

***Ab Initio* Studies of Rhodium(I)–*N*-Alkenylamide Complexes with *cis*- and *trans*-Coordinating Phosphines: Relevance for the Mechanism of Catalytic Asymmetric Hydrogenation of Prochiral Dehydroamino Acids**

Achim Kless,* Armin Börner, Detlef Heller, and Rüdiger Selke

Max-Planck-Gesellschaft, Arbeitsgruppe "Asymmetrische Katalyse" at the University of Rostock, Buchbinderstrasse 5-6, D-18055 Rostock, Germany

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A theoretical study on cationic Rh(I)–*N*-alkenylamide complexes is presented, which are important intermediates in the asymmetric hydrogenation affording *N*-acylamino acids. The assumption of different intermediates investigated is based on the inter- and intramolecular equilibrium of diastereomeric complexes in the hydrogenation mechanism. The geometry optimizations were performed at the MP2 level of theory using relativistic pseudopotentials for rhodium, followed by QCISD(T) single-point calculations. The intermediates containing *cis*- or *trans*-coordinated phosphines have been compared structurally and energetically, and the influence of solvents is discussed. In the equilibrium consisting of uncoordinated substrate and substrate complexes, all tautomeric complexes were found in the calculation and have a minimum on the potential hypersurface. However, the occurrence of enamine/imine and amide/imine-ol tautomers could be excluded for the catalytic reaction, because they implement irreversible steps (C–H activation, deprotonation) which finish the catalytic cycle and may therefore be responsible for turnover-limiting steps. Only the calculation of an intermediate showing hetero- π -allyl type coordination can explain satisfactorily the crucial interconversion of the diastereomeric *major*/*minor* complexes in a noncoordinating medium. This intermediate is favored for the rationalization of the intramolecular equilibrium. For *trans*-coordinating diphosphine ligands a *T-shaped* intermediate with only a coordinated nitrogen atom is proposed.

Introduction

Chiral diphosphine ligands are widely used in asymmetric catalysis.¹ Most of them are chelating ligands. During complex formation with late transition metals, a *cis* orientation is adopted preferentially. There are only a few ligands which complex in a *trans* fashion.^{1b} The change of the complex geometry causes decisive changes in the catalytic cycle, giving rise to a different coordination mode of substrates. Novel intermediates have been formed, as a consequence. In this connection, the hydrogenation of prochiral dehydroamino acids affording products of academic and industrial interest (L-Dopa synthesis) is a broadly investigated reaction. Especially when functional groups in the backbone of the ligand are involved in the catalytic cycle or noncoordinating solvents are used, the mechanism can prefer other pathways.^{1c} Therefore, in such cases important details of the mechanism have still to be clarified. Such intermediates have so far not been investigated by NMR due to their small stationary concentration; consequently, *ab initio* calculations are the method of choice.²

For the hydrogenation mechanism with cationic Rh(I) complexes the importance of the intramolecular equilibrium between the diastereomeric rhodium–substrate complexes is documented.^{3a,b} Another pathway proceeds through the intermolecular equilibrium, wherein *major*/*minor* complexes convert via the solvent complex. That means that, in this isomerization process, the substrate is always coordinated to the rhodium (Scheme 1). Herein, we report that the formation of Rh(I)–*N*-alkenylamide complexes depends on the influence of *cis*- and *trans*-coordinating phosphines. The results are discussed in relation to the generally accepted mechanistic view.^{3c}

Computational Methods

The geometry optimizations were performed at the MP2 level of theory with the quadratic conversion algorithm, followed by QCISD(T) single-point calculations using GAUSSIAN 92/94.⁴ The core electrons (up to 3d) of rhodium were described by Hay-Wadt's effective core potential and the valence orbitals (4s, 4p, 4d, 5s, 5p) by a (5s5p4d)/[3s3p3d] set.⁵ All other atoms were represented by a double- ζ basis set.⁶

