Structure of the Diamine−Rh(I) Precursor in the Asymmetric Hydride Transfer Reduction of Ketones: A Theoretical and Experimental Approach

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Abstract: The nature of the Rh−diamine precursor in the catalytic cycle of the asymmetric hydride transfer reduction of carbonyl compounds was examined by both theoretical and experimental approaches. On the one hand, calculations based on the DFT theory were performed on various $[RhH(NH_3)_n(C_2H_4)_{4-n}]$ complexes, in the trigonal bipyramidal (TBP) and square pyramidal (SP) forms. Their geometry has been fully optimized, and it was found that the only stable complex corresponds to $n = 2$ in a TBP form, with the ethylenes in the equatorial plane. On the other hand, mass analyses of the synthesized complexes showed that their composition was $[Rh(COD)(diamine)]^+ X^-$ ($X^- = Cl^-$ or PF_6^-). Several experiments were performed to study the influence of the ligand stoichiometry, the nature of the diene (cyclooctadiene (COD) or others). Finally, the two methods converged and proved that the active species contains only one diamine and one diene bound to the metal.

1. Introduction

Phosphorus-containing ligands are well-known and used in asymmetric catalysis. Nevertheless, phosphine-based metal complexes present several drawbacks (price, instability) which generally limit their development to an industrial scale. Moreover, Stille's group[1] has demonstrated that heterogenization of such complexes is feasible but not easy. Therefore, efforts have been made to develop other classes of ligands that would be easily accessible, cheaper, more stable than phosphines, and potentially more suitable for heterogenization purposes. Nitrogen-containing compounds seem to fit such criteria, and considerable efforts are made in this field.

They can be efficient chiral modifiers in several homogeneous or heterogeneous asymmetric reactions such as allylic alkylation,[2] cyclopropanation,[3] epoxidation,[4] or hydroxylation.[5] Recently, Pfaltz,[6] Noyori,[7] and Mukaiyama[8] as well as reports from our laboratory[9,10] showed that nitrogen-containing ligands can be used in asymmetric reductions with similar or even higher selectivities than those obtained with the best chiral phosphines. They particularly proved to be efficient for the hydride transfer reduction of ketones, leading to optically active secondary alcohols. Chiral alkylphenanthrolines have been used by Gladiali *et al.*[11] with ee's up to 65% for the rhodium catalyzed reduction of acetophenone. We showed that the use of C_2 symmetric diamines can lead to methyl mandelate with nearly complete selectivity (ee > 99%) with a rhodium complex.[8] More recently, chiral thioureas derived from these C_2 symmetric diamines led to 87% ee in the ruthenium catalyzed reduction of acetophenone.[12]

Although these results are satisfactory in terms of efficiency and selectivity, the mechanism of the reaction has not been elucidated. The catalyst structure has not been completely defined. Only few X-ray structures of complexes have been reported for diamine derivative ligands. Recently, Noyori[13] published the structure of the supposed active species: only one diamine derivative ligand, (1*S*,2*S*)-*N*-*p* -toluenesulfonyl-1,2-diphenylethylenediamine, is bound to the ruthenium together with the η^6-arene moiety coming from the catalyst precursor.

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(1) Stille, J. K. Proc. IUPAC, *Macromol. Symp. 28th* **1982**, 263.

(2) Leutenegger, U.; Umbricht, G.; Fahrni, C.; von Matt, P.; Pfaltz, A. *Tetrahedron* **1992**, *48*, 2143.

(3) Bedekar, A. V.; Andersson, P. G. *Tetrahedron Lett.* **1996**, *37 (23)*, 4073.

(4) Jacobsen, E. N. in *Catalytic Asymmetric Synthesis*; Ojima, I., Ed.; VCH: New York, 1993; Chapter 4.2.

(5) Johnson, R. A.; Sharpless, K. B. In *Catalytic Asymmetric Synthesis*; Ojima, I., Ed.; VCH: New York, 1993; Chapter 4.4.

(6) (a) Müller, D.; Umbricht, G.; Weber, B.; Pfaltz, A. *Helv. Chim. Acta* **1991**, *74*, 232. (b) von Matt, P.; Pfaltz, A. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 566. (c) Zhou, Q. L.; Pfaltz, A. *Tetrahedron* **1994**, *50*, 4467. (d) Pfaltz, A.; von Matt. P.; Lloyd-Jones, C.; Minidis, A. B. E. *Helv. Chim. Acta* **1995**, *78*, 265.

(7) (a) Hashigushi, S.; Fujii, A.; Takehara, J.; Ikariya, T.; Noyori, R. *J. Am. Chem. Soc.* **1995**, *117*, 7562. (b) Ohkuma, T.; Ooka, H.; Ikariya, T.; Noyori, R. *J. Am. Chem. Soc.* **1995**, *117*, 10417.

(8) Nagata, T.; Yorozu, K.; Yamada, T.; Mukaiyama, T. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 2145.

