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A DFT Study of the Role of Water in the Rhodium-Catalyzed Hydrogenation of Acetone

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The positive effect of the addition of water to acetone hydrogenation by [RhH$_2$(PR$_3$)$_2$L$_2$]$^+$ catalysts has been studied by DFT calculations. The energetic profiles reveal that the more favourable mechanistic path involves a hydride migration to the ketone followed by a reductive elimination that is assisted by two water molecules.

Rhodium phosphine complexes are excellent catalysts for the hydrogenation of C-C double and triple bonds.[1,2] The first major publication in this area concerned the synthesis and catalytic hydrogenation behaviour of Rh(PPh$_3$)$_3$Cl (Wilkinson's catalyst) in the mid sixties.[3,4] In the late sixties it was found that cationic rhodium complexes with the formula [Rh(diene)L$_2$]$^+$ could prepared as tetraphenylborate or perchlorate salts in polar media through addition of a phosphine (L) to [Rh(diene)Cl]$_2$.[5] The cationic complexes were found to react with molecular hydrogen to give dihydrido complexes with the formula [RhH$_2$(PR$_3$)$_2$L$_2$]$^+$ (L = solvent) and to function as catalysts not only for the hydrogenation of olefins and alkynes,[6] but also of ketones at room temperature and atmospheric pressure.[7] Cationic complexes allow a wide variety of monodentate and bidentate phosphines to be used and many hydrogenation studies based on these catalysts, including enantioselective versions, have been reported.[8]

The reduction of ketones by cationic rhodium complexes[7] was found to be most efficient in the presence of small quantities of water (1%). It was suggested that water was necessary in order to facilitate the second proton transfer (Scheme 1, **3** to **4**), in such a way that deprotonation may be carried out by the hydroxyl ion (**5**), or by a water molecule, and protonation of the alkoxy-group may occur simultaneously or in a subsequent step. A similar mechanism was later proposed by Fujitsu and coworkers[9] for the catalytic hydrogenation of styrene oxide, and several aldehydes and ketones with cationic rhodium complexes, with complexes that contain the PEt$_3$ ligand being the most active among the ligands that were studied. An accelerating effect of water in the catalytic hydrogenation of carbon dioxide to formic acid by related rhodium cationic complexes has also been reported.[10] DFT calculations also have shown that water molecules play important roles in accelerating the rate of proton shuttling in a proton transfer step,[11] hydrogen activation,[12] transfer hydrogenation of ketones,[13] olefin epoxidation by hydrogen peroxide,[14] tautomerizacion,[15] and proton exchange processes.[16] Water also can behave as a cooperating ligand in metal-bifunctional catalytic process.[17] Finally, DFT studies have shown that 2-propanol can decrease the barrier of heterolytic splitting of H$_2$ on ruthenium by acting as a proton shuttle.[18]
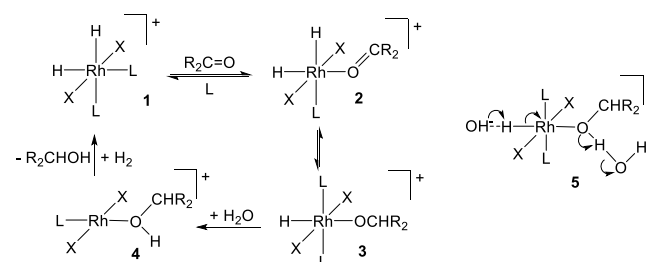
Scheme 1. X = PR$_3$, L = solvent

The role of water in the rhodium-catalyzed hydrogenation of ketones, first reported in 1970, remains an intriguing finding that has not been explained to our knowledge. In this work, we revisit this reaction using DFT methods, taking into account the specific characteristics of water such as polarity, hydrogen bond donor/acceptor capabilities, or self-ionization. The goal

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will be to evaluate the role of water molecules in the catalytic reaction.

