Catalytic Asymmetric Hydride Transfer Reduction of Ketones with Rhodium and Chiral Diamine Ligands: Approach of the Active Species Structure by DFT Calculations

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The structure of RhH(diamine)$(C_2H_4)_2$ complexes involved in the title reaction was studied by DFT calculations. The structures of all the possible diastereoisomers of the Rh complexes were optimized with either the (*R*,*R*)-*N*,*N*′-dimethyl-1,2-dimethylethylenediamine or the (*R*,*R*)-*N*,*N*′-dimethyl-1,2-diphenylethylenediamine (in both cases with the *threo* diamine). The diastereoisomer with all the substituents of the nitrogen atoms arranged *trans* to each other relative to the mean plane was found to be the most stable. Therefore, the active species involved in the title reaction has unambiguously a structure presenting a C_2-symmetry axis with stereogenic nitrogen atoms. This can be the key to enantioselectivity.

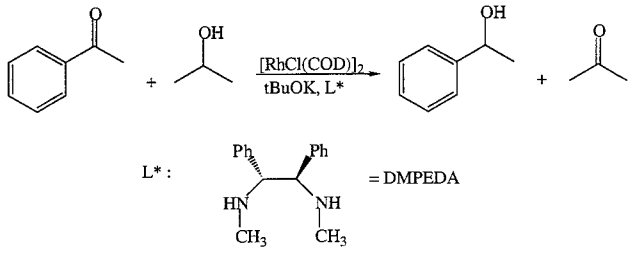
I. Introduction

Catalytic hydride transfer reaction allows the reduction of ketones into the corresponding alcohols with good to excellent enantioselectivity when chiral ligands are used. Among them, nitrogen compounds are of particular efficiency especially with rhodium and ruthenium precursors.[1,2] Some years ago, we have shown that *N*,*N*′-dimethyl-1,2-diphenylethylenediamine (DMPEDA) is a good ligand for the rhodium-catalyzed hydride transfer reduction of ketones (Scheme 1).[2]

With this system, 67% ee was measured on acetophenone. Recently, excellent results were also published by Noyori et al. with rhodium and (*R*,*R*)-*N*-(*p*-toluenesulfonyl)-1,2-cyclohexanediamine [Cp*RhCl(chiral diamine)].[3] Up to 97% enantiomeric excesses (ee) were measured for the reduction of acetophenone.

Our previous studies have shown that the substitution on the nitrogen atoms is of high importance and that it is necessary to have three different substituents on the nitrogen atoms to ensure good enantioselectivity.[4] Thus, when the nitrogen atoms of the diamine are not substituted (1,2-diphenylethylenediamine) or substituted by identical groups (*N*,*N*′-tetramethyl-1,2-diphenylethylenediamine), only 17% or 6% ee is obtained for the reduction of acetophenone against 67% with DMPEDA ($NHCH_3$). We assumed that the nitrogen atoms became stereogenic centers when bound to the rhodium and thus were responsible for the transfer of chirality. We also proposed that in this particular case the C_2-symmetry has to be kept in the catalytic active species in order to reach a good enantioselectivity. These hypotheses are based on our own experimental observations and also on the results published by Alexakis[5,6] and others.[7] These groups have shown by X-ray and NMR that, in the aminal structure derived from the DMPEDA, the methyl groups on the nitrogen atoms were in *trans* position compared with the phenyl groups on the carbon atoms in α position. In this case, the two nitrogen atoms are chiral centers of the same stereochemistry. We assume that it is the same feature when the diamine is bound to the rhodium, forming a five-

Scheme 1. Hydride Transfer Reduction of Acetophenone Using Rhodium and a Chiral Diamine



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(1) (a) Noyori, R.; Hashiguchi, S. *Acc. Chem. Res.* **1997**, *30*, 97. (b) Fache, F.; Schulz, E.; Tommasino, M. L.; Lemaire, M. *Chem. Rev.* **2000**, *100*, 2159.
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(4) Gamez, P.; Fache, F.; Lemaire, M. *Tetrahedron: Asymmetry* **1995**, *6*, 705.
(5) Alexakis, A.; Lensen, N.; Mangeney, P. *Tetrahedron Lett.* **1991**, *32*, 1171.
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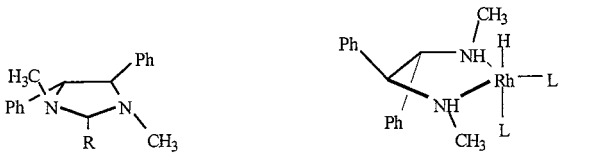
Scheme 2. Structure Analogy between Aminal and the Supposed Rhodium Active Species



Aminal Supposed rhodium complex

membered ring described in Scheme 2. Obviously, the understanding of the structure of the real active catalytic species is of crucial importance in order to design new, more efficient, and selective catalysts.