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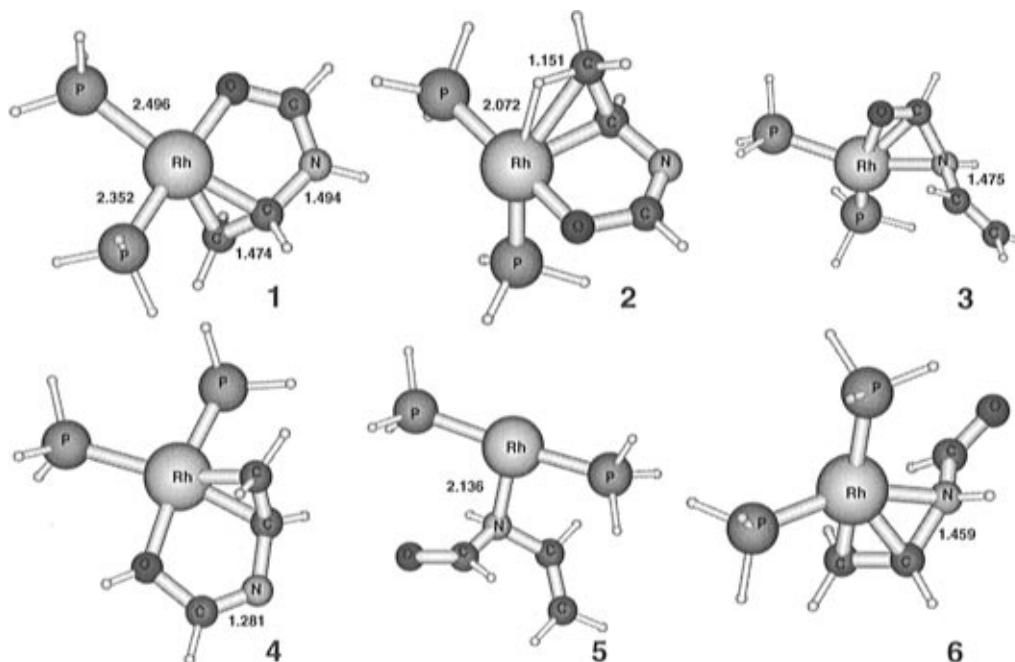
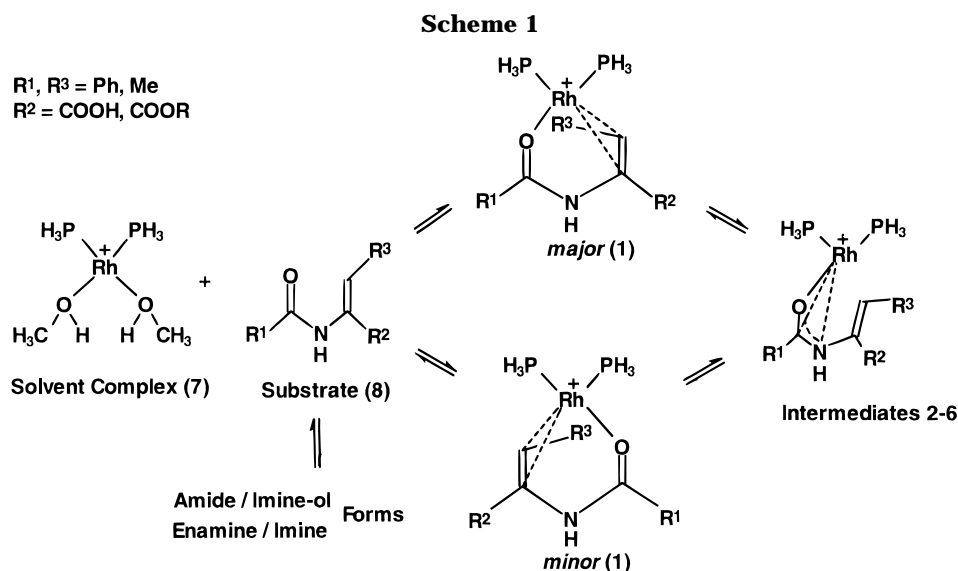


Figure 1. MP2-optimized geometries of rhodium(I)-N-alkenylamide complexes.



To get more information about the contribution of the entropy and enthalpy to the free energy of the reaction pathways, MP2 frequency calculations were carried out for all possible intermediates; the second derivatives were obtained analytically. All intermediates possessed no negative eigenvalues. The energies were corrected for zero-point energies, which lead to energy differences of about 2 kcal/mol. The larger Pople basis 6-31G* was employed for all atoms except rhodium on the SCF level to estimate the effects of polarization functions.

Results and Discussion

Due to the equilibrium between uncoordinated substrate and substrate complexes, all tautomeric complexes should be taken into account and have been investigated by *ab initio* methods. The substitution of the functional groups R¹-R³, especially the carboxylic group, by hydrogen does not give significant deviations

of the Rh-C or C-C double-bond distances. Considering the coordination modes of dehydro amino acids in rhodium(I) complexes, there are only a few possible intermediates possible that can explain the influence of coordinating or noncoordinating solvents or functional groups. All of the derived intermediates possess a minimum on the potential hypersurface. In a first step of our approach the minima are compared structurally (Figure 1) and energetically (Figure 2).

