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Highly Stereoselective Proton/Hydride Exchange: Assistance of Hydrogen Bonding for the Heterolytic Splitting of H_2

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The heterolytic activation of H_2 is of great importance in both biological systems (e.g., hydrogenases) and catalytic ionic hydrogenations.[1] For hydrogenations of carbonyl groups, Ru catalysts with primary amino ligands have been found to exhibit extraordinary activities.[2] This "NH effect" was attributed to a bifunctional mechanism with rate-determining heterolytic hydrogen splitting by intramolecular proton transfer from an η^2-H_2 ligand to a basic amido ligand, but calculated barriers for this step turned out to be too high in comparison with experimental results.[3] Furthermore, the acceleration of catalytic rates by alkali alkoxide cocatalysts, protic solvents, and hydrogenation products points toward the involvement of hydrogen bridging in bifunctional H_2 activation,[4] which was confirmed computationally.[5,4h] However, the body of experimental data, which allows for the quantification and precise mechanistic interpretation of this observation, remains very limited,[6] and most recently, kinetic studies have suggested direct proton transfer as originally proposed to be operative in the absence of base.[7]

Ir and Ru complexes with the PNP pincer ligand $HN(CH_2CH_2P^iPr_2)_2$ (*H*PNP) have been utilized as catalysts for hydrogenation of ketones and imines,[8] and cooperative, pyridine-based PNP ligands are active catalysts in acceptorless alcohol dehydrogenation.[9] Recently, we presented the dehydrocoupling of borane−amine adducts catalyzed by the amido complex $[Ru(H)PMe_3(PNP)]$ (**1**).[10] Complex **1** reversibly both eliminates and adds H_2, forming equilibria with $[Ru(H)PMe_3\{N(CHCHP^iPr_2)(CH_2CH_2P^iPr_2)\}]$ (**2**) and $[Ru(H)_2PMe_3(HPNP)]$ (**3**), respectively.[10a] Amino complex **3** features a trans-dihydride configuration with only one hydride in close proximity to the internal N−H acid, representing an ideal probe for studying hydrogen exchange processes of the syn H−N−Ru−H moiety referenced against the second hydride.

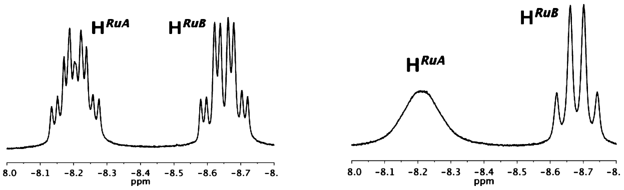
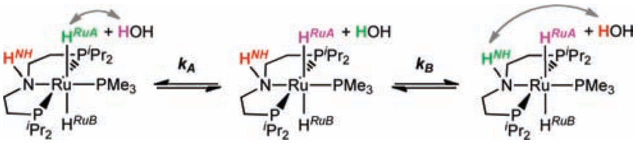


Figure 1. Hydride regions of the ^1H NMR spectra of (left) **3** and (right) **3** with 2 equiv of H_2O.

The ^1H NMR spectrum of complex **3** in THF-d_8 (Figure 1, left) exhibits two sharp signals in the hydride region at −8.20 (H^{RuA}) and −8.65 ppm (H^{RuB}). H^{RuA} can be assigned to the hydride adjacent to the PNP N−H proton (H^{NH}) using ^1H nuclear Overhauser effect NMR spectroscopy (NOESY). To account for possible chemical exchange of H^{RuA} with H^{NH}, the NOE signals were calibrated with proton distances obtained from a density functional theory (DFT) model of **3**. In the calculated structure, the $H^{RuA}\cdots H^{NH}$ distance ($d_A = 2.64$ Å) is very close to the distances between H^{RuB} and two C−H protons on the pincer backbone ($d_{B1} = 2.60$ Å; $d_{B2} = 2.81$ Å), which are equivalent on the NMR time scale. A comparison of the distances ($d_A{}^{-6}/d_B{}^{-6} = 1.14$)[11] with the integrals of the respective NOESY ($\tau_m = 1$ s) cross peaks ($I_A/I_B = 1.13$) suggests negligible H^{RuA}/H^{NH} chemical exchange on the experimental time scale. Accordingly, H_2 elimination from **3** proceeds very slowly, and full dehydrogenation toward **1** under vacuum at room temperature takes several hours.

Scheme 1. Exchange of H_2O with H^{RuA} and H^{NH} in Amino Dihydride Complex **3**



The addition of 2 equiv of water to a sample of **3** in THF-d_8 results in broadening of the hydride signals and breakdown of the H^{RuA}−H^{RuB} *J*-coupling (Figure 1, right).[12] The hydride chemical shift differences with respect to dry samples were very small [$\Delta\delta(H^{RuA}) = 0.01$ ppm; $\Delta\delta(H^{RuB}) = 0.03$ ppm], which would be in agreement with Ru−H/H_2O proton exchange via short-lived dihydrogen complexes.[13] Accordingly, below −50 °C, exchange was slow on the NMR time scale, giving two sharp hydride signals with similar $T_1{}^{\min}$ values [154 ms (191 K) for H^{RuA} and 172 ms (191 K) for H^{RuB} at 400 MHz] that are typical of terminal hydride ligands.[14] Addition of molecular sieves to this NMR sample resulted in full restoration of the "dry" ^1H NMR spectrum. Most significantly, at room temperature, the broadening of the H^{RuA} signal was considerably larger than for H^{RuB}, pointing toward very different exchange rates, as was further substantiated using T_1 measurements: above −50 °C, the apparent T_1 values derived from inversion recovery for H^{RuA} dropped as a result of rapid exchange, contrasting sharply with H^{RuB} (see the Supporting Information).