It has not been possible to obtain a crystal structure of the catalytic complex, probably because of the lower stability of nitrogen complexes compared with phosphorus analogues. Thus, to evaluate the hypotheses concerning the structure of the active complex, theoretical studies have been performed by our group.[8] We have shown that the active species involved in the reduction of ketones by hydride transfer possesses two sp^3 nitrogen atoms as σ ligands and two ethylenes as π ligands. This was afterward confirmed by experimental data. To go further in our structural approach of the active species, different complexes with diamine ligands bearing various substituents (methyl or phenyl groups) have been studied, and the resulting structures, optimized by DFT calculations, are discussed in this paper.

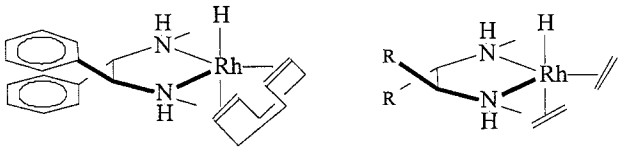
II. Methodology

1. Theoretical Calculations. The calculations were based on the density functional theory (DFT) at the generalized gradient approximation (GGA) level (Becke's 1988 functional[10] for exchange and Perdew−Wang's 1991 functional[11] for correlation). Some structures have been recalculated with the B_3-LYP hybrid functional, with no significant change in the relative energies. For the rhodium atom, we used the relativistic effective core potential of Hay and Wadt[12] with the corresponding double-ζ basis set. The 1s cores of N and C were also described by a pseudopotential,[13] and the corresponding basis set for the valence was of 4-1G type[14] with a d polarization function on N ($\alpha = 0.80$) and C ($\alpha = 0.75$) and a p polarization function on the hydride ($\alpha = 1.00$). The calculations were performed with the Gaussian 94 program.[9]

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.

The molecular mechanics calculations were performed with the MM+ method, which is mostly used for organic molecules.

Scheme 3. Experimental and Model Complexes



Experimental complex Model complex

We considered the Allinger[15] parametrization. The calculations were performed using the HyperChem software.

2. Model Complexes Used. Experimentally, the rhodium precursor is the dimer $[Rh(C_8H_{12})Cl]_2$ and the ligand used is the *threo* (*S*,*S*)-*N*,*N*′-dimethyl-1,2-diphenylethylenediamine (DMPEDA). We have previously shown that the active species in the catalytic cycle is most likely a rhodium complex with one hydride, one diamine (DMPEDA), and one diene (cyclooctadiene = COD) coordinated to the metal.[8]

A rhodium dimer containing ethylene was tested as a catalyst precursor and exhibited behavior similar to the COD precursor. To save computational time, we therefore modeled the COD ligand by two ethylene (C_2H_4) molecules (Scheme 3).

III. Results and Discussion

1. Conformational Study of the Free Diamine Ligands. The geometry of diamines with structures close to DMPEDA was studied. First, the phenyl groups on the carbon atoms have been replaced by methyl groups. Various positions of the substituents on the nitrogen atoms have been tested for the *threo* (*R*,*R*)- or (*S*,*S*)-$H_3CHN-CH(CH_3)-(H_3C)HC-NHCH_3$ diamine (DMMEDA, Scheme 4) and optimized.

The best conformation is the staggered *gauche* conformer **1**, the staggered *trans* conformer **2** being only 3 kJ/mol less stable. In the first structure, the diamine is not planar since the NCCN dihedral angle is 50.7°. The four methyl groups are alternatively placed on both sides of the mean plane of the molecule. In the second structure, the nitrogen atoms and the two carbon atoms are almost in the same plane (NCCN = 11°). In ligand **1**, the two nitrogen atoms point in the same direction and are ideally placed to interact with the metal. Not too much extra energy is required to turn these atoms toward the rhodium. Considering the Newmann projections of Scheme 4, one notices that the arrangement around the C−C bond is either C, N, N, C in **1** or N, C, C, N in **2**. If the relative stability were only based on steric considerations, that would mean that the interaction between two $NHCH_3$ groups is less destabilizing than that between two CH_3 groups. In fact, the H atom on one nitrogen points toward the other nitrogen, and therefore N−H hydrogen bonds are formed. The bond lengths are 2.6 Å, and the overlap populations (op) have a positive value of 0.013. To prove that the steric effects are not the only cause for the distinction between **1** and **2**, we also calculated the same conformers of the diamine bearing no methyl on the carbon nor on the nitrogen atoms. In this case no steric repulsion exists in conformer **2**. Our calculations showed that the *gauche* conformer **1** is more stable than the *trans* conformer **2** by 13 kJ/mol and that again hydrogen bonds are formed with N−H bond lengths of 2.54 Å. Therefore the staggered *gauche* conformation of the *threo* diamine is due to the existence of hydrogen bonds and not to steric

