ochoa de Echagüen, A. Oliva, R. M. Ortuño, J. Veciana, J. Vidal-Gancedo, *J. Am. Chem. Soc.* **1997**, *119*, 9992−10003.
[35] Other examples: K. Mikami, S. Matsumoto, Y. Okubo, M. Fujitsuka, O. Ito, T. Suenobu, S. Fukuzumi, *J. Am. Chem. Soc.* **2000**, *122*, 2236−2243.
[36] K. Yamaguchi, F. Jensen, A. Dorigo, K. N. Houk, *Chem. Phys. Lett.* **1988**, *149*, 537.
[37] K. P. Gable, F. A. Zhuravlev, *J. Am. Chem. Soc.* **2002**, *124*, 3970−3979.
[38] M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, V. G. Zakrzewski, J. A. Montgomery, Jr., R. E. Stratmann, J. C. Burant, S. Dapprich, J. M. Millam, A. D. Daniels, K. N. Kudin, M. C. Strain, O. Farkas, J. Tomasi, V. Barone, M. Cossi, R. Cammi, B. Mennucci, C. Pomelli, C. Adamo, S. Clifford, J. Ochterski, G. A. Petersson, P. Y. Ayala, Q. Cui, K. Morokuma, D. K. Malick, A. D. Rabuck, K. Raghavachari, J. B. Foresman, J. Cioslowski, J. V. Ortiz, A. G. Baboul, B. B. Stefanov, G. Liu, A. Liashenko, P. Piskorz, I. Komaromi, R. Gomperts, R. L. Martin, D. J. Fox, T. Keith, M. A. Al-Laham, C. Y. Peng, A. Nanayakkara, M. Challacombe, P. M. W. Gill, B. Johnson, W. Chen, M. W. Wong, J. L. Andres, C. Gonzalez, M. Head-Gordon, E. S. Replogle, and J. A. Pople, *Gaussian 98, Revision A.9*, Gaussian Inc., Pittsburgh PA, **1998**.
[39] P. J. Stephens, F. J. Devlin, C. F. Chabalowski, M. J. Frisch, *J. Phys. Chem.* **1994**, *98*, 11623.
[40] P. J. Hay, W. R. Wadt, *J. Chem. Phys.* **1985**, *82*, 270.
[41] P. C. Hariharan, J. A. Pople, *Theor. Chim. Acta* **1973**, *28*, 213.
[42] W. J. Hehre, R. Ditchfield, J. A. Pople, *J. Chem. Phys.* **1972**, *56*, 2257.
[43] G. Ujaque, F. Maseras, A. Lledós, *Int. J. Quantum Chem.* **2000**, *77*, 544−551.
[44] A. W. Ehlers, M. Böme, S. Dapprich, A. Gobbi, A. Höllwarth, V. Jonas, K. F. Köhler, R. Stegmann, A. Veldkamp, G. Frenking, *Chem. Phys. Lett.* **1993**, *208*, 111−114.

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