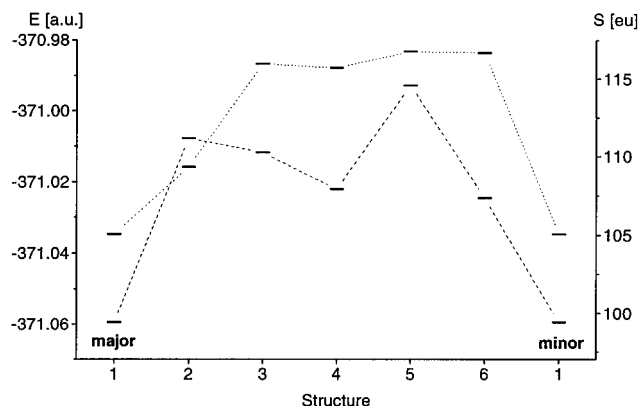
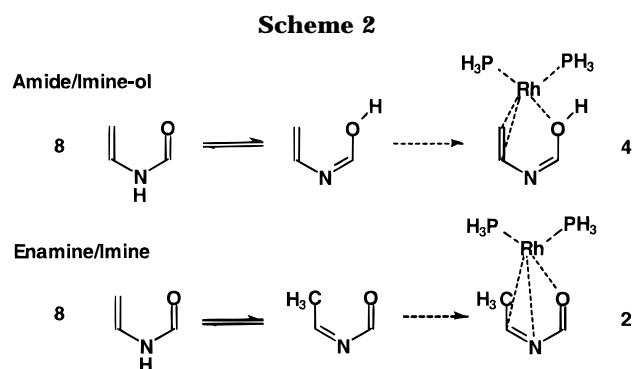
The thermodynamically most stable substrate complex is the metallacyclopropane **1**, already proved by an X-ray structure analysis (Table 1).⁷ By coordination of the C-C double bond to the rhodium atom a metallacyclopropane structure is formed with a C-C bond distance of 1.474 Å. This arrangement is favored due to the *trans* effect. In comparison to the C-C distance (1.382 Å) found in the X-ray structure, this C-C distance is always overestimated at this level of theory.

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Table 1. Energies and O–H/N–H-Frequencies

structure	QCISDT(T) + ZPE (au)	ZPE (kcal/mol)	MP2 (au)	HF (DZ) (au)	HF (6-31G*) (au)	ΔE to 1 (kcal/mol)	IR (cm ⁻¹)
1	-371.059 412 4	86.47	-371.098 648 6	-370.296 399 5	-370.520 682 8	0.0	3407 (N–H)
2	-371.007 782 6	85.07	-371.044 621 9	-370.221 340 6	-370.457 336 7	32.4	
3	-371.011 831 4	84.98	-371.042 047 1	-370.243 298 8	-370.472 579 1	29.8	3326 (N–H)
4	-371.022 055 6	84.70	-371.056 086 5	-370.252 245 8	-370.475 487 6	23.4	3491 (O–H)
5	-370.992 860 9	84.81	-371.016 356 7	-370.264 258 2	-370.490 980 2	41.7	3256 (N–H)
6	-371.024 555 3	85.41	-371.062 828 2	-370.256 849 8	-370.518 877 7	21.9	3318 (N–H)
7	-355.272 031 7	102.25	-355.326 523 2	-354.639 585 7	-354.830 624 4		3519 (O–H)
8	-246.178 180 0	53.04	-246.215 744 3	-245.726 895 8	-245.859 741 6		3425 (N–H)
9	-486.272 510 0	119.35	-486.328 962 7	-485.358 945 5	-485.623 867 9		3499 (O–H), 3392 (N–H)
MeOH	-115.189 010 0	32.08	-115.220 931 3	-115.012 898 1			3489 (O–H)

**Figure 2.** Comparison of Energies (dashes) and Entropies (dots).

Partially, this can be traced back to the P–Rh–P angle, which in nonchelating diphosphines is larger (95.7°) than in chelating diphosphines (83.0°, five-membered ring). All Rh(I) complexes of prochiral dehydro amino acids are complexed by such chelating ligands. The use of the model phosphine PH₃, instead of the sterically encumbered chelate diphosphines, might preclude the existence of some of the intermediates involved in the real reactions or change the relative stabilities of them. However, this model phosphine represents the unhindered case where all possible conformations can be adopted by the phosphines. In particular, a quantitative comparison between the *cis*- and the *trans*-coordinating phosphines is made possible.

An enamine/imine tautomerism (Scheme 2) generates the structure **2**, wherein the electron densities are shifted from N to O in analogy to the imine-ol tautomer **4**.⁸ The *trans* effect is weaker compared to that in the intermediate **1** and in examples **4** and **6**, described later.