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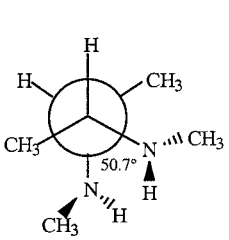
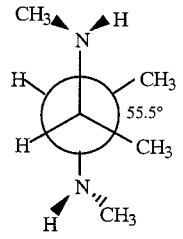
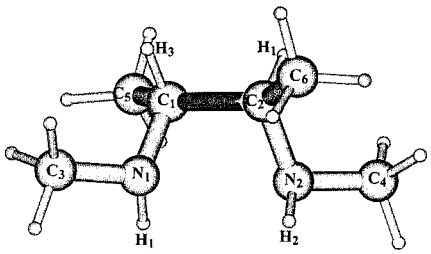
Scheme 4. Most Stable Conformations of the (*R*,*R*)-*N*,*N*′-Dimethyl-1,2-dimethylethylenediamine

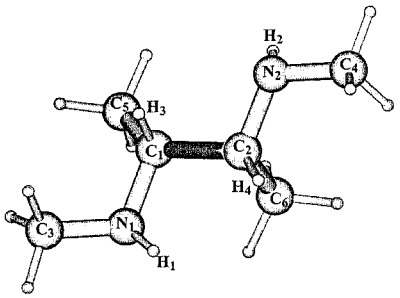


(R,R) staggered gauche
ΔE= 0 kJ/mol
Conformer **1**



(R,R) staggered trans
ΔE= 3 kJ/mol
Conformer **2**

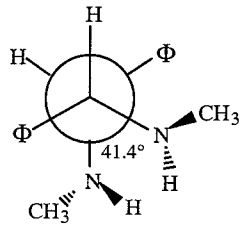




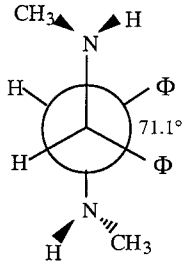
N_1-N_2	2.78 Å
N_1-C_1	1.48 Å
N_2-C_2	1.48 Å
C_1-C_2	1.56 Å
N_1-C_3	1.47 Å
N_2-C_4	1.47 Å
N_1-H_2	2.58 Å
N_2-H_1	2.60 Å
N_1-C_1-C_2-H_2	50.7 °

N_1-C_1	1.48 Å
N_2-C_2	1.48 Å
C_1-C_2	1.56 Å
N_1-C_3	1.47 Å
N_2-C_4	1.47 Å
N_1-H_2	3.89 Å
N_2-H_1	4.20 Å
N_1-C_1-C_2-H_2	169.0°

Scheme 5. Most Stable Conformations of the (*R*,*R*)-*N*,*N*′-Dimethyl-1,2-diphenylethylenediamine



(R,R) staggered gauche
ΔE= 0 kJ/mol
Conformer **1**



(R,R) staggered trans
ΔE= 2 kJ/mol
Conformer **2**

effects. However, when steric effects are added, the difference between **1** and **2** can change.

We have then calculated the same conformations for the *threo* DMPEDA with phenyl instead of methyl groups on the carbon atoms. The staggered *gauche* conformer (Scheme 5), where hydrogen bonds also exist, is slightly more stable than the *trans* one by 2 kJ/mol, as is the case for DMMEDA. Hence, the free diamine shows the same relative conformer stability either with methyls or with phenyls on the carbons. One must keep in mind that the reactions are done in solvent (2-propanol), which can change the conformer relative stabilities. We have therefore simulated the solvent effects by the polarizable continuum model (PCM) of Tomasi,[16] which considers the solute in a cavity of solvent only represented by its dielectric constant. We chose ethanol to model 2-propanol. The introduction of solvent effects increases the difference between the two conformers, the staggered *gauche* one being now 9 kJ/mol more stable. Hence the *threo* diastereoisomer of DMPEDA prefers the staggered *gauche* conformation, well adapted for the rhodium coordination.

We then studied the ligands *N*,*N*′-dimethyl-1,2-dimethylethylenediamine and *N*,*N*′-dimethyl-1,2-diphenylethylenediamine coordinated to the metal.

2. Rh−Diamine Complexes. As we have shown in the previous paragraph, the most stable conformer of the free *threo* diamine is in a staggered *gauche* conformation. All the substituents are placed alternatively above and below the mean plane of the molecule, which presents a C_2-symmetry axis. We studied the Rh−diamine complex in order to know if the ligand presents the same conformation when coordinated to the metal.

