Origin of the Enantioselectivity in the Hydrogen Transfer Reduction of Carbonyls by a Rhodium(I) Complex: A Theoretical Study

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Received February 13, 2001

Concerted mechanisms for the catalytic cycle of the carbonyl reduction by a rhodium(I) hydride complex were studied on the basis of DFT theoretical calculations. The first assumed mechanism consists of the direct transfer of a metal-bound hydride to the carbon of the carbonyl in concert with the coordination of the oxygen to the metallic center. In the second mechanism, the hydride of the complex and a proton of a nitrogen-containing ligand are transferred simultaneously to the carbonyl. Several substrates such as formaldehyde, acetone, and the experimentally used acetophenone were investigated as starting materials, and several nitrogen-containing ligands were considered. Each postulated intermediate was confirmed to be a stationary point on the potential energy surface, and transition states were characterized, except in the case of the first mechanism, where no transition state was found. All the activation barriers were calculated to be within the range of 3.9−18.7 kcal mol^{-1} and are consistent with experimental reaction rates. In the case of acetophenone, the calculations for chiral diamine ligands explain the origin of the observed enantioselectivity with a complete characterization of the diastereoisomer transition states.

I. Introduction

Catalytic asymmetric hydrogen transfer is a reaction of recent interest for the reduction of C═O leading to optically active secondary alcohols. It can be achieved with a transition metal, such as Ru(II), Rh(I), or Ir(I), bearing chiral ligands. Nitrogen-containing ligands are among the best, and many studies have shown their remarkable catalytic performance.[1−3] However, little is known experimentally about intermediates and reaction steps, except the recently published characterizations, by X-ray crystallography, of some intermediates with Ru(II) catalyst[4] and a kinetic study in the case of Rh(I).[5]

Two paths have been generally considered:[1] a stepwise process through an intermediate hydride complex (path A) and a process where the hydrogen is directly transferred from the secondary alkoxy complex to the substrate (path B). In the case of path A, two possibilities can also be considered: a two-step mechanism with coordination of the substrate followed by the insertion of the hydride in the double bond and, on the other hand, a concerted mechanism. Our purpose was to elucidate the mechanism of this reaction in the case of rhodium(I) catalysts bearing chiral diamine ligands, by means of DFT calculations, to find the origin of enantioselectivity. Understanding the detailed mechanism of the reaction should allow us to gain insights into the design of catalysts with improved enantioselectivity.

In previous studies, we investigated the nature of the ligands and the structure of the supposed hydride intermediate complex of path A[6] and we studied a two-step mechanism for the hydride transfer.[7] In the present paper we will present our results for the concerted reaction mechanism of path A.

The first possible mechanism for the hydride transfer step has been postulated by Gladiali in the case of the reduction of acetophenone by 2-propanol with a Rh(I) complex.[8] It is shown in Scheme 1. This cycle can be started with the postulated hydride complex **1**.[6] The first step is concerted and involves the coordination of the acetophenone in concert with the hydride transfer to form an alkoxy complex. The second step is an exchange with the 2-propanol solvent, followed by the reverse reaction of the first step, which leads to the regeneration of the hydride complex **1**. A second concerted mechanism

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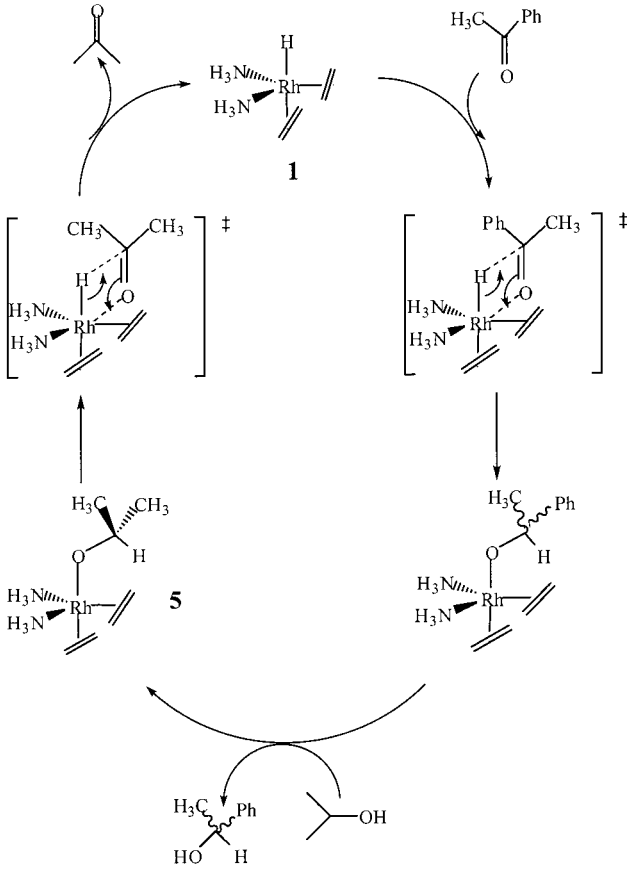
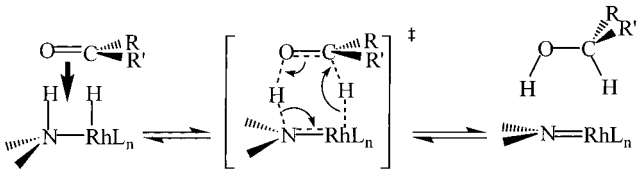
10.1021/om010120v CCC: $20.00
Publication on Web 05/01/2001

Scheme 1. Catalytic Cycle Proposed by Gladiali for the Concerted Reduction of Acetophenone with the Rh(I) Hydride Complex 1



Scheme 2. Schematic Mechanism for the Transfer of both the Hydride and an Amine Proton from the Hydride−Rh Complex to the Carbonyl



that can be envisaged involves a double hydrogen transfer from the complex to the ketone, following Scheme 2. Recently such a mechanism has been proven experimentally for the same reaction, but with a Ru(II) complex.[4] This mechanism is completely concerted and avoids the passage through alkoxy complexes.