(9) (a) Gamez, P.; Fache, F.; Mangeney, P.; Lemaire, M. *Tetrahedron Lett.* **1993**, *34*, 6897. (b) Gamez, P.; Fache, F.; Lemaire, M. *Tetrahedron: Asymmetry* **1995**, *6*, 705. (c) Gamez, P.; Dunjic, B.; Fache, F.; Lemaire, M. *Tetrahedron: Asymmetry* **1995**, *6*, 1109.

(10) Fache, F.; Gamez, P.; Nour, F.; Lemaire, M. *J. Mol. Catal.* **1993**, *85*, 131.

(11) Gladiali, S.; Pinna, L.; Delogu, G.; De Martin, S.; Zassinovich, G.; Mestroni, G. *Tetrahedron: Asymmetry* **1990**, *1*, 635.

(12) Touchard, F.; Gamez, P.; Fache, F.; Lemaire, M. *Tetrahedron Lett.* **1997**, *38 (13)*, 2275.

(13) Haack, K.-J.; Hashiguchi, S.; Fujii, A.; Ikariya, T.; Noyori, R. *Angew. Chem., Int. Ed. Engl.* **1997**, *36* (3), 285.

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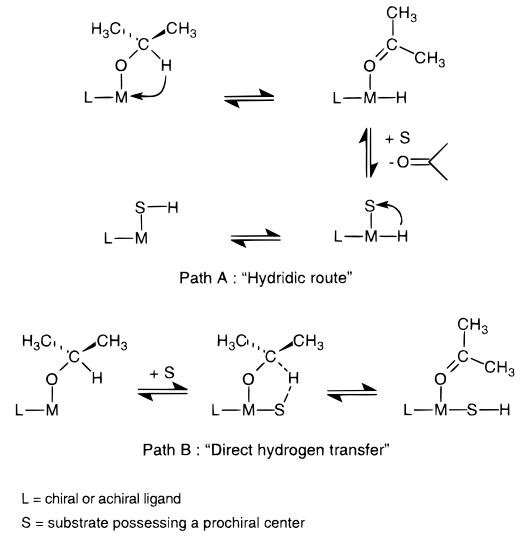

Figure 1. Possible paths for the hydrogen-transfer reactions.

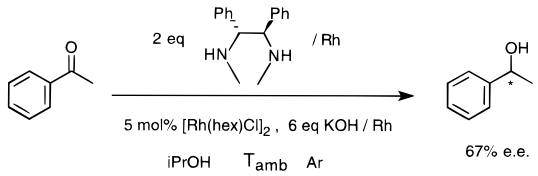

Figure 2. Asymmetric hydride transfer reduction of acetophenone.

Some mechanisms have been proposed for the asymmetric hydrogen transfer reaction.[14] Two general paths could be envisaged (Figure 1): a stepwise process through a hydride complex (path A) and a concerted process where the hydrogen is directly transferred from the secondary alcohol to the substrate (path B). In the catalytic cycle proposed by Gladiali *et al.*,[11] the active complex is a pentacoordinated rhodium hydride with two phenanthroline ligands (path A).

Recently, we reported 67% ee at 100% conversion for the hydride transfer reduction of acetophenone using *N*,*N*′-dimethyl-1,2-diphenyl-1,2-ethanediamine and $[Rh(hex)Cl]_2$ as metallic precursor[9] (Figure 2). Furthermore, we obtained 60% ee at 100% conversion, with $[Rh(COD)Cl]_2$, using polyureas[15] synthesized using different diisocyanates and the same diamine, showing that heterogenization of our system is successful.

Our purpose was to elucidate the mechanism of this reaction. Many facts related to the active species remain unknown. We wanted to find out the factors influencing the enantioselectivity in order to be able to optimize them. Therefore, we combined a theoretical and an experimental study.

Gladiali's proposed cycle was used as initial hypothesis although in our system diamines are sp^3 ligands, whereas phenanthrolines are sp^2 ligands. Hence, we investigated the structure of the supposed initial d^8 complex $[RhHL_2]$ with L = diamine or cyclooctadiene (the metallic precursor of our system is $[Rh(COD)Cl]_2$).

From an experimental point of view, we synthesized rhodium−diamine complexes and studied the influence of the metallic precursor, the cyclooctadiene, and the ligand stoichiometry. From a theoretical point of view, we fully optimized the d^8 complex with different ligands (amines or alkenes).

2. Theoretical Study

The d^8 ML_5 complexes have been extensively studied at the semiempirical EHT level.[16−19] The influence of the ligand nature on the structure has been elucidated together with the preferred position of the π-ligand, like ethylene. Moreover, ab initio calculations have been performed on d^8 five coordinated Rh complexes such as $[RhH(C_2H_4)(CO)_2PH_3]$. Morokuma[20] has studied the relative stability of the different geometries of this complex and shown that all the equilibrium structures in the catalytic cycle are "trigonal bipyramidal".

In our calculations, we modeled the diamine ligand by two NH_3 and the cyclooctadiene (COD) ligand by two ethylene C_2H_4 molecules.