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One hydrogen atom of the methyl group is involved in the coordination (agostic H). The elongated C–H distance of 1.151 Å (C–H = 1.090 Å would be normal at this level of theory) and the H–Rh distance of 2.072 Å show clearly that C–H activation can occur.⁹

The intermediate **4** can be derived from the amide/imine-ol tautomerism (Scheme 2) of the substrate.¹⁰ For the *Z* type of the imine-ol form the coordination of oxygen is preferred for steric reasons. It might be possible to create a butadiene-like coordination with the nitrogen in the case of the *E* type.¹¹ Rhodium(I) is flexible enough to catch the conformational changes of the tautomers. In structure **4** the rhodium increases the acidity of the hydroxy group. Therefore, this intermediate is stabilized in basic solvents, where deprotonation and formation of neutral Rh complexes can take place. Both tautomers (**2** and **4**) can be excluded for the catalytic cycle, because they involve irreversible steps which terminate the catalytic cycle. Such species may be responsible for turnover-limiting steps.

Transition-metal amidates are well-known and are often described by η^2 (O,N)-type bonding. However, late transition metals from the second row seem to have a preference for η^3 -hetero- π -allyl-like coordination, which depends on the participating heteroatoms and the topologic circumstances of the system considered.¹² It is interesting to note that such a coordination mode was never discussed in the mechanism of the catalytic asymmetric hydrogenation. The intermediate **3** is a π -allyl type complex derived from the amidate substructure. This allylic structure is characterized by elongated bonds (C–O = 1.345 Å; N–C = 1.492 Å) and O–Rh (2.176 Å), C–Rh (2.052 Å), and N–Rh (2.144 Å) distances being of the same order of length. The bond distance of 1.475 Å between the nitrogen atom and the olefin indicates a single bond, and therefore, free rotation around this bond is possible. This rotation is required for the interconversion of the diastereomeric substrate complexes. It is noteworthy that this intermediate should be favored to explain the intramolecular equilibrium, because neither the coordination of a solvent nor a supporting functional group in the back-

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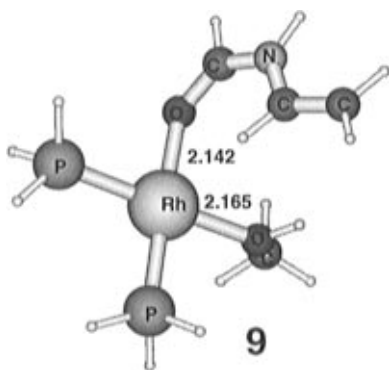


Figure 3. η^1 -Coordinated substrate.

bone of the ligand is necessary. The activation energy which is at least necessary for the rotation of the C–N single bond between structures **1** and **3** is in the range of 29.8 kcal/mol and corresponds to the dissociation energy of the metallacyclopropane structure in compound **1**. In comparison to the metallacyclopropane structures (**1**, **4**, **6**), there is no *trans* effect in the η^3 -type bonding. Therefore, the topological requirements for *cis*-coordinating diphosphine ligands to adopt such a coordination are small. This coordination mode is also postulated for Rh(I)–amidate complexes in the catalytic cycle of amide-directed hydrocarbonylation of alkenamides.¹³

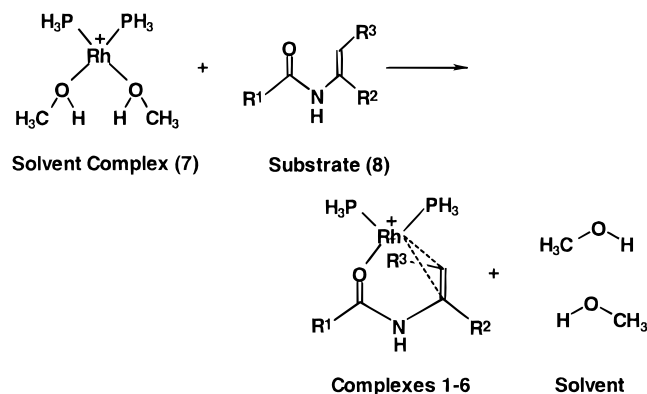
An alternative mechanism for the interconversion via the intermediate **3** is the π – σ – π interconversion.¹⁴ We assume that one intermediate with a nonchelating σ bond formed by donation of a free electron pair of the carbonyl oxygen to the rhodium is possible (Figure 3). Such coordination must be stabilized by additional solvent molecules, e.g. methanol,¹⁵ or ligands bearing methoxy or hydroxy groups in their backbone.¹⁶ In cases without a coordinating solvent molecule, the structure lies about 35 kcal/mol higher in energy related to a nonstationary point.