2.1. Rhodium−*N*,*N*′-Dimethyl-1,2-dimethylethylenediamine Complexes. We studied different trigonal-bipyramidal rhodium complexes. The methyl groups on the carbon atoms were placed in a *trans* position (*threo* diastereoisomer), either in axial position or in equatorial position. The methyl groups on the

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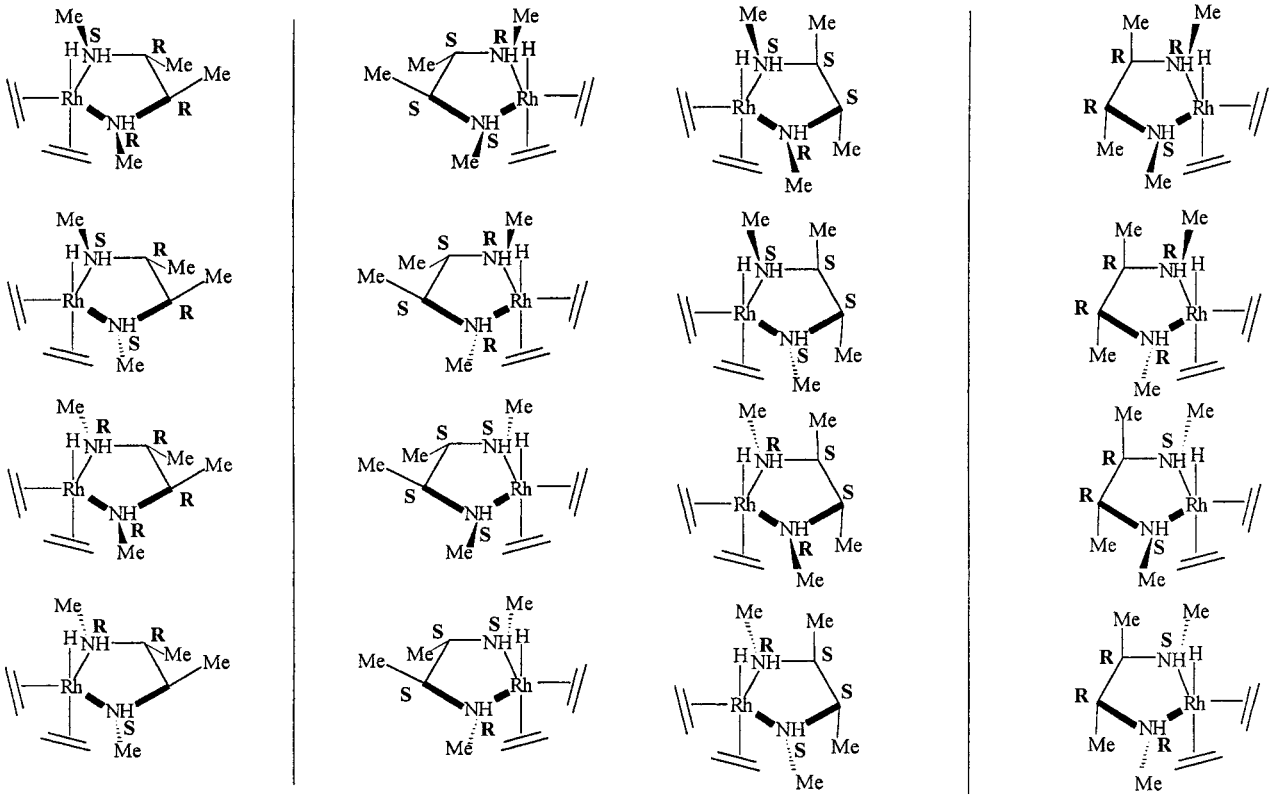
Scheme 6. Sixteen Possible Rhodium−*N,N′*-Dimethyl-1,2-dimethylethylenediamine Complexes

Complexes with methyl groups on the C atoms in equatorial position Complexes with methyl groups on the C atoms in axial position



Complexes of type **3** Complexes of type **4** Complexes of type **5** Complexes of type **6**

nitrogen atoms were placed in different positions. Sixteen complexes are possible (Scheme 6).

Complexes of type **3** and **4**, as well as complexes of type **5** and **6**, are enantiomers and therefore have the same energy. For practical reasons, the calculations were performed on the diastereoisomers **3** and **5**, which led to the geometry optimization of eight structures. The largest energy difference between the eight optimized complexes is 29 kJ/mol. The energy differences between the four most stable complexes are given in Table 1. Complexes **7** and **8** are separated by 3 kJ/mol. These structures are shown in Scheme 7. The most stable complex **7** corresponds to the structure of the diamine ligand where all the methyl groups are successively in *trans* position relative to the mean plane, which means the presence of a C_2-symmetry axis. Thus, the nitrogen atoms are stereogenic centers with the same configuration. In complex **8**, the methyl groups on the nitrogen atoms are placed above the mean plane of the molecule. The C_2-symmetry axis is not held in that case, and the nitrogen atoms of the diamine present a *meso* configuration. In the case of structure **9**, where the methyls on the carbons are axial, the most stable isomer has the methyls on the nitrogens *cis* to the methyls on the carbons instead of being alternate. That means that the steric effects between the methyls on N_1 and C_2 or N_2 and C_1 are stronger than those between the methyls on N_1 and C_1 or N_2 and C_2 (see Scheme 7 for numbering).