2.1. Methodology. The calculations were based on the density functional theory (DFT) at the generalized gradient approximation (GGA) level. They were performed with the Gaussian 94 program.[21] We used the Becke's 1988 functional[22] for exchange and the Perdew-Wang's 1991 gradient corrected functional[23] for correlation. For the Rh atom, we used the relativistic effective core potential of Hay and Wadt with the corresponding double ζ basis set.[24] For C, N, and H atoms, in the study of $[RhH(NH_3)_4]$, we used the double ζ basis of Dunning[25] augmented by a polarization d function on N atoms ($\alpha = 0.80$) and a p function on the hydride ($\alpha = 1.00$). For the calculations on $[RhH(NH_3)_2(C_2H_4)_2]$, a pseudopotential was also used for N and C atoms.[26] The corresponding basis set was of 4-1G type[27] (Table A, Supporting Information) with a d function on N ($\alpha = 0.80$) and C ($\alpha = 0.75$) and a p function on the hydride ($\alpha = 1.00$).

All the structures given in the text were fully optimized using the gradient technique. The binding energies were calculated as the difference between the energy of the whole molecule and the energies of the two isolated parts. A negative value means that the bond is stabilizing.

2.2. Study of $[RhH(NH_3)_4]$ and $[RhH(NH_3)_3]$. (a) $[RhH(NH_3)_4]$. The d^8 complex $[RhH(NH_3)_4]$ is a model for the supposed $[RhH(diamine)_2]$ initial complex of Gladiali's cycle.[11] It is well-known that ML_5 complexes can be stable in a trigonal-bipyramidal (TBP) or square-pyramidal structure (SP).[19] Four structures are possible: a trigonal-bipyramidal form with H in axial or equatorial position and a square-pyramidal complex with H in apical or basal position (Figure 3).

(14) Zassinovich, G.; Mestroni, G. *Chem. Rev. (Washington, D.C.)* **1992**, *92*, 1051.
(15) Gamez, P.; Dunjic, B.; Fache, F.; Lemaire, M. *J. Chem. Soc., Chem. Commun.* **1994**, 1417.
(16) Rossi, A. R.; Hoffmann, R. *Inorg. Chem.* **1975**, *14*, 365.
(17) Albright, T. A.; Burdett, J. K.; Whangbo, M. H. In *Orbital Interaction in Chemistry*; J. Wiley & Sons, Inc.: 1985.
(18) Albright, T. A.; Hoffmann, R.; Thibeault, J. C.; Thorn, D. L. *J. Am. Chem. Soc.* **1979**, *101*, 1 (14), 3801.
(19) Albright, T. A. *Tetrahedron* **1982**, *38*, 1339.
(20) Kuga, N.; Su-Qian Jin; Morokuma, K. *J. Am. Chem. Soc.* **1988**, *110*, 3417.
(21) *Gaussian 94* (*Revision D.1*); Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Gill, P. M. W.; Johnson, B. G.; Robb, M. A.; Cheeseman, J. R.; Keith, T. A.; Petersson, G. A.; Montgomery, J. A.; Raghavachari, K.; Al-Laham, M. A.; Zakrzewski, V. G.; Ortiz, J. V.; Foresman, J. B.; Cioslowski, J.; Stefanov, B. B.; Nanayakkara, A.; Challacombe, M.; Peng, C. Y.; Ayala, P. Y.; Chen, W.; Wong, M. W.; Andres, J. L.; Replogle, E. S.; Gomperts, R.; Martin, R. L.; Fox, D. J.; Binkley, J. S.; Defrees, D. J.; Baker, J.; Stewart, J. P.; Head-Gordon, M.; Gonzalez, C.; People, J. A. Gaussian, Inc.: Pittsburgh, PA, 1995.
(22) Becke, A. D. *Phys. Rev. A* **1988**, *38*, 3098.
(23) Perdew, J. P.; Wang, Y. *Phys. Rev. B* **1992**, *45*, 13244.
(24) Hay, P. J.; Wadt, W. R. *J. Chem. Phys.* **1985**, *85*, 299.
(25) Dunning, T. H., Jr.; Hay, P. J. In *Modern Theoretical Chemistry*; Schaefer III, H. F., Ed.; Plenum: New York, 1976; pp 1−28.
(26) Bouteiller, Y.; Mijoule, C.; Nizam, M.; Barthelat, J. C.; Daudey, J. P.; Pelissier, M. *Mol. Phys.* **1988**, *65*, 295.
(27) Bouteiller, Y.; Mijoule, C.; Nizam, M.; Barthelat, J. C.; Daudey, J. P.; Pelissier, M. Private communication (Table A, Supporting Information).
(28) Mangeney, P.; Tajero, T.; Grosjean, F.; Normant, J. F. *Synthesis* **1988**, 255.

