Catalytic Hydrogenation

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Efficient Homogeneous Catalytic Hydrogenation of Esters to Alcohols**

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The reduction of esters to the corresponding alcohols is an important reaction in organic synthesis. Compared with traditional procedures using stoichiometric amounts of metal hydride reagents (e.g. $LiAlH_4$),[1] the catalytic hydrogenation of esters to alcohols, which generates no waste, is attractive environmentally and economically [Eq. (1)]. Het-

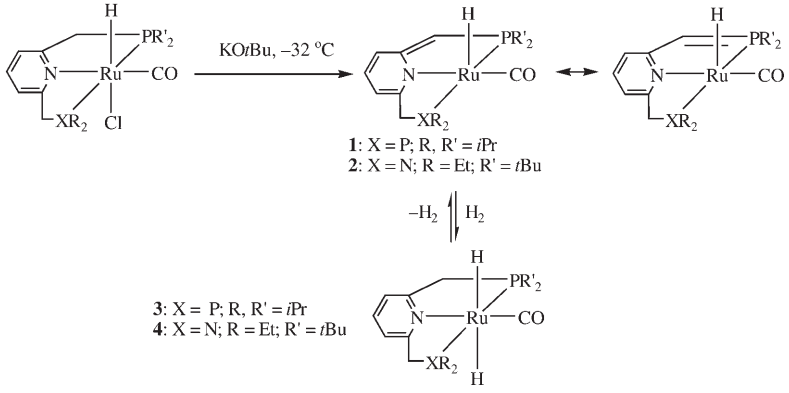
$$RCOOR' + 2\,H_2 \xrightarrow{\text{catalyst}} RCH_2OH + R'OH \qquad (1)$$

erogeneous hydrogenation of some fatty esters is practiced industrially at relatively high temperatures (200–300 °C) and high hydrogen pressures (200–300 atm) using transition-metal catalysts,[2] while homogeneous systems capable of hydrogenation of esters are very scarce[3–7] and mostly limited to activated esters. In these systems, large amounts of additives, such as an organic base,[3] inorganic acids,[3] salts,[5,6] zinc,[7] and fluorinated alcoholic solvents[3] were needed to obtain high conversion of esters into alcohols. Grey and coworkers[4] reported that the anionic ruthenium hydride complex $K_2[(PPh_3)_3(PPh_2)Ru_2H_4]\cdot(C_6H_{14}O_3)_2$, catalyzed the hydrogenation of activated esters, while ethyl acetate was hydrogenated to ethanol in only 8% yield and aromatic esters (e.g. methyl benzoate) were not hydrogenated with this catalyst.

We are aware of only two homogeneously catalyzed systems that are effective for the hydrogenation of nonactivated esters (i.e. esters in which there is no electron-withdrawing group adjacent to the carbalkoxy group).[3,7] Elsevier and Teunissen[3] reported a system of $[Ru(acac)_3]$ (acac = acetylacetonate) with $MeC(CH_2PPh_2)_3$, which effectively catalyzed the hydrogenation of benzyl benzoate to benzyl alcohol at 120 °C under 84 atm of H_2; this system required fluorinated alcohols (CF_3CH_2OH or $CF_3CH(OH)CF_3$) as solvents and an excess of triethylamine. Nomura et al.[7] reported that using $[Ru(acac)_3]$ with excess $P(n\text{-}C_8H_{17})_3$ in the presence of zinc in polar solvents at 200 °C and 10 atm H_2, methyl phenylacetate underwent hydrogenation and transesterification, the latter often being the major process.

Herein we report the hydrogenation of non-activated esters to the corresponding alcohols under relatively mild, neutral conditions, with no additives being required. The reaction is catalyzed by a ruthenium hydride complex based on the pincer ligand PNN (2-(di-*tert*-butylphosphinomethyl)-6-(diethylaminomethyl)pyridine). A comparison with the analogous PNP system reveals a major ligand effect, attributable to ligand hemilability.

The new PNP complex **1** was prepared by deprotonation of the chloro hydride complex [(PNP)RuHCl(CO)][8] with KO*t*Bu at −32 °C in 85% yield (Scheme 1).[9,10] The $^{31}P\{^1H\}$ NMR spectrum of **1** shows two groups of doublets at $\delta = 67.0$ and 66.3 ppm with $J_{PP} = 256.0$ Hz, corresponding to the two magnetically different phosphorus atoms of the *i*Pr-PNP ligand. The hydride ligand exhibits a triplet at $\delta = -13.02$ ppm ($J_{PH} = 24.0$ Hz) in the ^1H NMR spectrum. A one-proton doublet at $\delta = 3.85$ ppm ($J_{PH} = 12.0$ Hz) in the ^1H NMR spectrum and a broad singlet at $\delta = 39.0$ ppm in the $^{13}C\{^1H\}$ NMR spectrum indicate formation of an anionic PNP system (also confirmed by ^{13}C-DEPT and J_1-HMQC NMR spectra). The CO ligand gives a band at 1888 cm^{-1} in the IR spectrum.