However, we cannot conclude that complex **7** is the only possible structure since the energy difference between complexes **7** and **8** is only 3 kJ/mol. This small energy difference can be considered at the limits of the calculation method. It can be noted however that the comparison concerns conformers with very similar structures, which renders the energy differences more reliable.

We have then performed the same calculations in the case of the more realistic phenyl substituents (DMPEDA).

2.2. Rhodium−*N,N′*-Dimethyl-1,2-diphenylethylenediamine Complexes. We have thus replaced the methyl groups on the carbon atoms by phenyl groups in the four most stable complexes, **7**−**10**, in order to study a more realistic complex. The bond lengths and angles in the starting structures are those found respectively in complexes **7**−**10**. We have first optimized the relative positions of the phenyl groups using HyperChem, keeping all the atoms frozen, except those of the phenyl groups. The geometries obtained were further optimized using DFT calculations. The calculated complexes include a large number of atoms and are at the limit of practical sizes for DFT calculations (a geometry optimization can require 14 days on a workstation). The energy differences between the four optimized complexes found are presented in Table 2, and the structures of the two most stable complexes are shown in Scheme 8.

We observe that the most stable isomer is **11**, which corresponds to a geometry where the methyl and phenyl groups are alternatively placed on both sides of the diamine mean plane, giving a C_2-symmetry axis molecule with stereogenic nitrogen atoms. This geometry

Table 1. Energy Differences between the Four Most Stable Rhodium−*N*,*N*′-Dimethyl-1,2-dimethylethylenediamine Complexes

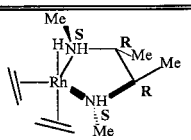
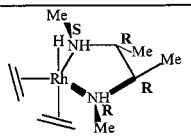
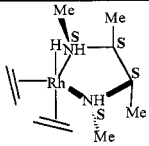
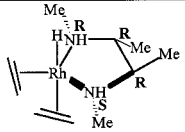
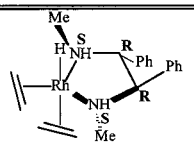
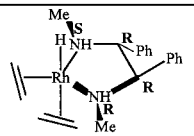
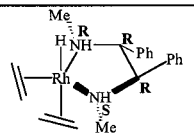
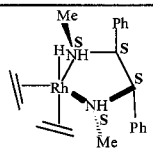
Optimised Rh-diamine complex	ΔE (kJ.mol^{-1})	C_2 axis
 **7**	0	yes
 **8**	3	no
 **9**	6	yes
 **10**	8	no

Table 2. Energy Differences between the Four Most Stable Rhodium−*N*,*N*′-Dimethyl-1,2-diphenylethylenediamine Complexes

Optimised Rh-diamine complex	ΔE (kJ.mol^{-1})	C_2 axis
 **11** eq to **7**	0	yes
 **12** eq to **8**	11	no
 **13** eq to **10**	15	no
 **14** eq to **9**	28	yes

is similar to that of complex **7** obtained previously. However, the energy difference between **11** and the other structures is higher than in the case of **7** (11 vs 3 kJ/mol). In this case, contrary to what was obtained with the methyl groups, the calculations show that there is clearly one structure of the Rh(DMPEDA) complex more stable than the others, in which the nitrogen atoms are stereogenic centers. The energies of structures **11** and **12** have been recalculated with the B_3LYP functional, giving a difference of 13 kJ/mol (instead of 11 kJ/mol). Therefore the results do not seem to be dependent on the choice of the GGA functional. Thus, unlike what occurs for the free diamines, the substituents on the carbons have a non-negligible influence on the relative stability of the complexes. Effectively, due to the constraint of the cycle, the dihedral angle between the phenyl rings cannot increase like it did in the free diamine (compare this angle in Scheme 4, 55° and in Scheme 5, 71°).

These relative stabilities can be explained by the following. The complexes can be considered as built by the interaction of DMPEDA with the metallic fragment $RhH(C_2H_4)_2$. The binding energy between these fragments can be decomposed in the sum of two terms. The first one is the deformation energy E_{def}. Effectively, in the complexes the fragments are deformed compared with their separated geometries. For instance, in free diamine (Scheme 4) a rotation around the N_2C_2 bond is necessary to put the lone pair of N_2 in the right direction for the interaction with Rh. The reference for the deformation energy of the diamine is the most stable conformer **1** shown on Scheme 5. The second term is

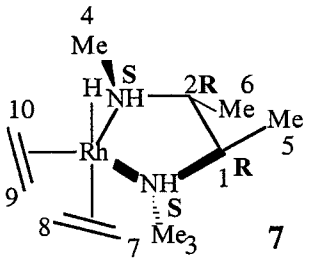
Table 3. Deformation Energies, E_{def}, of the Diamine and of the Metallic Fragments in 11−14, Total Deformation Energies, E_{def}(tot), and Interaction Energies, E_{int}, between the Fragments (in kJ/mol)