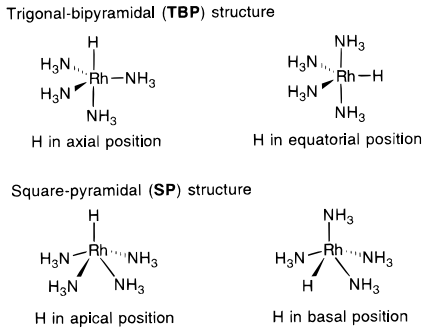

Figure 3. Possible ML_5 complex structures.

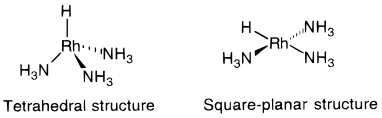

Figure 4. Possible ML_4 complex structures.

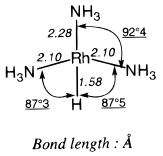

Figure 5. Most stable structure of ML_4 [$Rh(NH_3)_3H$].

A geometry optimization has been performed on each structure. Whatever the initial structure, a NH_3 is moved out of the coordination sphere, either in the equatorial plane in the trigonal-bipyramidal (TBP) structures or in apical position in the square-pyramidal (SP) form (H basal), to give a square-planar ML_4 complex: [$Rh(NH_3)_3H$]. In the SP structure with H in apical position, one of the four equivalent basal NH_3 is eliminated to give the same ML_4 complex. Therefore, it seems that a complex containing four NH_3 groups is not stable.

(b) [$RhH(NH_3)_3$]. To evaluate the NH_3 binding energy, the ML_4 [$Rh(NH_3)_3H$] complex has also been studied. Different geometries are possible: a tetrahedral or a square-planar structure (Figure 4).

After optimization, the most stable structure (Figure 5) is the square-planar form, in agreement with the above results.

The molecule is almost planar. The nitrogen lying trans to H is further from the rhodium atom than the others (2.28 Å instead of 2.10 Å). This is due to the hydride trans influence. The ligands cis to H are bent toward H which is less sterically hindered than NH_3. A similar geometry has been obtained by Morokuma[20] for the [$RhH(C_2H_4)(CO)_2PH_3$] complex.

2.3. Study of [$RhH(NH_3)_2(C_2H_4)_2$]. As was concluded in the previous section, it seems that a four amine coordinated structure is not stable. Hence we envisaged, contrary to Gladiali's proposal, that the rhodium complex could contain one cyclooctadiene ligand. Calculations have been performed on model ML_5 [$Rh(NH_3)_2(C_2H_4)_2H$] complexes with two ethylenes and two NH_3's. Several positions of the five ligands have been considered. To simulate the real complex (cyclooctadiene and diamine), the two ethylenes are in cis position one with another as well as the two NH_3 groups. Therefore, six complexes have been optimized. The starting structures **I**−**VI** have the same standard values for the geometry (Rh−N = 2.3 Å; Rh−H = 1.6 Å; Rh−C = 2.15 Å; $L_{eq}RhL'_{eq}$ = 120°). Relative energies of the standard geometries used as starting points for the optimization are given in Figure 6. These structures are divided into two groups leading to two stable forms.

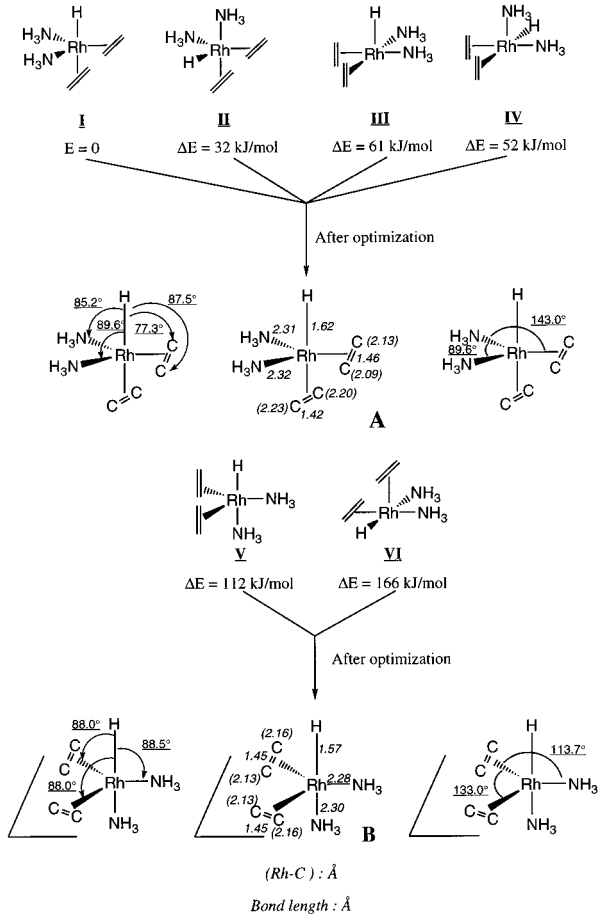

Figure 6. Stable structures of the [$Rh(NH_3)_2(C_2H_4)_2H$] complex.