In the first part of this study, we have performed calculations with NH_3 and C_2H_4 ligands. To study the enantioselectivity, in the second part, a model chiral diamine was used instead of NH_3. The carbonyls considered are formaldehyde, acetone, and the experimentally used prochiral acetophenone.

II. Methodology

Calculations were based on the density functional theory (DFT) at the generalized gradient approximation (GGA) level. They were performed with the Gaussian 94 and 98 programs.[9] We used Becke's 1988 functional[10] for exchange and Perdew-Wang's 1991 gradient-corrected functional[11] for correlation. The PW91 functional gives a good evaluation of the weak interactions, while hybrid functionals such as B3LYP do not.[12] Nevertheless, for comparison, the last example has been recalculated with the B3LYP functional on geometries previously optimized. For the Rh atom, we used the relativistic effective core potential of Hay and Wadt (with 4s and 4p in the valence) and the corresponding double-ζ basis set.[13] A pseudopotential was also used for C, N, and O atoms.[14] The corresponding double-ζ valence basis set was of 41G type[15] with a d polarization function on N ($\alpha = 0.80$), C ($\alpha = 0.75$), and O ($\alpha = 0.85$). For H atoms, we used the Duning double-ζ basis set with a 2p polarization orbital on the hydride ($\alpha = 1.0$).

Geometries of reactants and products were fully optimized without any symmetry constraints. Transition state geometries were found via the quasi-Newton algorithms[16] QST2 and QST3. All transition states were characterized by determining the number of imaginary frequencies,[17] and a further characterization of the transition states was achieved by calculation of the intrinsic reaction coordinate (IRC)[18] leading to the corresponding energy minima.

III. Results and Discussion

A. Concerted Mechanism with $HRh(C_2H_4)_2(NH_3)_2$ (1). In a previous study,[6] we investigated the various structures of the d^8 model hydride 18-electron complex **1** as the assumed starting point of the catalytic cycle. It is built with model NH_3 and C_2H_4 ligands. In this section, we discuss in detail the potential energy surface associated with the concerted hydrogen transfer catalyzed by this active complex in the case of formaldehyde and acetone as substrates.

(a) Formaldehyde. In the exploration of the hydrogen-transfer process for the reduction of formaldehyde, we have considered the approach of the formaldehyde molecule to **1**. Formaldehyde was positioned between the NH_3 ligands, with the C═O bond almost perpendicular to the Rh−H one and with the carbonyl carbon 3 Å from H. The hydride was spontaneously transferred to the carbon of the formaldehyde, and a hydrogen of one NH_3 group moved to the oxygen to form methanol. The structure obtained after optimization is the hydrogen-bonded structure **2** (Figure 1), in which methanol is associated with the Rh complex by two hydrogen bonds: one between a hydrogen of the NH_3 ligand and the oxygen and the other between the hydrogen of the hydroxyl group and the nitrogen of the NH_2 ligand.

It is known (according to NMR results) that complexes similar to **1** have acidic protons on the amino groups.[4] The calculated Mulliken charges and overlap popula-

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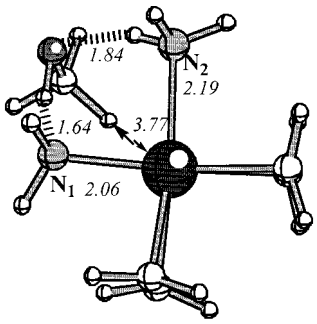

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Figure 1. Selected geometrical parameters of optimized structure (Å) for the hydrogen-bonded product **2**.

tions confirm this issue. On the free NH_3 molecule, the Mulliken charges are 0.291 on H and −0.870 on N, and the overlap population between N and H is 0.338. In comparison, on the NH_3 ligands in **1**, the Mulliken charges are respectively 0.365 and −0.869 on H and N, and the overlap population is 0.309. One can conclude that the hydrogens on the NH_3 in the complex have a more acidic character. Rhodium is responsible for this acidic character by withdrawing electron density from H through the N, without modification of the N electron density.

The Rh complex in product **2** is an approximately planar 16-electron complex. The N_1−Rh bond is shorter than the N_2−Rh bond (respectively 2.06 and 2.19 Å), which means that the N_1−Rh bond has a significant double-bond character. The resulting molecular complex **2** is 30 kcal mol^{-1} lower in energy than the two isolated molecules: the reaction is highly exothermic.

(b) Acetone. When the approach of the acetone molecule to **1** is the same as for formaldehyde, the precursor complex **3** is formed. In **3** (Figure 2), the two reactants (**1** and acetone) are associated by hydrogen bonds between the oxygen of acetone and one hydrogen of each NH_3 group (both distances between H and O are 2.25 Å). This starting reactant is formed without any barrier, and it is 3.3 kcal mol^{-1} lower than the two isolated molecules. One can notice that there is an interaction between the carbon of the acetone and the rhodium-bound hydride, with a distance of 2.96 Å. The small but positive overlap population between H and C is also consistent with the presence of this interaction (0.024 as compared to 0.025 for the two hydrogen bonds). The reaction is favored by the existence of this molecular precursor, since the two reactants are kept close together.

The resulting hydrogen-bonded complex **4**, corresponding to the transfer of two hydrogen atoms from **1** to acetone, was also optimized (Figure 2). In **4**, the two products are associated by hydrogen bonds and the structure is similar to that of **2**, where 2-propanol has replaced methanol. **4** is 12.2 kcal mol^{-1} lower than **3**; thus, the reaction is also exothermic.

