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Evidence for a ruthenium dihydride species as the active catalyst in the $RuCl_2(PPh_3)$-catalyzed hydrogen transfer reaction in the presence of base

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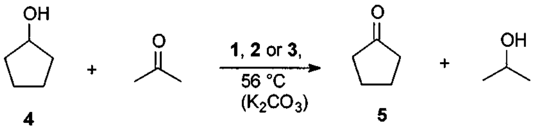
The role of the base in $RuCl_2(PPh_3)_3$-catalyzed hydrogen transfer reactions is to generate a highly active $RuH_2(PPh_3)_3$ catalyst from the dichloride *via* two consecutive alkoxide displacement–β-elimination sequences.

In 1991 we reported on a dramatic rate acceleration in the $RuCl_2(PPh_3)_3$-catalyzed transfer-hydrogenation of ketones upon addition of a catalytic amount of base.[1] The accelerating effect of the base was in the order of 10^3–10^4, and this provided a viable procedure for transfer hydrogenation. This remarkable effect was subsequently extended to other hydrogen transfer reactions,[1b] and by using it in the reversed direction, procedures for ruthenium-catalyzed Oppenauer oxidation were developed.[2] Further developments of the ruthenium-catalyzed transfer hydrogenations[3,4] into enantioselective versions have been recently realized by several groups.[5–10]

The effect of base in the iridium-catalyzed[10b–11] transfer hydrogenation has also been observed, but the role of base has remained unclear.[12] In our previous work on the use of $RuCl_2(PPh_3)_3$ **1** as a catalyst we proposed that a ruthenium alkoxide is formed with a subsequent β-elimination[13] to give a ketone and $Ru(H)Cl(PPh_3)_3$ **2**. The latter was proposed to act as the active catalyst. We have now studied the mechanism of this reaction and found that formation of a ruthenium dihydride species is responsible for the dramatic rate acceleration.

The reaction of $RuCl_2(PPh_3)_3$ **1** with isopropanol in the presence of base was studied by ^1H NMR spectroscopy with the aim of detecting complexes, which are possible active catalytic intermediates in transfer hydrogenation reactions. Treatment of $RuCl_2(PPh_3)_3$ with isopropanol and KOH at room temperature under argon gave a doublet of a triplet at δ −10.15 (J_{PH} 35.2, 42.2 Hz) and a broad singlet at δ −7.07 in an integral ratio of 3 : 1.[14] According to literature data the multiplet at δ −10.15 was assigned as $RuH_2(PPh_3)_3$ **3′**[15] and the singlet at δ −7.07 as $Ru(H_2)H_2(PPh_3)_3$.[16] Thus, the mole ratio between the complexes is 6 : 1. To further establish the assignments, reference samples of $RuH_2(PPh_3)_4$ **3**[17] and $Ru(H_2)H_2(PPh_3)_3$[16] were prepared according to literature procedures. Addition of **3** to the reaction sample increased the multiplet at δ −10.15. The doublet of triplet coupling pattern and the presence of free PPh_3 according to ^{31}P NMR clearly indicate that in solution $RuH_2(PPh_3)_4$ **3** dissociates a phosphine to give $RuH_2(PPh_3)_3$ **3′**. Also, addition of $Ru(H_2)H_2(PPh_3)_3$ to the reaction sample increased the broad singlet at δ −7.07. Furthermore, the ^{31}P NMR of the reaction sample and the reference samples established the assignments made. It is not yet clear which role $Ru(H_2)H_2(PPh_3)_3$ plays in the catalytic reaction but it is known[15a,18] that in the presence of ketones $Ru(H_2)H_2(PPh_3)_3$ easily dissociates its H_2 ligand. This will generate the active catalyst $RuH_2(PPh_3)_3$ **3′** and also lead to some 'hydrogen-leakage' in the hydrogen transfer reaction.[19]

The observation that a ruthenium dihydride complex is formed when $RuCl_2(PPh_3)_3$ reacts with isopropanol in the presence of base has interesting mechanistic implications for $RuCl_2(PPh_3)_3$-catalyzed hydrogen transfer reactions. To obtain further evidence for a dihydride species as the active catalyst, we studied the catalytic hydrogen transfer between cyclopentanol and acetone employing three different catalyst sources: $RuCl_2(PPh_3)_3$ **1**, $Ru(H)Cl(PPh_3)_3$ **2**,[20] and $RuH_2(PPh_3)_4$ **3**[17] [Fig. 1, eqn. (1)].