The self-dissociation of water is an endergonic process with a ΔG value of 19.1 kcal mol^{-1}, at 25°C and 1 bar, based on experimental conductivity measurements.[19] Therefore, any alternative catalytic cycle that has an overall activation barrier below 19.1 kcal mol^{-1} should be considered as an energetically more favourable route. In Scheme 2 we propose three reaction mechanisms involving water molecules as alternatives to the water self-dissociation mechanism (path **a**). The alcohol product can be obtained from **3** through reductive elimination from alkoxide and hydride ligands cis to one another to yield Rh(I) complex **4** (path **b**). This process could take place in absence of water via a three center transition state. However, water molecules may act as a proton shuttle between the hydride and the oxygen of the alkoxide ligand and release the ring stain of a possibly highly strained transition state.
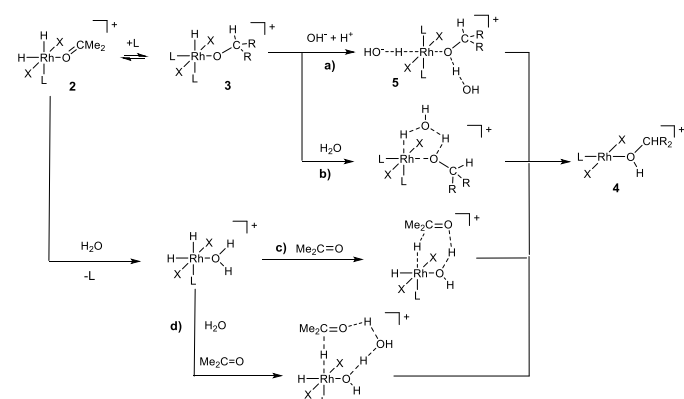
Scheme 2. Mechanistic proposal for the role of water in hydrogenation of ketones

Ketones can be hydrogenated without coordination of the substrate to the metal, i.e., following an outer sphere mechanism.[20] A proton from a XH group (usually an amine) coordinated to the metal is transferred to the O atom while a hydride on the metal is transferred to the C atom. Recently, the role of a strong base in ketone hydrogenation using iridium complexes with "non N-H" ligands has been unraveled by Lledós and Poli.[21] Coordination of a water molecule to the metal in intermediate **2** (path **c**) may create a metal-ligand bifunctional catalyst through a hydroxo species. Additional water molecules could assist the proton transfer process as indicated in path d. The proposed pathways are in agreement with the reported isotopic experiments without considering enol structures. Thus, in this work, all mechanistic pathways proposed in Scheme 2 are calculated at the B3LYP-D3(PCM)/def2-TZVP//B3LYP-D3/def2-SVP computational level (see the ESI† for details).

The energetic profile for the catalytic cycle following a reductive elimination mechanism (path **b** in Scheme 2) is shown in Figure 1. The generation of a vacancy at **A** (**2**) trans to the hydride upon decoordination of acetone (L) leads to an energy increase of 0.6 kcal mol^{-1} due to the strong trans labilizing effect of the hydride ligand. Therefore, we can assume that a five-coordinate dihydride would rearrange readily and lead to different isomers. Hence, for all calculated structures, all possible isomers have been considered and only those with the lowest energy are shown in the energetic profile. Isomerization of **A** to **A'**, in which the phosphine ligands are cis to one another, increases the energy by 2.7 kcal mol^{-1}. Migratory insertion of the ketone into the Rh—H bond leading to the alkoxy complex (**3**) is characterized by **TS-A'B** having the energetic barrier of 17.2 kcal mol^{-1} (Other possible structures for **TS-A'B** that lead to higher barriers are reported in the ESI). The reductive elimination of 2-propanol from intermediate **B** (or **3**) through **TS-BC** requires overcoming an energetic barrier of 30.3 kcal mol^{-1}, which is not plausible
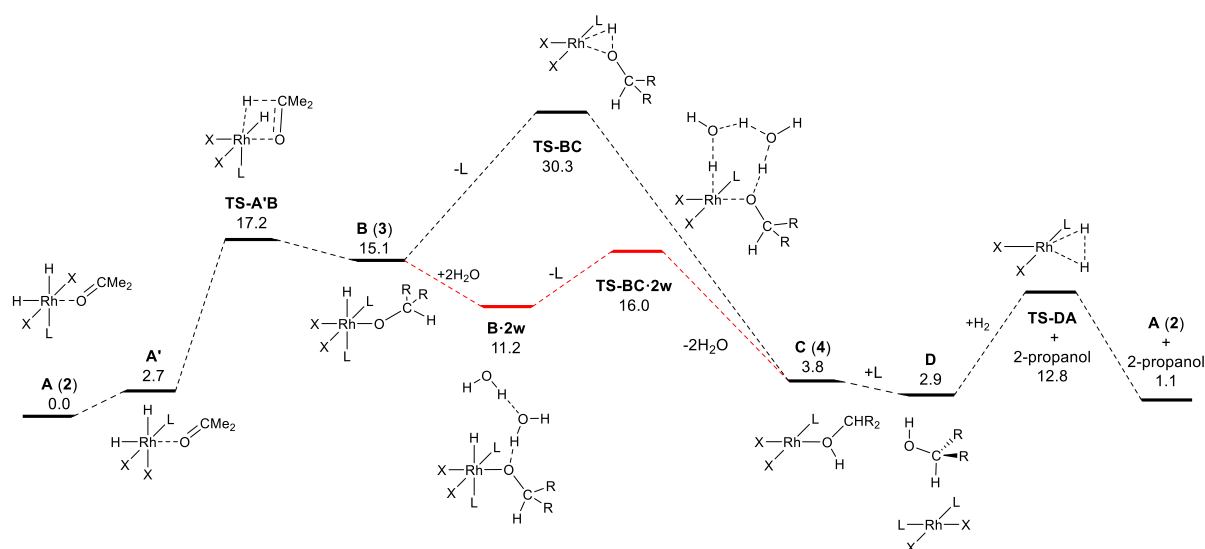