In contrast to the case of formaldehyde, the reaction from **3** to **4** does not proceed without a barrier and we have located a transition state, $\mathbf{TS_{3\rightarrow 4}}$ (Figure 2), on the potential surface. In $\mathbf{TS_{3\rightarrow 4}}$, the hydride is close to the carbon (1.73 Å), and the Rh−H length (1.67 Å) is slightly longer than it was in **3** (1.62 Å). The H−N bond to be broken is almost the same as in **3** (1.04 Å vs 1.03 Å). The vibrational analysis shows that the normal mode with an imaginary frequency is a linear combination of the two forming H−C and H−O bonds. This transition state has a reactant-like character: in fact, there is only a rotation of the ketone, without any significant deformation of the Rh complex. Therefore, it is early and the activation energy is only 4.4 kcal mol^{-1}.

To get more detailed information about the change in geometry between $\mathbf{TS_{3\rightarrow 4}}$ and the product **4**, we have computed the reaction pathway starting from $\mathbf{TS_{3\rightarrow 4}}$ in the direction of the product (IRC[18]). From $\mathbf{TS_{3\rightarrow 4}}$, the hydride begins to be transferred to the carbon of the acetone and, at the same time, the H of one NH_3 ligand gets closer to the oxygen. Simultaneously, the other NH_3 ligand moves to the vacant site (former hydride site) to generate the Rh complex in a square-planar structure, while the configuration of the two ethylene ligands does not vary much. The newly formed 2-propanol molecule stays in the coordination sphere of **3** anchored by hydrogen bonds. This concerted mechanism is represented schematically in Scheme 2.

From these two cases with formaldehyde and acetone as substrates, we can conclude that an easy mechanism for the reaction is the direct formation of the expected alcohol (methanol or 2-propanol) via the transfer of both the hydride and an amine proton of the Rh(I) hydride complex. While this work was in progress, such a mechanism has been proposed by Noyori et al.[4] for the same reaction catalyzed by a Ru(II) complex. In this case, the intermediate complexes have been isolated and analyzed by X-ray spectra. Theoretical studies of this reaction with Ru(II) complexes appeared very recently.[19]

Nevertheless, we tried also to find a transition state corresponding to Gladiali's postulated mechanism,[8] which yields directly the ML_5 acetoxy complex **5** as the product (Figure 3). This complex has already been studied,[7] and the structure of Figure 4 is the most stable isomer of all possible ones. When formaldehyde is put parallel to the Rh−H bond with O at 2.4 Å from Rh and C at 1.75 Å from H and the geometry totally relaxed, it goes away from the metal. When, with the same geometry as a starting point, the distance Rh−O is maintained constant, one NH_3 moves away and formaldehyde coordinates to Rh in the η^2 form previously described[7] and the mechanism of the hydride transfer is that already studied. Thus, we can conclude that the concerted mechanism postulated by Gladiali is not possible with the studied complex.

(c) Why are the Reactivities of Formaldehyde and Acetone toward the Hydride Different? As described above, the reduction of formaldehyde takes place without any barrier, whereas with acetone a 4.4 kcal mol^{-1} activation energy is calculated. Assuming that frontier orbitals control the reactivity, we will examine the energy difference between these orbitals. The stabilizating interaction is between the carbonyl LUMO, that is the CO π^* orbital (π_{CO}^*), and the HOMO of the hydride−Rh complex **1** (with a main character on the metal s and $d_{x^2-y^2} + d_{z^2}$ orbitals and an antibonding mixing with the hydride *s* orbital). Effectively, the HOMO of $\mathbf{TS_{3\rightarrow 4}}$ is formed by the bonding interaction

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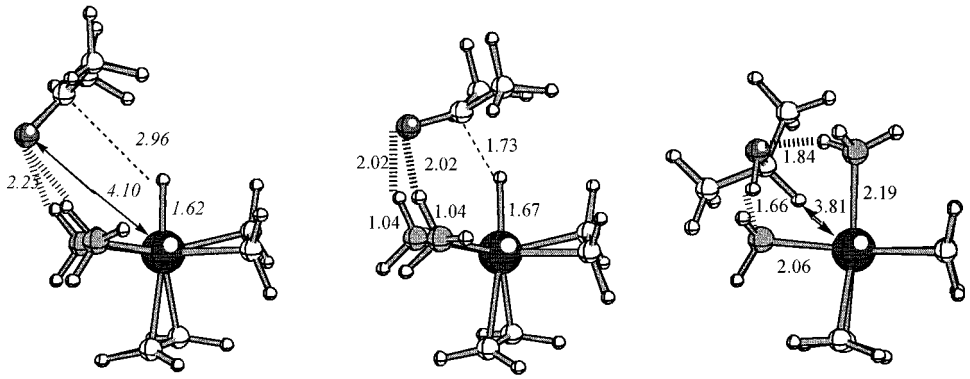

3 *(-3.3)* **$TS_{3->4}$** *(1.1)* **4** *(-15.5)*

Figure 2. Selected geometrical parameters of optimized structures (Å) for the precursor complex **3**, the transition state $\mathbf{TS_{3\rightarrow4}}$, and the product **4**. Energies (kcal mol^{-1}) in parentheses are relative to **1** + acetone.

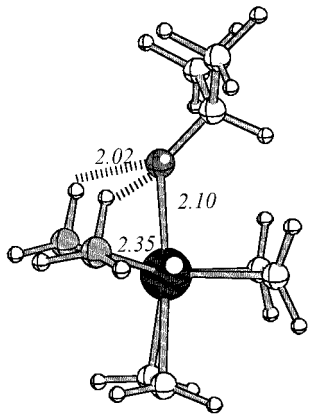

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Figure 3. Optimized geometry (Å, deg) for the product **5** in the case of Gladiali's cycle.

between the complex HOMO and the acetone LUMO, which gives a bonding interaction between the s orbital of the hydride and a p orbital of the carbon (an illustration of the orbital interactions in the TS HOMO will be given further in section B (b)). In general, the metal's occupied d orbitals lie lower in energy than the ligand's unoccupied ones. Actually, π_{CO}* was calculated at −2.4 eV in formaldehyde and −1.5 eV in acetone, and the complex HOMO was calculated at −3.2 eV. Therefore, the energy difference (0.8 eV vs 1.7 eV) is in favor of a greater reactivity of formaldehyde toward the hydride.