Both stable structures are trigonal bipyramids with ethylenes in equatorial position (structure **B**) or in axial and equatorial position (structure **A**). In both cases, hydride prefers the axial position (Figure 6). Comparing the starting structures, it is noticeable that **II** is 32 kJ/mol less stable than **I**, which is in agreement with the theoretical and experimental results obtained by Rossi and Hoffmann.[16] In a d^8 TBP complex, the best σ-donor ligand prefers the axial position over the equatorial one. On the contrary, it has been found by calculations that in SP complexes the best σ-donor prefers the basal position over the apical one (**IV** is 9 kJ/mol more stable than **III**). Rossi and Hoffmann[16] have also shown that, in these complexes, the π ligands have better interactions in the basal plane. Effectively, **IV** is more stable than **VI** by 114 kJ/mol.

The most stable form (TBP or SP) for ML_5 d^8 complexes depends strongly on the ligand nature. With the ligands considered here, the TBP structure is preferred over the SP one. The important orbitals of structures **I** and **IV** are presented in Figure 7 (**IV**, in Figure 6, can be drawn as **IVa** by rotation of the axis).

In **I**, the d_{xy} orbital, antibonding with the NH_3's, that would be the HOMO in a complex with four σ-donors, is in fact stabilized by the bonding interaction with the π^*_{cc} (vide supra). In **IVa**, the HOMO is the d_y^2 orbital which has the symmetry to interact with π_{cc} but not with π^*_{cc}. Moreover, d_y^2 is antibonding with π_{cc} and remains high in energy. This explains why the optimized structure is a TBP one, whatever the initial complex.

It is noteworthy that, in structure **B**, the four carbons are in the same equatorial plane, despite the steric hindrance (the angle between the midpoint of the C═C bonds in structure B is ca.

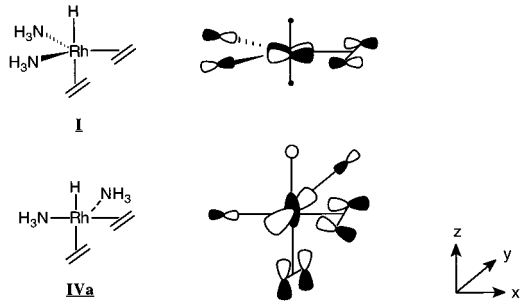

Figure 7. $[Rh(NH_3)_2(C_2H_4)_2H]$ SP and TBP structure orbitals.

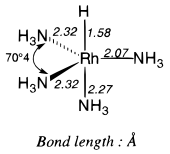

Figure 8. Trigonal-bipyramidal $[Rh(NH_3)_4H]$ complex structure.

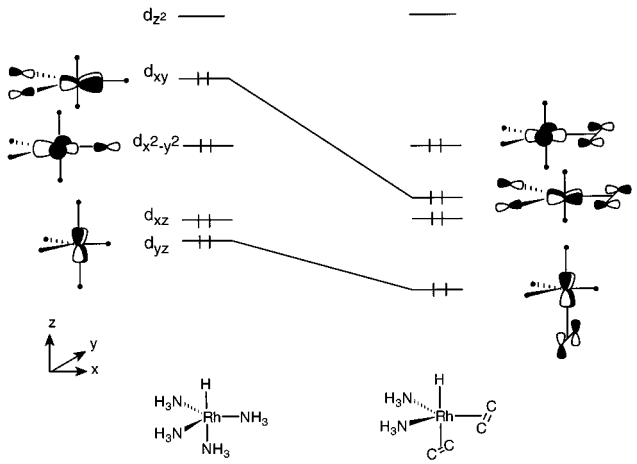

Figure 9. Trigonal-bipyramidal $[Rh(NH_3)_4H]$ and $[Rh(NH_3)_2(C_2H_4)_2H]$ orbital interaction diagram.

133° instead of 89.6° between the NH_3 ligands in structure **A**). Albright[19] and Morokuma[20] have already described that unsaturated molecules prefer the equatorial position in a trigonal bipyramid. Moreover, they prefer to be in the equatorial plane rather than perpendicular to it. These two results are due to the fact that the Rh d_{xy} orbital is hybridized away from the NH_3 ligands (see Figures 7 and 9) and has therefore a better overlap with the π orbitals of the unsaturated molecule than the d_{xz} and the d_{yz} which are involved in the equatorial perpendicular position and in the axial position, respectively. For this reason structure **B** is more stable than structure **A**, by 53 kJ/mol.

Dissociation energies have been studied. In all cases, the MHL_3 complex, obtained after dissociation of the structures **A** and **B**, has been fully optimized. It is worth emphasizing that, in both cases, the NH_3 ligand dissociates more easily than ethylene. In structure **A**, the NH_3's are not strongly bound (15 kJ/mol) compared to 74 or 83 kJ/mol, depending on the position of the leaving ethylene. In structure **B**, the NH_3 dissociation energy is about 52 and 98 kJ/mol for ethylene. Whatever the structure, the MHL_4 complexes are always more stable than the MHL_3 + L structure, indicating that complexes **A** and **B** are stable.