Figure 1. Gibbs relative energy in acetone solution (ΔG in kcal mol^{-1}) of the ketone hydrogenation catalyzed by **2** following the migratory insertion/reductive elimination path (**b**). Only the structures of the lowest energy isomers are shown.

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under mild reaction conditions. Inspection of the key geometrical parameter of **TS-BC** (See ESI) shows that the angle H-Rh-O involved in the reductive elimination is 46°, so ring strain could be a cause for the high energy of this transition state.

In order to reduce the barrier imposed by a three-membered ring structure, one to three water molecules were added to intermediate **B** and **TS-BC** in order to simulate the effect of water molecules in the formation of hydrogen bonds and in assisting proton transfer processes. The dependence of the energetics versus the number of water molecules (0-3) is shown in Table 1. Intermediate **B** is slightly stabilized by hydrogen bonding interactions when two water molecules are included (11.2 kcal mol^{-1}). However, the reductive elimination transition structure (**TS-BC**) is strongly stabilized when two water molecules are included, which reduces the energetic difference from 30.3 kcal mol^{-1} to 16.0 kcal mol^{-1} (2w). Key geometrical data of **TS-BC·2w** are shown in the ESI†. Beyond **TS-BC**, the Rh(I) square planar intermediate **C**, corresponding to **4**, can release 2-propanol and the catalytic cycle can be closed through oxidative addition of molecular hydrogen to intermediate **D** via **TS-DA** with a relative energy of 12.8 kcal mol^{-1}. The cis arrangement of phosphine ligands is slightly more favourable than a trans arrangement for all calculated structures except complex **A** (see ESI). The energy span for the calculated energy profile shows a value of 17.2 kcal mol^{-1} from the starting complex **A** to the transition structure of highest energy (**TS-A'B**) provided that two water molecules are present to reduce the energetic cost of the reductive

elimination step. The relative Gibbs free energy for the two alternative pathways (**c-d**), following the outer sphere mechanism for ketone hydrogenation, is shown in Figure 2. The cycle starts by the replacing a coordinated ketone with a

Table 1. Gibbs free energy (in kcal mol$^{-1,}$ relative to A and isolated molecules) for structures **B** and **TS-BC** considering some discrete water molecules (0w-3w).