Of course, the destabilizating four-electron interactions between the occupied orbitals of the complex and of the molecule play also a role. They cannot be easily quantified. Nevertheless, one can suppose that they are larger for acetone than for formaldehyde because of the methyl groups.

The two considered kinds of interactions lead to the same conclusion: that is, a greater reactivity of formaldehyde as compared to acetone.

B. Concerted Mechanism with a Rh Complex Bearing a Chiral Diamine. (a) The Diamine Considered. The best real catalysts in fact bear secondary diamines as chiral ligands.[2b] For example, (*S*,*S*)-*N*,*N*′-dimethyl-1,2-diphenyl-1,2-ethanediamine, (*S*,*S*)-DMPEDA, has been extensively used. When bound to rhodium, the nitrogen atoms become stereogenic centers. We showed previously that in the preferred geometry of the coordinated (*S*,*S*)-DMPEDA, they have a *R* configuration.[20] In this geometry, the hydrogens on the carbons and nitrogens in the cycle are trans respective to each other with a N−H bond on one side pointing toward the Rh−H bond and the N−H on the other side pointing in the opposite direction (Figure 4). Other configurations for the nitrogen atoms are associated with diastereoisomeric complexes which are less stable by 2.6−6.6 kcal mol^{-1} and show a less favorable N−H orientation for reaction. In part A, we showed that a hydrogen on the same side as the hydride is crucial to anchor the carbonyl and to stabilize the transition state, via a hydrogen bond. These considerations led us to study the influence of the *R* configuration of this particular nitrogen without explicitly considering the chirality of the carbons. Thus, we have studied the concerted mechanism with complex **6** as catalyst (Figure 4), where the structure arising at the nitrogen atom is kept but the phenyl groups are replaced by hydrogen atoms. It allows us to study the enantioselectivity of the reaction: experimentally with the (*S*,*S*)-DMPEDA ligand, and for acetophenone, the (*R*)-1-phenylethanol enantiomer is favored with an ee of 67%.[2b] For this purpose, we considered the reduction of acetone and acetophenone. For the latter, two different approaches can be considered with respect to the prochiral faces. Therefore, we studied the enantioface differenciation.

(b) Acetone. In the case of acetone, we can locate a hydrogen-bound molecular complex, **7** (Figure 5). In **7**, there is a hydrogen bond between acetone and the hydrogen borne by the amino group of **6**. In addition the interaction between the hydride and the carbon of the carbonyl, as described above for the model complex, is maintained (overlap population of 0.01). Therefore, the acetone is close to the hydrogens to be transferred. This structure is relatively rigid. This precursor structure is 4.8 kcal mol^{-1} more stable than the two isolated reactants. The hydrogen bond is stronger than in **3** (2.09 Å in **7** instead of 2.25 Å in **3**), but the carbon is farther from the hydride (3.35 Å vs 2.96 Å). To avoid the steric

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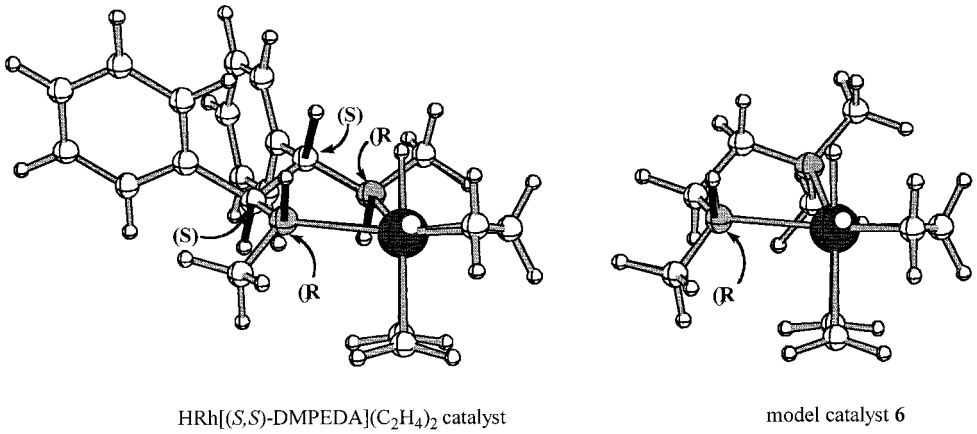

Figure 4. Preferred geometry of the real catalyst with (*S,S*)-DMPEDA as ligand and of the considered model complex **6** used in calculations.