2.4. Influence of the Nature of the Ligands on the Stability of $RhHL_4$ Complexes: Orbital Interactions. The difference of stability between $[Rh(NH_3)_4H]$ and $[Rh(NH_3)_2(C_2H_4)_2H]$ can be explained taking the orbital interactions into account. As the leaving NH_3's are in the equatorial plane of the trigonal bipyramid, we compared structure **A** to the corresponding one with four NH_3 groups. The geometry of the latter has been chosen as follows: the Rh−NH_3 bond lengths in the equatorial plane are equal to those found in complex **A** (2.32 Å), and the other Rh−NH_3 bond lengths have been optimized (Figure 8).

For the sake of clarity, the ligands are considered along the axis (x or z) and in the (xy) plane, the real structures being distorted, to a small extent, from this ideal geometry.

Then, we evaluated the NH_3 dissociation energy in this complex. According to the different complexes and ligand energies, the dissociated $[Rh(NH_3)_3H]+NH_3$ structure is 133 kJ/mol more stable than the $[Rh(NH_3)_4H]$ complex.

To explain this result, we compared the orbital interactions in the two complexes (Figure 9).

According to the diagram, in the highest occupied orbital of the complex with four NH_3 groups, the bond between the metal d_{xy} orbital and the equatorial NH_3 p orbitals is antibonding. This orbital is high in energy, which strongly destabilizes the molecule. Therefore, the four nitrogen ligand complex is not stable. The rhodium cannot complex four σ-donor ligands. An equatorial NH_3 has to be removed to stabilize the molecule. The high d_{xy} orbital which is now nonbonding is stabilized, whereas the other orbitals do not vary much.

In the case of $[Rh(NH_3)_2(C_2H_4)_2H]$, the HOMO is lowered thanks to the bonding interaction between the metal d_{xy} orbital and the equatorial ethylene π^* orbital (back-bonding interaction). The π-acceptor ligand lying in the pyramid plane stabilizes the high orbital.

The nonbonding metal d_{yz} orbital of the $[Rh(NH_3)_4H]$ complex is stabilized in the same manner in the $[Rh(NH_3)_2(C_2H_4)_2H]$ structure due to the bonding interaction with the axial olefine π^* orbital (back-bonding interaction). This d-level stabilization by back-donation is a well-known effect.[19] Therefore, the two olefine and two NH_3 coordinated complex is stable. Combining σ-donor and π-acceptor ligands stabilizes the structure. These theoretical results lead one to think that the active complex includes a diene and a diamine.

3. Experimental Study

Gladiali used rhodium complexed by phenanthroline ligands (sp^2) to reduce acetophenone and came to the conclusion that two bidentate ligands (four nitrogen atoms) were bound to the metal. Thanks to X-ray structures, Noyori proved that, for the same reaction, only one bidentate diamine derivative ligand (sp^3 type) was coordinated to the ruthenium. Taking into account the theoretical results, it seems that our system is close to Noyori's one. To confirm or reject these features, we tried to synthesize and isolate different complexes with one or two diamine ligands. To our knowledge, no X-ray structures have been obtained for complexes with four σ-donor ligands.

3.1. Synthesis of a Rhodium−Diamine Complex. The diamine and the rhodium precursor were stirred at room temperature in dichloromethane. A yellow precipitate appeared. It was then filtered and dried. Several amounts of diamine (1, 2, or 10 equiv), as well as different counteranions (Cl^-, PF_6^-) were used, but analyses showed that only one complex is obtained. According to mass analyses, only one diamine and one cyclooctadiene are coordinated to the rhodium. Regardless of the quantity of ligand, the complex always has the same composition (Figure 10). It is in complete agreement with the theoretical result, which shows that four σ-donor ligands cannot be coordinated to the metal, whereas a complex with two σ-donor and two π-acceptor ligands is stable.

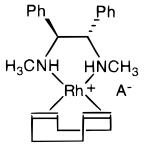

Figure 10. Synthesized rhodium−diamine complex.

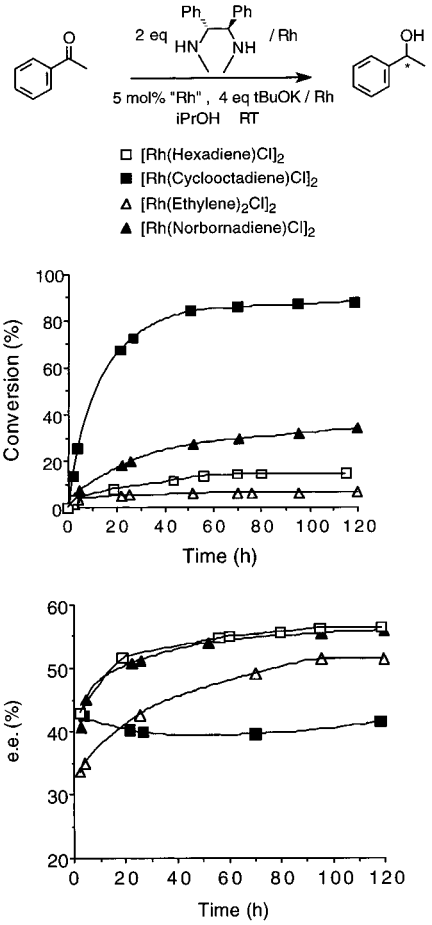

Figure 11. Metallic precursor influence on activity and selectivity.