(1)

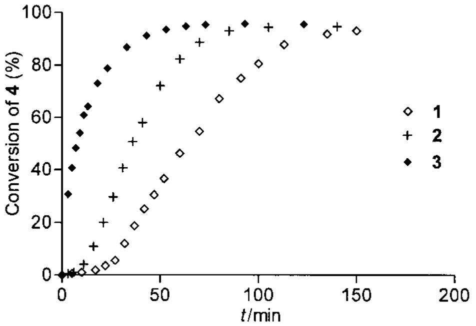
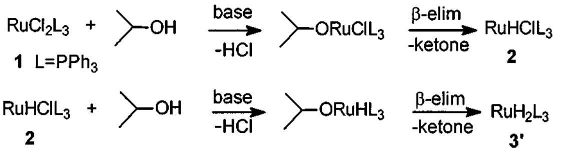


Fig. 1 Ruthenium-catalyzed hydrogen transfer from cyclopentanol to acetone with $RuCl_2(PPh_3)_3$ **1**, $Ru(H)Cl(PPH_3)_3$ **2**, or $RuH_2(PPh_3)_4$ **3** at 56 °C in the presence of K_2CO_3. In each experiment 0.2 mol% of ruthenium catalyst was employed.

The conversion of **4** to **5** was monitored by GC. Significant differences were observed in the reaction rates for the three catalyst precursors. Thus, there were observable induction periods for the complexes **1** and **2**, with the longest induction period for **1**. For the dihydride complex **3** there was a fast initial rate, without any sign of an induction period. Catalyst **3** showed identical reactivity also in the absence of base, whereas **1** and **2** were inactive under these conditions. The longer induction period for **1** compared to **2** is explained by eqns. (2) and (3). The two chlorides in **1** are removed in two consecutive alkoxide displacement–β-elimination sequences whereas for **2** only one such sequence is requried [eqn. (3)].[21,22]

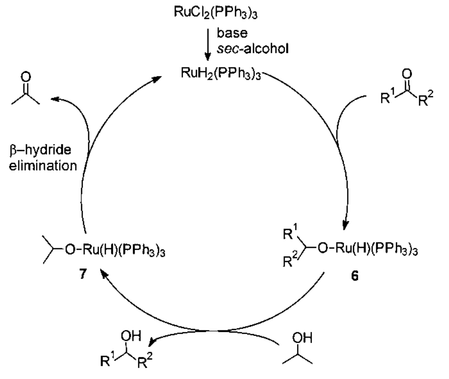


(2)

(3)

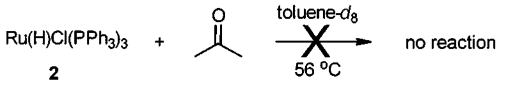
The mechanism for the ruthenium-catalyzed hydrogen transfer is depicted in Scheme 1. It is interesting that once the ruthenium dihydride has been generated the base is no longer required, which was confirmed by experiments (*vide supra*).

Additional support for a dihydride as the active catalyst was obtained from stoichiometric reactions of **2** and **3′** with acetone in toluene-d_8 [eqns. (4) and (5)] monitored by ^1H NMR. Thus, it was found that monohydride **2** did not react with acetone at

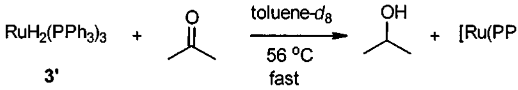


Scheme 1 Mechanism of $RuCl_2(PPh_3)_3$-catalyzed hydrogen transfer.

56 °C, whereas the dihydride **3′** (generated from **3** *in situ*) rapidly ($t_{\frac{1}{2}} \approx 5$ min) reduced acetone to isopropanol. This rules out **2** as the active catalyst. In the catalytic system (Scheme 1), where there is a large excess of alcohol, it is likely that proton transfer from isopropanol to the alkoxy group in **6** takes place. This leads to an exchange of alkoxy groups on ruthenium to give **7**. In eqn. (5) there is no excess of alcohol and a formal reductive elimination to give a Ru(0) species would predominate.



(4)



(5)

Apparently, exchange of the chloride ligand of **2** to a hydride **3′** leads to dramatic changes in the electronic structure of the ruthenium catalyst, which facilitates the hydride addition to a ketone. Preliminary theoretical calculations on the formaldehyde complex **8** and the corresponding alkoxy adduct **9** for ruthenium monohydride (X = Cl) and ruthenium dihydride (X = H) were performed at the DFT/DZ + P level of theory.[23] The calculations show that for the monohydride **8** (X = Cl) the reaction is thermodynamically unfavored by 5.3 kcal mol^{-1} (Fig. 2). This implies that the alkoxy chloride **9** (X = Cl) is unstable and will undergo facile β-elimination to give the keto compound and the hydride.[24] In the case of the dihydride complex the equilibrium is slightly shifted toward adduct **9**, the free energy difference being about 1 kcal mol^{-1}.

8 X = Cl (0)
X = H (0)

9 X = Cl (+5.3)
X = H (-1.3)

Fig. 2 Energies (kcal mol^{-1}) of structures **8** and **9** for dihydride (X = H) and monohydride (X = Cl).

In conclusion, the experimental results indicate that ruthenium dihydride $RuH_2(PPh_3)_3$ is the active catalyst in base-accelerated $RuCl_2(PPh_3)_3$-catalyzed hydrogen transfer reactions.[25] Furthermore, it is shown that the monohydride **2** is not the active catalyst. Theoretical calculations support the observation that a chlororuthenium monohydride is unreactive towards hydride addition to a keto group.

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