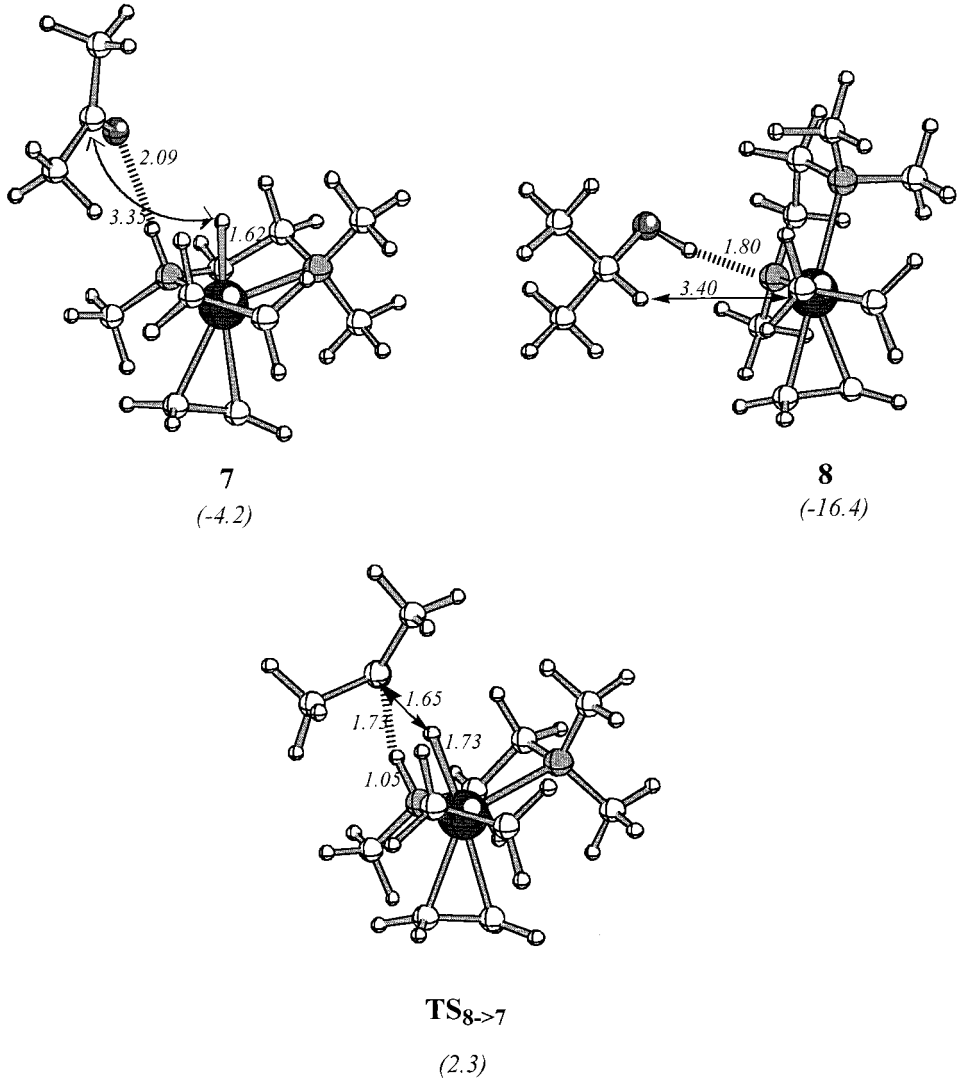

Figure 5. Selected geometrical parameters of optimized structures (Å) for the precursor complex **7**, the transition state $\mathbf{TS_{7\rightarrow 8}}$ and the product **8**. Energies (kcal mol^{-1}) in parentheses are relative to **6** + acetone.

hindrance between a methyl group bound to the second nitrogen and that of acetone, acetone is not positioned above complex **6** but beside it so that the carbonyl plane is almost perpendicular to the equatorial plane.

The product **8**, corresponding to the transfer of two hydrogens, is 12.2 kcal mol^{-1} lower than **7** so that the reaction is exothermic. In **8** (Figure 5), the Rh complex has a square-planar geometry and its structure is similar to **4**. Since the second nitrogen does not bear any hydrogen, 2-propanol is kept in the coordination sphere of the Rh complex by only one hydrogen bond (length 1.80 Å).

Starting from **7**, we found the transition state $\mathbf{TS_{7\rightarrow 8}}$ for this concerted transfer of both a proton and the

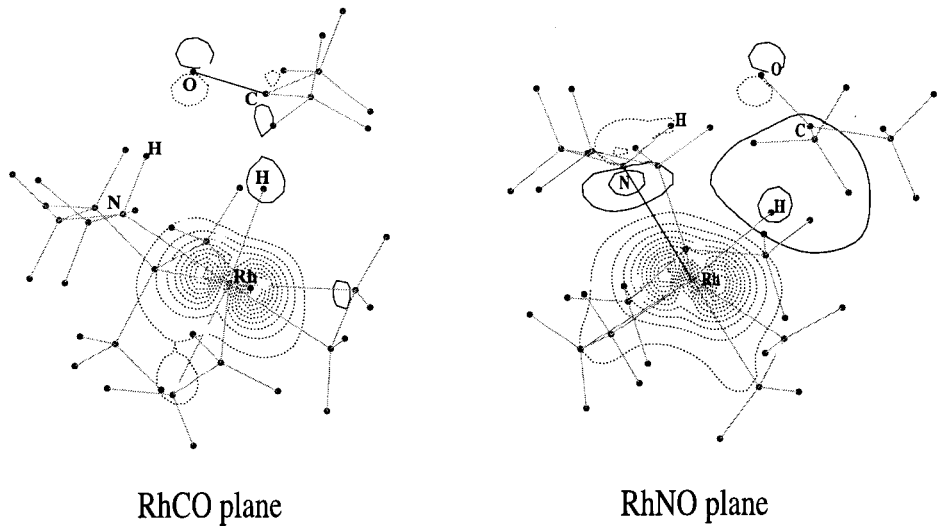

Figure 6. Contour map of the HOMO of the transition state $\mathbf{TS_{3\rightarrow4}}$ in the planes RhCO and RhNO. The solid and dashed lines indicate opposite signs.