	B	TS-BC
0w	15.1	30.3
1w	18.9	26.6
2w	11.2	16.0
3w	17.4	18.2

water molecule which can interact with the substrate via hydrogen bonding through a second water molecule (**E·2w**). This step is nearly isoenergetic to **A** (+0.8 kcal mol^{-1}). The concerted double hydrogen transfer H$^-$/H$^+$ from the hydride to the acetone carbon atom and from the coordinated water molecule to the acetone oxygen atom takes place through **TS-EF·1w** which has a high barrier of 43.8 kcal mol^{-1}, corresponding to path **c**. Assistance of 1 or 2 extra water molecules (path **d**) to the proton transfer process from the water ligand to the oxygen atom of the ketone reduces the energetic cost to 25.1 kcal mol^{-1} (**TS-EF·2w**) and 27.5 kcal mol^{-1} (**TS-EF·3w**), yielding intermediate **F·2w** and the alcohol. Inspection of the molecular geometry of **TS-EF·2w** (see ESI†), shows that the second water molecule relaxes the geometrical constrain in the proton transfer process. The catalyst may be regenerated by reductive elimination of the hydride
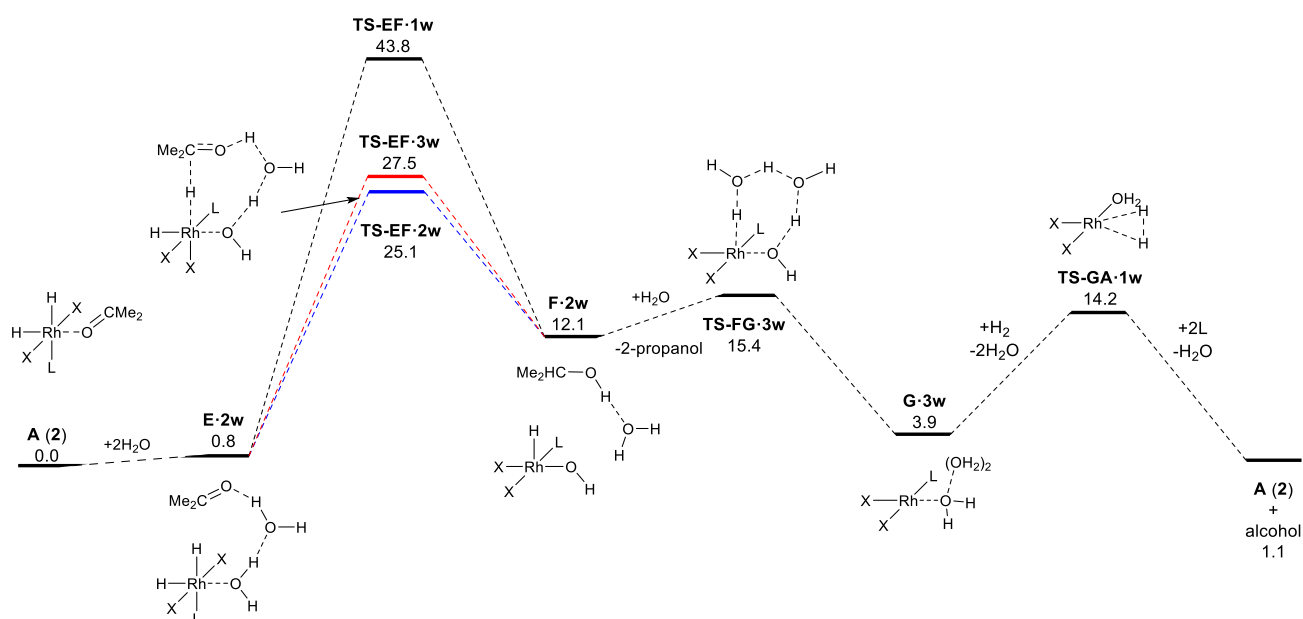
Figure 2. Gibbs relative energy in acetone solution (ΔG in kcal/mol) of the ketone hydrogenation catalysed by **2** following the double hydrogen transfer path with assistance of 1 to 3 water molecules. Only the lowest energy structural isomers are shown.

and the OH group through **TS-FG·3w** via an affordable energetic barrier (15.4 kcal mol^{-1}) to yield the Rh(I) intermediate **G·3w** followed by oxidative addition of molecular hydrogen across **TS-GA·1w** with a relative energy of 14.2 kcal mol^{-1}. The calculated energetic span for path **d** when two water molecules are included is 25.1 kcal mol^{-1}.

In summary, the DFT calculated energetic profiles reveal that the mechanistic path of lowest energetic span (17.2 kcal mol^{-1}) involves a hydride migration to the ketone in the rate limiting step followed by a reductive elimination that is assisted by two water molecules. For the outer sphere mechanism the energetic span is 25.1 kcal mol^{-1}. Because the former value is lower that the energy necessary for the self-dissociation of water, it is the energetically preferred reaction pathway. In addition, the presence of water molecules may assist proton transfer processes by reducing the energy of transition structures corresponding to processes of reductive elimination (or oxidative addition) involving a hydride and a coordinated ketone.

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