Intermediate **3** is not the only way to form a η^3 -coordinated complex. Considering the other functionality of the substrate, the vinylamine substructure can form the stable complex **6**. In contrast to the intermediate **3**, the *trans* effect is considerable (P–Rh distance elongated by 0.08 Å) and can be attributed to the C=C double bond, independent of the bonding mode.¹⁷

The second nonchelating intermediate **5** is characterized by a single N–Rh bond and spans the largest energetic range of 41.7 kcal/mol related to the substrate complex **1**.¹⁸ The P–Rh–P angle of nearly 180° is entirely different compared to other complexes. The substrate in this case is not acting as a chelating ligand, and the P–Rh–P substructure reacts as a weak bidentate Lewis acid, affording a *T-shaped* molecule with a free coordination site.¹⁹ For short-bridged *cis*-coordinating diphosphines yielding a five- or seven-membered-

Scheme 3

R₁, R₂, R₃ = H



ΔG [kcal/mol]	ΔH [kcal/mol]	ΔS [eu]
- 19.3 (1)	- 13.3 (1)	20.0 (1)
- 52.7 (3)	- 43.6 (3)	30.5 (3)
- 64.8 (5)	- 55.5 (5)	31.3 (5)
- 44.5 (6)	- 35.2 (6)	31.2 (6)

Table 2. Entropies of Intermediates and Starting Materials

structure	entropy (eu)	structure	entropy (eu)
1	105.05	6	116.68
2	109.34	7	130.62
3	115.96	8	68.87
4	115.70	9	142.47
5	116.75	MeOH	57.01

ring system, the coordination type **5** can be excluded. Because of torsional hindrance, the diphosphines cannot adopt such an orientation. This does not hold for *trans*-coordinating diphosphines and shows here an extraordinary position of these ligands in asymmetric catalysis.^{1b}

Thermodynamics. Calculations with cationic rhodium-complexes neglect the influences caused by weakly coordinated anions such as BF_4^- or SbF_6^- . This leads to larger energy differences between the intermediates. Therefore, if a coordinating solvent is present, a participation of the solvent complex is adopted (Scheme 3). The most important IR frequencies (Table 1), which are scaled by a factor of 0.9472, and the contribution of the entropy to the overall energy of the systems (Table 2) are given.

As seen in Table 1, as expected, the O–H vibration band lies lower than the N–H vibration. The difference between the coordinated and the uncoordinated O–H group can be neglected. In contrast to O–H, the N–H vibration depends on the bonding mode and shows significant shifts to shorter wavelengths when the substrate is coordinated. This feature is independent if the N–H function coordinates directly to the rhodium atom or takes other coordination modes.

Among all intermediates considered, the calculated entropy of the complex **1** shows the smallest value. The other intermediates, especially the η^3 -coordinated species, have entropies which are up to 10% higher. Therefore, the intramolecular equilibrium should be favored entropically at higher temperatures. This assumption is based on the pronounced chelate effect indicated by a positive reaction entropy. If the reaction is carried out in methanol as solvent, the liberation of methanol in the overall reaction can be neglected from an entropic point of view. In this case the reaction entropy adopts a negative value.

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From the calculated energies and entropies, the overall thermodynamic data for the intermolecular equilibrium was obtained (Scheme 3). The formation of the *trans*-coordinated structure **5** proceeds with the largest free energy, and in comparison with structure **15** is thermodynamically more comparable to structures **3** and **6**. We conclude that the concentration of the intermediates **2–6** increases while the concentration of the substrate complex **1** decreases.

In summary, five new coordination modes of *N*-alkenylamides in cationic Rh(I) complexes were found. They are close together in energy and must be included in the considerations of inter- and intramolecular equilibria. Only by assuming formation of the intermediate **3** can the interconversion of the two diastereomeric complexes in a noncoordinating medium be explained. The lowest activation energy for the rotation around the C–N single bond is about 29.8 kcal/mol (Table 1), in the range of the dissociation energy of the metallacyclopropane substructure of compound **1**. The intermediates **2** and **4** are held responsible for turnover-

limiting steps due to irreversible reactions. For *trans*-coordinating diphosphines the intermediate **5** is likely. Other features which show the extraordinary position of *trans*-coordinating diphosphines in related catalytic reactions are currently under investigation.

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Supporting Information Available: A listing of the computational results with full geometries and energies, including tables of bond distances and angles of all compounds (20 pages). Ordering information is given on any current masthead page.

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