	E_{def} diamine	E_{def} $RhH(C_2H_4)_2$	E_{def}(tot)	E_{int}
11	25	15	40	−143
12	37	12	49	−141
13	35	14	49	−137
14	24	13	37	−113

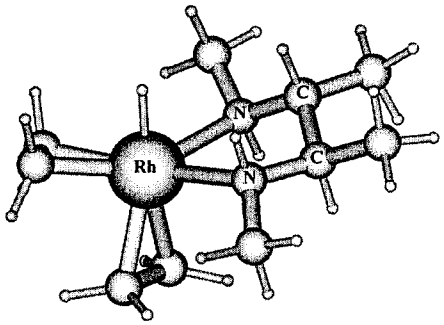
the interaction energy E_{int} between the deformed fragments, calculated as the difference between the complex energy and the energies of these fragments. The results are given in Table 3.

The $RhH(C_2H_4)_2$ fragment is deformed in each complex, but the associated deformation energies are rather equivalent. If we now consider the diamine fragment, DMPEDA is slightly more stable in geometry **14** than in geometry **11** (Δ = 1 kJ/mol), although the phenyl rings are in axial position. The total deformation energy is hence smaller in **14** than in **11**. Therefore the stability of **11** is not governed by an adequate arrangement of the substituents in the diamine moiety but by a stronger interaction of the fragment molecular orbitals, as evidenced by an interaction energy difference of 30 kJ/mol. The main interaction occurs between the HOMO of the diamine, which is the antibonding combination of the nitrogen lone pairs, and the LUMO of the metallic part, which is the d_{xy} orbital if the RhNN plane is the *xy* plane. The diamine HOMO for **11** is higher than for **14** by 12.5 kJ/mol, and on the contrary, the metal LUMO for **11** is lower than for **14** by 11.6 kJ/mol. Therefore

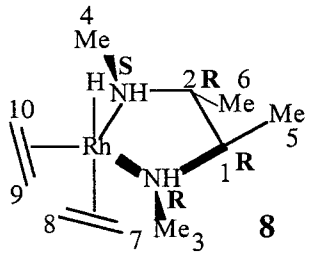
Scheme 7. Most Stable Structures of the Rhodium−*N,N′*-Dimethyl-1,2-dimethylethylenediamine Complexes 7 and 8



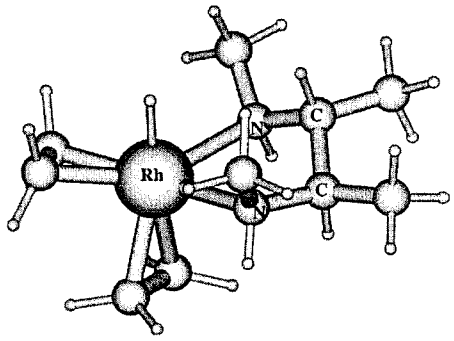
7



Bond length (Å)		Angle (°)		Diedre angle (°)	
Rh-H	1.62	N_1-Rh-N_2	75.5	H-Rh-N_1-C_1	-94.8
Rh-N_1	2.36	Rh-N_1-C_1	111.2	H-Rh-N_2-C_2	64.8
Rh-N_2	2.32	Rh-N_2-C_2	110.6	N_1-C_1-C_2-N_2	-55.1
N_1-C_1	1.49	N_1-C_1-C_2	109.4	H-Rh-N_1-C_3	131.6
N_2-C_2	1.49	N_2-C_2-C_1	109.4	H-Rh-N_2-C_4	-62.1
C_1-C_2	1.56			Rh-N_1-C_1-C_5	162.2
Rh-C_7	2.20			Rh-N_2-C_2-C_6	169.6
Rh-C_8	2.23				
Rh-C_9	2.13				
Rh-C_{10}	2.09				
C_7-C_8	1.42				
C_9-C_{10}	1.46				



8

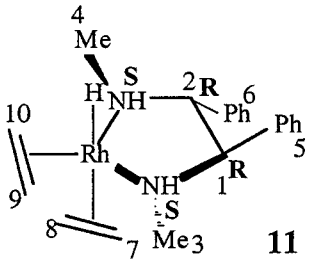


Bond length (Å)		Angle (°)		Diedre angle (°)	
Rh-H	1.62	N_1-Rh-N_2	76.5	H-Rh-N_1-C_1	-96.4
Rh-N_1	2.32	Rh-N_1-C_1	109.4	H-Rh-N_2-C_2	71.9
Rh-N_2	2.34	Rh-N_2-C_2	109.4	N_1-C_1-C_2-N_2	-59.1
N_1-C_1	1.50	N_1-C_1-C_2	109.7	H-Rh-N_1-C_3	33.2
N_2-C_2	1.49	N_2-C_2-C_1	107.9	H-Rh-N_2-C_4	-55.1
C_1-C_2	1.56			Rh-N_1-C_1-C_5	171.5
Rh-C_7	2.20			Rh-N_2-C_2-C_6	168.3
Rh-C_8	2.24				
Rh-C_9	2.13				
Rh-C_{10}	2.09				
C_7-C_8	1.42				
C_9-C_{10}	1.46				