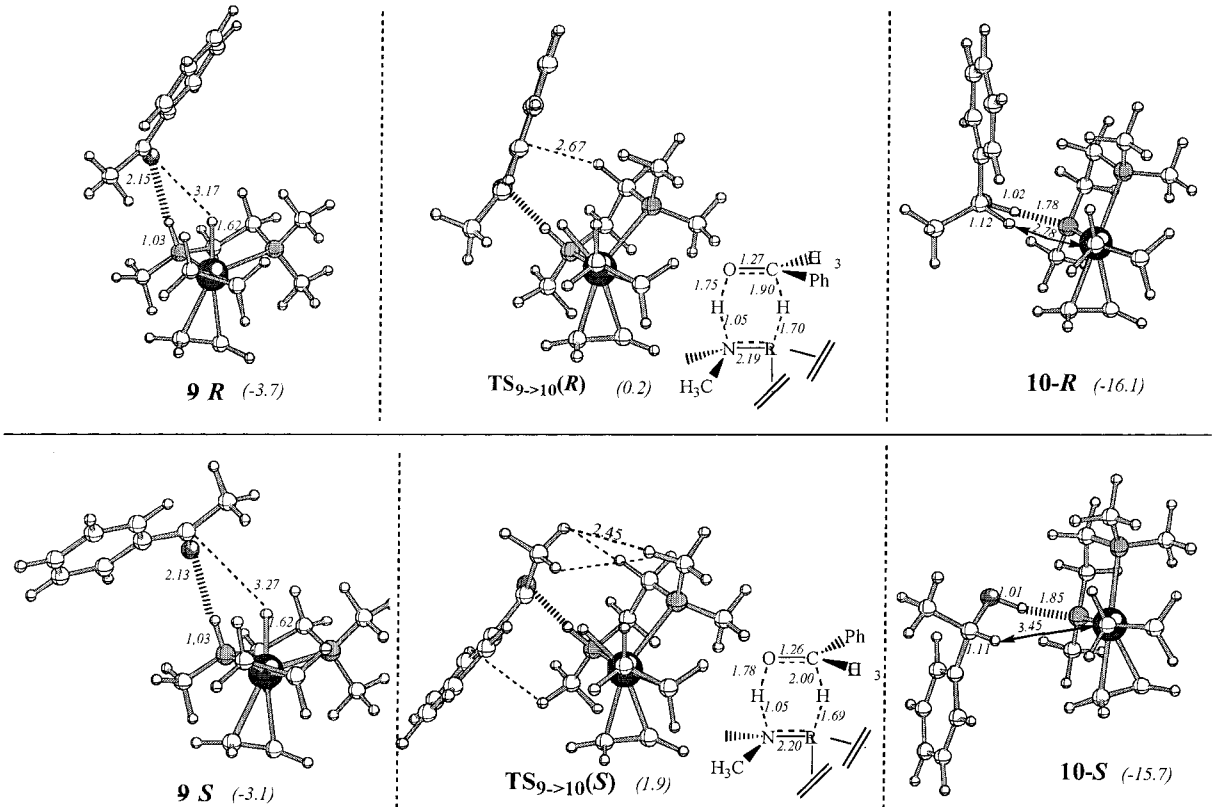

Figure 7. Selected geometrical parameters of optimized structures (Å) for the two diastereoisomeric precursor complexes **9**, the two transition states $\mathbf{TS_{9\rightarrow10}}$, and the two products **10**. The energies (kcal mol^{-1}) are relative to **6** + acetophenone.

hydride from complex **6** to acetone (Figure 5). The barrier is 6.5 kcal mol^{-1}. $\mathbf{TS_{7\rightarrow8}}$ is a six-membered cyclic transition state, and the six atoms involved are almost in the same plane (the deviation from the average plane is only 12°). IRC calculations confirm that this saddle point actually connects **7** and **8**. In this transition state the geometry of the Rh complex is almost the same as in the free complex **6** (except the Rh−H bond and the N−H bond, which are elongated to 1.73 Å and 1.05 Å, respectively) and the C−H and O−H bonds are not completely formed (1.65 and 1.73 Å, respectively). Hence, $\mathbf{TS_{7\rightarrow8}}$ is early. The orbital interactions between the six atoms are illustrated in Figure 6 by plots of the electronic density for the HOMO orbital. In the RhCO plane one observes the bonding interaction of H with π^* CO and the antibonding interaction of the hydride with the rhodium. In the RhNO plane, one notices a bonding interaction of H (from N−H) with the oxygen atom, whereas the N−H interaction is still bonding, which reflects the early character of the transition state.

The transition state $\mathbf{TS_{7\rightarrow8}}$ is similar to that obtained with the model complex ($\mathbf{TS_{3\rightarrow4}}$): the relevant geometrical parameters are almost the same. Therefore, the study of this reaction with the model hydride complex **1** gives a good prediction for this concerted mechanism.