Proton exchange rates of H_2O (4.25 equiv) with H^{RuA} [$k_A = 337(20)$ L mol^{-1} s^{-1}] and H^{NH} [$k_B = 8.0(4)$ L mol^{-1} s^{-1}] in THF-d_8 were derived using ^1H 2D NMR exchange spectroscopy (EXSY) combined with simultaneous fitting of several 2D spectra at different mixing times (Scheme 1).[15,16] This method offers the opportunity to study simultaneous multisite exchange over a wide dynamic range of exchange rates without the isotope effect inherent in H/D exchange kinetics. The k_A value is surprisingly high, considering the low acidity of water in such a nonpolar solvent. Most intriguingly, within experimental error, no direct exchange of H_2O

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with H^{RuB} was found. Stereoselective dihydrogen bonding has been observed previously, e.g., for [Re(*cis*-H)$_2$(CO)(NO)(*trans*-PR$_3$)$_2$] with alcohols, and was attributed to different relative ligand hydridicities and steric effects.[17] However, H^{RuA} and H^{RuB} are in very similar steric environments, and the trans dihydride configuration suggests comparable basicities of the hydride ligands. Therefore, the highly site-selective hydride/H_2O exchange and large exchange rate for H^{RuA} can best be rationalized in terms of directing H^{NH}/OH_2 hydrogen bonding. To further probe for the influence of the amine proton, the nitrogen atom was blocked by methylation (see the Supporting Information). Addition of 2 equiv of H_2O to [Ru(H)$_2$PMe$_3$(*Me*PNP)] [**5**; *Me*PNP = MeN(CH$_2$CH$_2$P^{i}Pr$_2$)$_2$] in THF-d_8 did not result in considerable broadening of either of the two hydride signals, and the mutual *J*-coupling was retained. Finally, the H_2O exchange rates with the hydrides of **5** as derived using ^{1}H 2D EXSY [0.07(3) and 0.03(2) L mol^{-1} s^{-1}] were very similar to each other and ~4 orders of magnitude smaller than k_A, supporting the idea that stereoselective H^+/H^- exchange in **3** is directed by H^{NH}.[18]

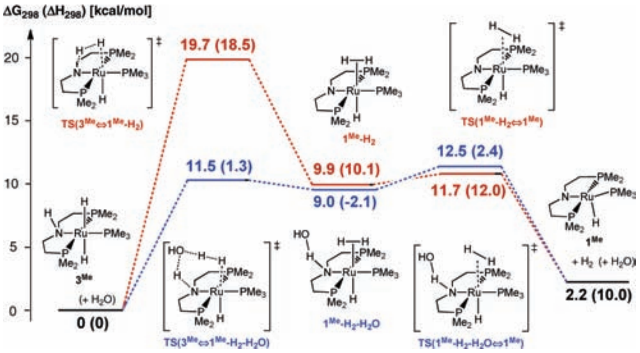

Figure 2. DFT calculations (B3LYP/6-31+G**) for heterolytic hydrogen splitting in THF (blue) with and (red) without water assistance.[19]

Since the intermediate dihydrogen complex that accounts for H^+/H^- exchange should be on the reaction path of H_2 activation by **1** as well, these results suggest that water lowers the barrier for heterolytic hydrogen splitting. Therefore, H_2 addition to model complex $\mathbf{1^{Me}}$ with and without H_2O was examined using DFT calculations (Figure 2). Addition of H_2 to amide $\mathbf{1^{Me}}$ is slightly exergonic ($\Delta G = -2.2$ kcal/mol). The water-free mechanism exhibits a barrier of $\Delta G^\ddagger = 9.8$ kcal/mol for rate-determining proton transfer from the H_2 ligand to N in the four-membered-ring transition state $\mathbf{TS(3^{Me}{\Leftrightarrow}1^{Me}{-}H_2)}$. In contrast, hydrogen bonding of the amido and H_2 ligands with water via six-membered-ring transition state $\mathbf{TS(3^{Me}{\Leftrightarrow}1^{Me}{-}H_2{-}H_2O)}$ lowers this barrier by $\Delta\Delta G^\ddagger = 8.2$ kcal/mol, in agreement with our proton exchange experiments.[19] Overall, the computed reaction profile compares well with calculations by Brandt, Andersson, and co-workers[5] on alcohol-assisted hydrogen activation in the diamine diphosphine model system [Ru(*trans*-H)$_2$(*cis*-PH$_3$)$_2$(H$_2$NCH$_2$CH$_2$NH$_2$)].

The unusual stereoselectivity of H^+/H^- exchange and the computational results strongly emphasize the role of hydrogen-bonding networks with Brønsted acids as weak as H_2O for heterolytic H_2 splitting by Ru−amide hydrogenation catalysts. In view of the ubiquitous availability of water, this mechanism might be relevant for both catalysis and biological heterolytic H_2 activation.

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Supporting Information Available: Full preparative, analytical, and computational details. This material is available free of charge via the Internet at http://pubs.acs.org.

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(18) H^+/H^+ exchange involving amine N−H and water O−H (k_B) could occur directly with N−H hydrogen-bonded water without Ru−H involvement; the slow exchange (0.14 s^{-1}) of H^{RuA} with H^{RuB} can best be explained by amine inversion upon such H^{NH} exchange with water.

(19) $\mathbf{3^{Me}{-}H_2O}$ with water hydrogen-bonded to H^{NH} was found to be slightly endergonic with respect to $\mathbf{3^{Me}}$ ($\Delta G = +2.0$ kcal/mol, $\Delta H = -7.5$ kcal/mol; see the Supporting Information).

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