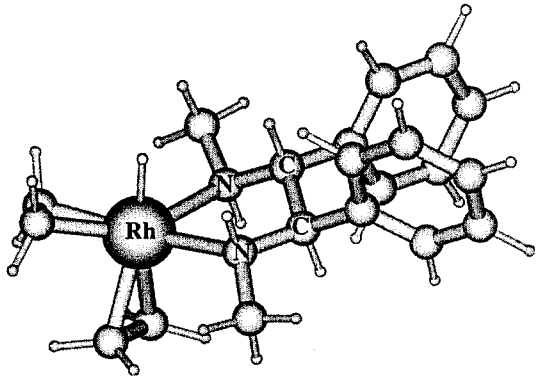
the interaction is stronger for **11** than for **14**. Hence the relative stability of the complexes **11** and **14** is not due to steric effects but rather to electronic effects. Structures **12** and **13**, compared with **11**, yield both a reduced interaction energy and a larger deformation energy for the diamine part. Thus the stability difference between **12** and **13** is also rather due to electronic effects. On the contrary, steric effects dominate for the comparison between **11** and **12** or **13**.

The energy differences have been calculated for gas phase molecules. The solvation could play an important role. It is expected however that the similar molecules

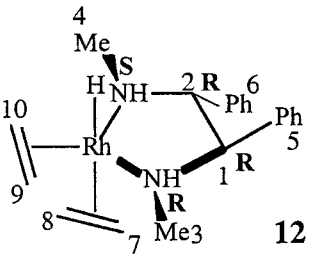
Scheme 8. Most Stable Structures of the Rhodium−*N,N′*-Dimethyl-1,2-diphenylethylenediamine Complexes 11 and 12



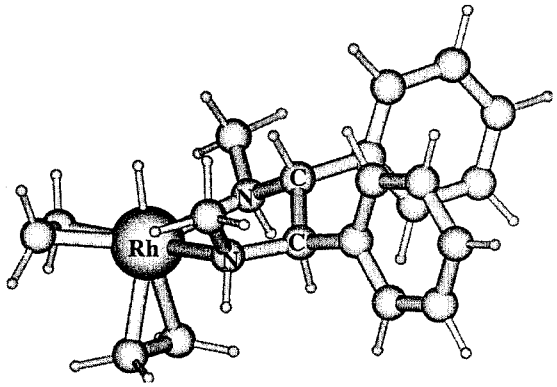
11



Bond length (Å)		Angle (°)		Diedre angle (°)	
Rh-H	1,62	N_1-Rh-N_2	75,7	H-Rh-N_1-C_1	-87,3
Rh-N_1	2,35	Rh-N_1-C_1	111,3	H-Rh-N_2-C_2	61,1
Rh-N_2	2,31	Rh-N_2-C_2	110,0	N_1-C_1-C_2-N_2	-50,7
N_1-C_1	1,49	N_1-C_1-C_2	110,7	H-Rh-N_1-C_3	137,7
N_2-C_2	1,49	N_2-C_2-C_1	110,1	H-Rh-N_2-C_4	-65,5
C_1-C_2	1,56			Rh-N_1-C_1-C_5	153,9
Rh-C_7	2,21			Rh-N_2-C_2-C_6	171,0
Rh-C_8	2,23				
Rh-C_9	2,13				
Rh-C_{10}	2,09				
C_7-C_8	1,42				
C_9-C_{10}	1,46				