To complete the catalytic reaction cycle, the hydride

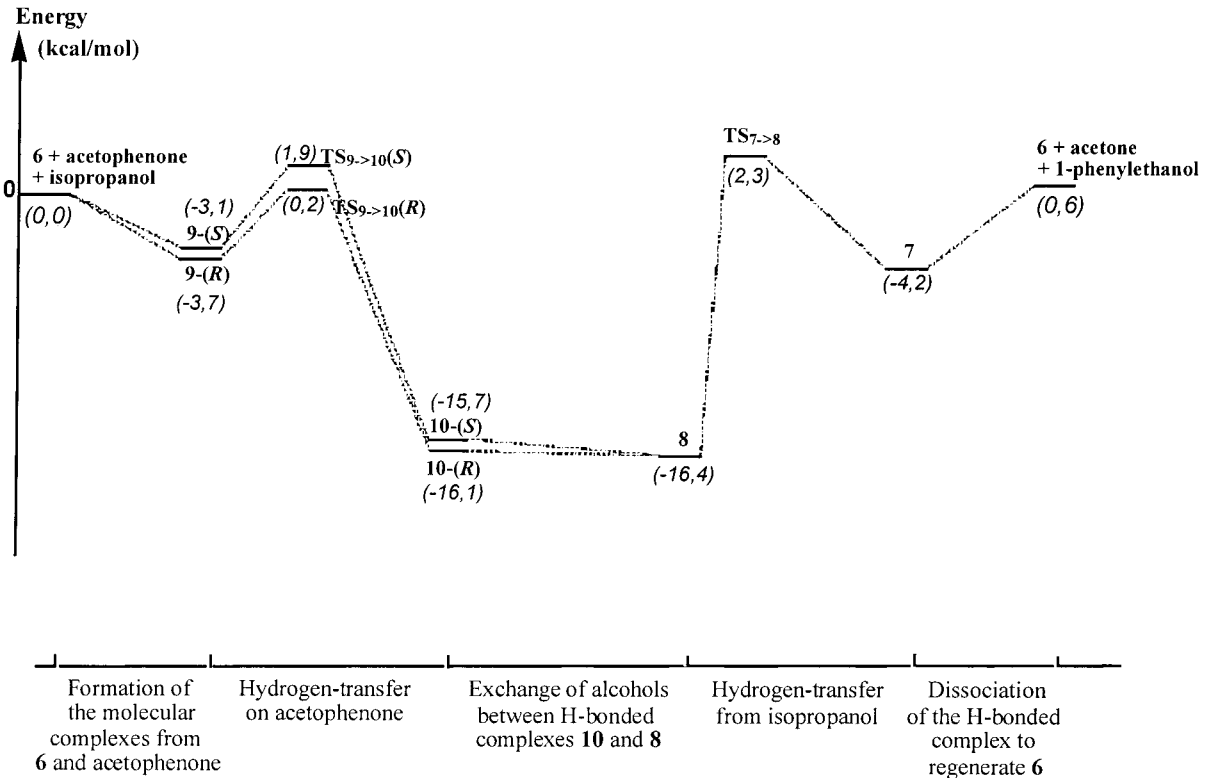

Figure 8. Calculated reaction profile (kcal mol^{-1}) of the entire catalytic cycle for the hydrogen transfer between acetophenone and 2-propanol catalyzed by **6**. All the energies reported refer to the reference state "**6** + acetophenone + 2-propanol". See text for details.

complex **6** needs to be regenerated from **8**. This is performed by just the reverse reaction **8** → **7**, starting from a 2-propanol molecule of the solvent. From the results above, this reverse reaction is associated with the highest energy barrier on the cycle: 18.7 kcal mol^{-1}. This barrier is reasonable so that the catalytic cycle is active. In addition, the fact that there is an excess of 2-propanol ("solvent") explains that the equilibrium can be displaced and hence the kinetic and thermodynamic conditions are not limiting.

(c) Acetophenone. Acetophenone exhibits two prochiral faces and two possible molecular precursor complexes. If the *re* face interacts with the Rh−H moiety and N−H, after optimization **9-(*R*)** is obtained as starting reactant (Figure 7). It corresponds to the phenyl ring pointing toward the methyl group borne by the tertiary amine (nitrogen bearing the two methyl groups). In this case, the hydrogen bond is 2.15 Å and the carbon-hydride interaction is associated with a distance of 3.17 Å (overlap population is 0.01). For the *si* face, we locate the diastereoisomer **9-(*S*)** (Figure 7), where the acetophenone methyl group points toward the tertiary amine. The hydrogen bond is almost the same (2.13 Å) and the C−H interaction is a little weaker (3.27 Å for the hydride−carbon distance and the overlap population is 0.007). The carbonyl plane is almost parallel to the equatorial plane of **6**. There is a small energy difference between the two structures (**9-(*R*)** is energetically favored by 0.6 kcal mol^{-1}).

We have located the transition states **TS$_{9\to10}$(*R*)** and **TS$_{9\to10}$(*S*)** (Figure 7) for the hydride and proton concerted transfers. With **9-(*R*)** and **9-(*S*)** as starting points, the reaction barriers are 3.9 and 5.0 kcal mol^{-1}, respectively. The energy difference between the two diastereoisomeric transition states is 1.7 kcal mol^{-1}. This difference is subtle and certainly not far from the accuracy of energies of GGA functionals. However in our case, very similar structures are compared, which differ only by a few interactions, so that energy comparisons are more reliable. Single-point calculations have been performed with the B3LYP functional. The reaction barriers are 6.5 and 8.4 kcal mol^{-1}, and the energy difference between the two diastereoisomeric transition states is 2.1 kcal mol^{-1}. Hence, both functionals give the same trend, although the values are slightly higher with B3LYP. In conclusion, the *R* pathway is kinetically favored. Moreover, this energy difference result can be qualitatively explained in terms of steric interactions between hydrogens. There are three distances between hydrogens which are smaller than the sum of van der Waals radii in **TS$_{9\to10}$(*S*)** (the shortest is 2.45 Å between acetophenone and amine methyl groups) and only one in **TS$_{9\to10}$(*R*)** (2.67 Å between hydrogens of the phenyl ring and of the diamine CH_3). An indirect probe of this steric interaction is the deformation of the diamine ligand. The calculated deformation energy has been found to be 0.5 kcal mol^{-1} larger in the **TS$_{9\to10}$(*S*)** structure than in **TS$_{9\to10}$(*R*)**.

Going through these saddle points, we found one stationary point each for the structures **10-(*R*)** and **10-(*S*)**. They correspond to the product: the resulting ML_4 Rh complex associated by a hydrogen bond with respectively (*R*)- or (*S*)-1-phenylethanol (Figure 7). Since, in each case, these products are lower in energy than the reactants, the transfer is exothermic ($\Delta E = -12.4$ kcal mol^{-1} for the *R* product and −12.6 kcal mol^{-1} for the *S* product).