The complexes thus obtained turned out to be efficient catalysts.

3.2. Influence of the Metallic Precursor. If the isolated complex is the true catalyst, the nature of the metallic precursor and particularly the diene may have an influence on the reaction. On the contrary, if two diamine ligands are coordinated to the rhodium, like Gladiali's proposed active complex, the nature of the diene will not have any influence on activity and selectivity. To ascertain one of these hypotheses, several metallic precursors with different dienes were used under the same conditions for the reduction of acetophenone. The results are shown in Figure 11.

The nature of the metallic precursor has an influence on both activity and selectivity. When ethylene is used, 51% ee is obtained but conversion is very low. Hexadiene and norbornadiene give approximately the same ee, 55% and 56% respectively, higher than for cyclooctadiene (47%) but with lower conversions.

The nature of the diene has an influence on the reaction, which tends to prove that the diene is coordinated to the metal in the active complex.

3.3. Influence of an Excess of Cyclooctadiene. We postulated that the cyclooctadiene coordinated complex could be the precursor of the active complex in the catalytic cycle

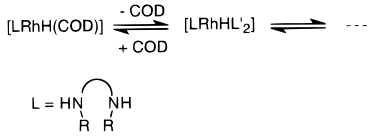

Figure 12. Possible structures of the active complex in the catalytic cycle.

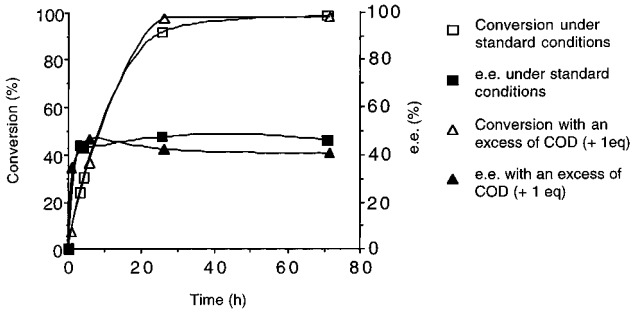

Figure 13. Influence of cyclooctadiene on reaction. Conditions: [acetophenone] = 3×10^{-2} mol/L; [Rh]/[substrate] = 5 mol %; [ligand]/[Rh] = 2; [tBuOK]/[Rh] = 4. Ligand = (1*R*,2*R*)-(+)-*N*,*N*′-dimethyl-1,2-diphenyl-1,2-ethanediamine. "Rh" = $[Rh(COD)Cl]_2$.

Table 1. Influence of the Stoichiometry of Ligand on the Asymmetric Reduction of Acetophenone[a]

entry	[ligand]/[Rh]	convn (%)	ee (%)
1	1	93	39
2	2	98	47
3	3	98	46
4	4	64	43

[a] 50 h of reaction. [acetophenone] = 3×10^{-2} mol/L. [Rh]/[substrate] = 5 mol %; [tBuOK]/[Rh] = 4; ligand = (1*R*,2*R*)-(+)-*N*,*N*′-dimethyl-1,2-diphenyl-1,2-ethanediamine. "Rh" = $[Rh(COD)Cl]_2$.

(Figure 12). Other ligands L′ (L′ = solvent, substrate, ...) could substitute the cyclooctadiene. In that case, an excess of COD should deplace the equilibrium in favor of [LRhH(COD)], which should have an influence on the rate of the reaction.

A test was performed using excess of cyclooctadiene: 1 equiv of cyclooctadiene is added before the introduction of the substrate. Results are shown in Figure 13.

According to Figure 13, it seems that excess of cyclooctadiene has no real influence on activity or selectivity. This result as well as the previous ones (Figure 11) confirms the presence of the diene in the active complex of the catalytic cycle.

3.4. Influence of the Ligand Stoichiometry. In our previous studies,[9] we used to add 2 equiv of ligand per metal atom. In these conditions, the catalytic system was proved to be always stable. Considering both our theoretical calculations and our first experimental results, we wanted here to examine closely the ligand stoichiometry. Different amounts of diamine were engaged in the reaction. Results are shown in Table 1.

Whatever the ligand-to-metal ratio, approximately the same ee is obtained. The use of 4 equiv of diamine decreases the reactivity (entry 4). According to entry 1, it seems that 1 equiv of diamine is enough. However, in that case, problems of reproductibility have been encountered: metallic rhodium happened to be formed, leading to racemate phenylethanol. When 2 equiv of ligand are in solution, the excess of diamine must stabilize the complex, preventing the formation of black particules of rhodium. However, only one diamine is coordinated to the metal.