12

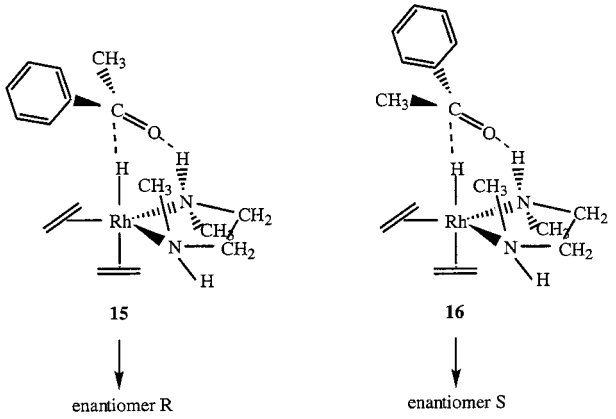


Bond length (Å)		Angle (°)		Diedre angle (°)	
Rh-H	1,61	N_1-Rh-N_2	76,7	H-Rh-N_1-C_1	-95,4
Rh-N_1	2,32	Rh-N_1-C_1	109,2	H-Rh-N_2-C_2	69,6
Rh-N_2	2,33	Rh-N_2-C_2	109,0	N_1-C_1-C_2-N_2	-60,3
N_1-C_1	1,50	N_1-C_1-C_2	109,2	H-Rh-N_1-C_3	34,3
N_2-C_2	1,50	N_2-C_2-C_1	107,4	H-Rh-N_2-C_4	-57,2
C_1-C_2	1,56			Rh-N_1-C_1-C_5	172,8
Rh-C_7	2,21			Rh-N_2-C_2-C_6	171,9
Rh-C_8	2,24				
Rh-C_9	2,13				
Rh-C_{10}	2,10				
C_7-C_8	1,42				
C_9-C_{10}	1,48				

presented here show small differences in solvation energies.

3. Discussion on the Enantioselectivity. In **11** (Scheme 8), with respect to the plane formed by the Rh and the two nitrogen atoms, the hydride is on the same side as a hydrogen on one N and a methyl on the other N. In the course of our study of the title reaction, we are currently examining various mechanisms.[17] The

Scheme 9. Two Possible Approaches of Acetophenone on the Hydride Rhodium Complex $RhH(C_2H_4)_2$(*N*,*N*′-dimethylethylenediamine)



most probable one involves the approach of the ketone above the hydride and needs the presence of one H on a nitrogen to make a hydrogen bond between C═O and N−H. For the approach of acetophenone on a complex similar to **11** (with only hydrogens on the carbons of the diamine), two possibilities exist giving the *R* or the *S* isomer of phenylethanol (Scheme 9). Our calculations show that the corresponding transition states are separated by 7 kJ/mol in favor of **15**, which corresponds to a 95:5 ratio. This means that the reaction is enantioselective. Moreover the most stable transition state yields the *R* isomer, as found experimentally. Hence a good agreement exists between theory and experiment for the configuration of the reaction product. Preliminary results show that, with phenyls on the carbons of the diamine, the difference between the two transition states is larger, and hence the reaction is more enantioselective. It was therefore fundamental to demonstrate that the reactive complex has unambiguously one majority configuration with an asymmetric environment on the N atoms.

IV. Conclusion

Starting from previous results,[8] we studied rhodium hydride complexes where the metal was bound to two ethylenes and one chiral diamine. We first studied the structure of the free (*N*,*N*′-dimethyl)- and (*N*,*N*′-diphenyl)-1,2-dimethylethylenediamines. The most stable conformer of the *threo* diamines is in a staggered *gauche* conformation for both molecules. We showed that these conformations are stabilized by hydrogen bonds between the two amino groups and that steric effects play a secondary role. In this geometry, the nitrogen atoms are ideally placed to coordinate the rhodium without a too strong distortion of the molecule.

Concerning the Rh complexes bearing phenyl groups on the diamine carbons, there is unambiguously a structure more stable than the others: it corresponds to a conformation of the diamine ligand where all the substituents are arranged in an alternative *trans* manner and where the C_2-symmetry is conserved. An analysis of the stability order of the four considered complexes shows that the result obtained is not intuitive, since the most stable structure for the diamine is associated with the less stable complex (Table 3). Electronic effects are thus important, in addition to steric effects.

We showed also that on such a complex having a C_2-symmetry axis and one H on the nitrogen atoms, the approach of acetophenone is enantioselective, leading to the *R* enantiomer when the starting diamine is *threo* (*S*,*S*), in agreement with the experimental results.

Therefore, the enantioselectivity of the reaction could be explained by two main reasons. The first one is the existence of a large excess of one enantiomer of the starting hydride Rh complex. The second one is that this complex has an asymmetric structure at the N atoms, which induces a clear distinction for the approach of a prochiral ketone on its two faces. The knowledge of these factors allows us to search how to improve the enantioselectivity. We have shown that replacing the methyl groups on the diamine carbon atoms by phenyl groups significantly increased the differences in energy between the considered complexes. To further enlarge the effect, it could be interesting to increase the bulkiness of the substituents on the carbons of the diamine, for example by replacing the phenyl groups by naphthyl ones. Previous experimental results[2] showed that electronic effects on the ketone play a role in the enantioselectivity since substituents with electon-donor or -withdrawing character gave different ee's. Another way to enhance the enantioselectivity could thus be to change the donor character of the diamine by substituting the nitrogens by groups other than methyls.

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(17) (a) Guiral, V.; Delbecq, F.; Sautet, P. *Organometallics* **2000**, *19*, 1589. (b) Guiral, V.; Delbecq, F.; Sautet, P. Submitted.