(d) Catalytic Cycle. Figure 8 summarizes the previous results and shows the calculated energy profile for the entire catalytic cycle, with the Rh complex bearing

the diamine ligand model **6** of the (*S,S*)-DMPEDA chiral diamine, acetophenone as substrate, and 2-propanol as hydrogen donor. In this profile, the additional molecules (acetophenone and 2-propanol) are considered at infinite distance (except in the cases explicitly mentioned). The energy difference between the final state and the initial state of the cycle is the energy of reduction of acetophenone and of oxidation of 2-propanol. This reaction is calculated to be almost thermoneutral (in fact endothermic by 0.6 kcal mol^{-1}), which is a known result.[21] Activation energies are reasonable. They are smaller than the ones obtained in the case of the two-step mechanism previously studied,[7] which requires an activation energy of 23.6 kcal mol^{-1}. Thus, this concerted mechanism with direct formation of the alcohol seems more probable than the two-step one. Furthermore, it explains the experimental preferential formation of the (*R*)-1-phenylethanol.[2b] Moreover, our study shows that the hydrogen transfer reduction of carbonyls by a hydride−Rh(I) complex does not follow the mechanism suggested by Gladiali et al.[8] which involves an alkoxy complex.

We have seen that it is essential for the activity and selectivity of the studied pathway that the diamine bear at least one hydrogen on one nitrogen atom. Experimentally, however, the reaction also takes place when no hydrogen is present at the nitrogen. Thus, what is the reaction mechanism in the case of tertiary amines?

C. Concerted Mechanism with a Rh Complex Bearing Tertiary Amines. Experimental results[2b] show that tertiary amine ligands exhibit almost the same activity as primary or secondary ones, but very poor enantioselectivity. Therefore, we have studied the mechanism with a hydride complex bearing two trimethylamine ligands, with formaldehyde and acetone as reactants.

Calculations were performed with a hydride complex carrying two ethylene ligands and two trimethylamine ligands, $HRh(C_2H_4)_2[N(CH_3)_3]_2$. First, for formaldehyde and acetone, molecular precursors have been characterized; the carbons of the carbonyls are positioned 2.15 and 3.80 Å above the hydride, respectively. They are located 2 kcal mol^{-1} (formaldehyde) and 1.1 kcal mol^{-1} (acetone) lower in energy than isolated molecules. From these starting points we have employed the reaction coordinate method to force the hydride to get closer to the carbon until the H−C distance reaches the usual value for a H−C bond. At each point the geometry has been optimized. For both carbonyls, the energy continuously increased by 20 kcal mol^{-1} and we could not find any transition state. Therefore, the direct formation of the alcoholate product is not conceivable.

A possible reaction mechanism is the two-step one,[7] which does not involve the presence of any hydrogen on nitrogen ligands and which is not stereoselective. This would explain the low enantioselectivity observed for such ligands.

The concerted mechanism of path B via a metal-coordinated alkoxide complex is also available in the case of tertiary amine ligands. It was also studied. A cyclic transition state such as the one proposed for Meerwein−Ponndorf−Verley reduction[21,22] is involved. With the model ligands (C_2H_4 and NH_3) and with acetone as the carbonyl species, the activation barrier is around 22 kcal mol^{-1}, which shows that it is a realistic mechanism. However, it is not enantioselective since it involves a step of decoordination of one amine group, leading to a square-planar ML_4 complex. More details on this mechanism will be given elsewhere.

IV. Conclusion

Within the framework of DFT calculations, we have studied two possible concerted mechanisms for the reduction of carbonyls catalyzed by a Rh(I)−hydride complex. On the basis of these calculations, we showed that the mechanism postulated by Gladialy is not realistic. In contrast, a concerted transfer of both the hydride and a proton (present on the amine ligand) is very probable in the case of primary or secondary amine ligands.

Effectively, the thermodynamic profile of the full cycle is found to be smooth, without excessive barriers, the overall reactions being quasi-thermoneutral. The first step corresponds to the transfer of two hydrogens from the hydride complex to the acetophenone leading to the formation of (*R*)- or (*S*)-1-phenylethanol. This step has a low activation barrier (3.9−5 kcal mol^{-1} depending on the coordinated face of acetophenone) and is exothermic (by 12.4−12.6 kcal mol^{-1}). Hence, when a model diamine ligand with the structure found to be the most stable for the real chiral diamine is used, the activation energies to form the diastereomeric transition states are different by 1.1 kcal mol^{-1}. Therefore, this first step controls the enantioselectivity, favoring the production of the *R* isomer. The following step (oxidation of 2-propanol) regenerates the active catalyst. It is the crucial step of the catalytic cycle for the activity because it has the highest activation barrier (18.7 kcal mol^{-1}) and is significantly endothermic (by 12.2 kcal mol^{-1}). However, the barrier remains reasonable and, overall, is lower than the one obtained in the case of the two-step mechanism described previously (23.6 kcal mol^{-1}).[7] Therefore, when catalysts bearing secondary or primary amines are used, it is clear that the concerted pathway is favored over the two-step one. Moreover, this concerted mechanism can explain the observed enantioselectivity, which was not the case for the two-step mechanism.

On the other hand, for Rh complexes with tertiary amine we conclude that this concerted mechanism cannot be envisaged. Consequently, the two-step mechanism via a hydride complex (path A)[7] or the concerted mechanism via an alkoxy complex (path B) (with a cyclic transition state such as that proposed for Meerwein−Ponndorf−Verley reduction[21,22]), which does not require a primary or secondary amine ligand, can be assumed. These pathways are not enantioselective, which explains the absence of selectivity observed for tertiary amines.

A more detailed study on the factors governing the enantioselectivity is in progress, especially the effect of phenyl groups on the carbons of the diamine. Kinetics arguments will be given.

Acknowledgment. This work was aided by computational support of the Pôle Scientifique de Modélisation Numérique at ENS-Lyon. We are grateful to Dr. Vincent Robert for valuable discussions.

OM010120V

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