4. Conclusion

Both theoretical and experimental results lead to the conclusion that the active complex in the catalytic cycle of the

asymmetric reduction of carbonyl compounds is most likely a rhodium complex with one diamine and one diene coordinated to the metal. This complex is different from the active species proposed by Gladiali. It may be due to the nature of the ligands. Diamines are sp^3 ligands, whereas phenanthrolines are sp^2 ligands. We have shown that four σ-donor ligands cannot be bound to the rhodium. Nevertheless, Gladiali's catalytic system is quite different due to the π-orbitals of the phenanthrolines, which can play a role in back-donation, so that his proposed cycle remains possible. Besides, Noyori has evidenced that the ruthenium catalyzed transfer hydrogenation takes place by way of a metal hydride (Figure 1, path A) rather than the metal alkoxides (Figure 1, path B). As for our rhodium−diamine system, this mechanistic aspect is under current research in our laboratory.

As we have shown that the nature of the diene has a great influence on the reaction, it seems worthwhile to study complexes with a chiral diene. Moreover, further works are still under progress to optimize the diamine ligand structure.

Experimental Section

General Experimental Procedures. All the commercially available products were used without further purification. Conversion and enantiomeric excess (ee) were monitored by gas chromatography using a CYDEX B chiral column. ^{1}H- and ^{13}C NMR spectra were recorded on a Bruker-AM200 FT spectrometer with chloroform-*d* as solvent. Chemical shifts are reported in parts per million (ppm), and coupling constants are reported in Hertz (Hz). All reactions were performed in screw-top V−Vials (Aldrich Z11,515-0). The *N*,*N*′-dimethyl-1,2-diphenyl-1,2-ethanediamine was synthesized according to a method already described by Mangeney et al.[28]

Asymmetric Hydride Transfer Reduction of Acetophenone. The (1*R*,2*R*)-(+)-*N*,*N*′-dimethyl-1,2-diphenyl-1,2-ethanediamine (0.0125 mmol, 2 equiv/Rh, except otherwise stated), the metallic precursor (0.0062 mmol Rh), and potassium *tert*-butoxide (0.0250 mmol, 4 equiv/Rh) were dissolved in 2-propanol (4 mL) and stirred for 1 h. The acetophenone (0.125 mmol) was then added.

[RhCl(COD) (1*R*,2*R*)-(+)-*N*,*N*′-dimethyl-1,2-diphenyl-1,2-ethanediamine] Synthesis. The metallic precursor $[RhCl(COD)]_2$ (0.52 mmol Rh) and the diamine (1.04 mmol, 2 equiv/Rh) were separately dissolved in 2.5 mL of CH_2Cl_2. The two solutions were mixed, and a yellow powder immediately precipitated. The solution was stirred overnight and then filtered. The precipitate was dried under vacuo (yield = 85%). ^{1}H NMR ($CDCl_3$) (*J* in Hertz) δ 7.27−7.11 (m, 10H), 4.27 (m, 4H, COD), 4.17 (dd, 2H, J = 2.9; 8.9), 2.71 (d, 6H, J = 5.8), 2.38−2.36 (m, 4H, COD), 1.76−1.71 (m, 4H, COD). HRMS calculated mass for $C_{24}H_{32}N_2Rh$: 451.1620523 g/mol. Found mass: 451.163800 g/mol. Anal. Calcd for $C_{24}H_{32}N_2RhCl$: C, 59.21; H, 6.62; N, 5.75; Cl, 7.28; Rh, 21.44. Found: C, 59.12; H, 6.60; N, 5.57; Cl, 7.08; Rh, 20.01.

[$RhPF_6$(COD) (1*R*,2*R*)-(+)-*N*,*N*′-dimethyl-1,2-diphenyl-1,2-ethanediamine] Synthesis. The metallic precursor $[RhCl(COD)]_2$ (1 mmol Rh) and KPF_6 (1.3 mmol) were dissolved in a 1:1 mixture of CH_2Cl_2/H_2O (10 mL). The diamine (2.04 mmol) was then added to the solution. After 15 min of stirring, the two phases were separated. The organic phase was washed twice with 5 mL of water and then dried over $MgSO_4$. Et_2O was added slowly until a white precipitate was obtained (yield = 98%). ^{1}H NMR ($CDCl_3$) (*J* in Hertz) δ 7.27−7.12 (m, 10H), 4.17 (m, 4H, COD), 3.91 (dd, 2H, J = 2.9; 8.5), 3.54−3.43 (m, 2H), 2.33−2.20 (m, 4H, COD), 2.08 (d, 6H, J = 5.8), 1.63−1.58 (m, 4H, COD); ^{13}C NMR ($CDCl_3$) δ 135.5, 128.9, 128.6, 127.7, 82.9, 82.6, 82.4, 82.2, 72.6, 35.3, 31.8, 28.2. HRMS calculated mass for $C_{24}H_{32}N_2Rh$: 451.1620523 g/mol. Found mass: 451.1626000 g/mol.

Supporting Information Available: Basis sets for C and N atoms (1 page). See any current masthead page for ordering and Web access instructions.

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