Scheme 1.

A single-crystal X-ray diffraction study of **1** (Figure 1) indicates a distorted square-pyramidal geometry around the Ru^{II} center, with the CO ligand coordinated *trans* to the pyridinic nitrogen atom and the hydride located in the apical position (Ru-H1r 1.48(11) Å). It is noted that the bond length of C1–C2 (1.450(9) Å) is significantly shorter than that of C7–C6 (1.552(9) Å) while the bond length of C1–P1 (1.803(6) Å) is shorter to a smaller extent than that of P2–C7 (1.843(7) Å), indicating that the dearomatic configuration of **1** contributes much more than that of the aromatic phosphor–ylide configuration in the solid state (see Scheme 1 for resonance forms).

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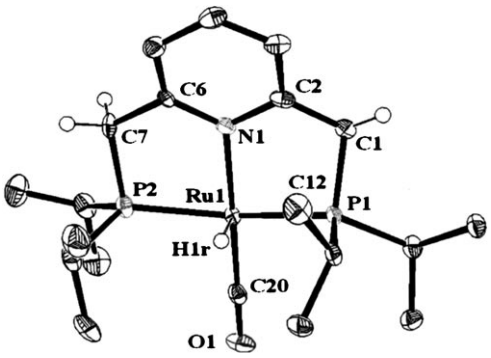


Figure 1. ORTEP diagram of a molecule of complex **1** with the thermal ellipsoids set at 50% probability. Selected bond lengths [Å] and angles [°]: Ru1–C20 1.844(7), Ru1–N1 2.163(5), Ru1–P1 2.350(2), Ru1–P2 2.291(2), Ru1–H1r 1.48(11), C1–C2 1.450(9), P1–C1 1.803(6), P2–C7 1.843(7), C6–C7 1.552(9); C20-Ru1-N1 171.4(2), P1-Ru1-P2 153.1(1), H1r-Ru1-P1 72(4), H1r-Ru-P2 85(4).

Upon treatment of complex **1** with dihydrogen, the *trans* dihydride complex **3** is quantitatively formed (see Scheme 1). This complex can also be prepared by treatment of the corresponding hydridochloride complex with $NaHBEt_3$.[9] Complex **3** slowly looses H_2 at room temperature to regenerate complex **1**. The PNN complex **2** was recently reported by us,[8] although crystals suitable for a single-crystal X-ray diffraction study could not be obtained. This complex shows analogous reactivity with dihydrogen, and it catalyzes the dehydrogenation of primary alcohols to esters.[8,11]

Complexes **1** and **2** were studied as catalysts for the hydrogenation of esters. Upon treatment of ethyl benzoate with dihydrogen (5.3 atm) at 115°C for 16 h with a catalytic amount of **3** (1 mol%), 7.5% conversion of the ester to yield 7% of benzyl alcohol and 7.5% of ethanol were obtained. Performing the reaction at 140°C resulted in 12% conversion to these alcohols. A trace amount of the transesterification product benzyl benzoate was also formed (Table 1, entries 1 and 2).

Remarkably, using complex **2** (1 mol%) as catalyst under the same conditions (115°C) for 4 h resulted in 99.2% conversion of ethyl benzoate into benzyl alcohol and ethanol (Table 1, entry 3). Hydrogenation of hexyl hexanoate resulted in formation of 1-hexanol in 82% yield after 5 h (entry 4). Ethyl acetate was hydrogenated to ethanol under similar conditions in almost 86% yield (entry 8). Reaction of benzyl benzoate with dihydrogen resulted in almost quantitative yield of benzyl alcohol after 7 h (entry 5); Reaction at room temperature led to quantitative formation of the *trans* dihydride ruthenium complex **4**, although no alcohol was formed. The aromatic methyl benzoate is quantitatively hydrogenated to benzyl alcohol and methanol (entry 6) in a relatively short time (4 h). As expected, the activated ester dimethyl terephthalate is converted into the corresponding dialcohol, 1,4-dimethanolbenzene, in high yield (97%) under our conditions (Table 1, entry 10). In a previous report, dimethyl phthalate was hydrogenated to phthalide using a ruthenium hydride complex in a yield of 11.5% after 144 h at 180°C under a hydrogen pressure of 128 atm.[5a] The bulky ester, *tert*-butyl acetate, was not effectively hydrogenated (10.5% conversion after 24 h; Table 1, entry 9), probably because of steric reasons.

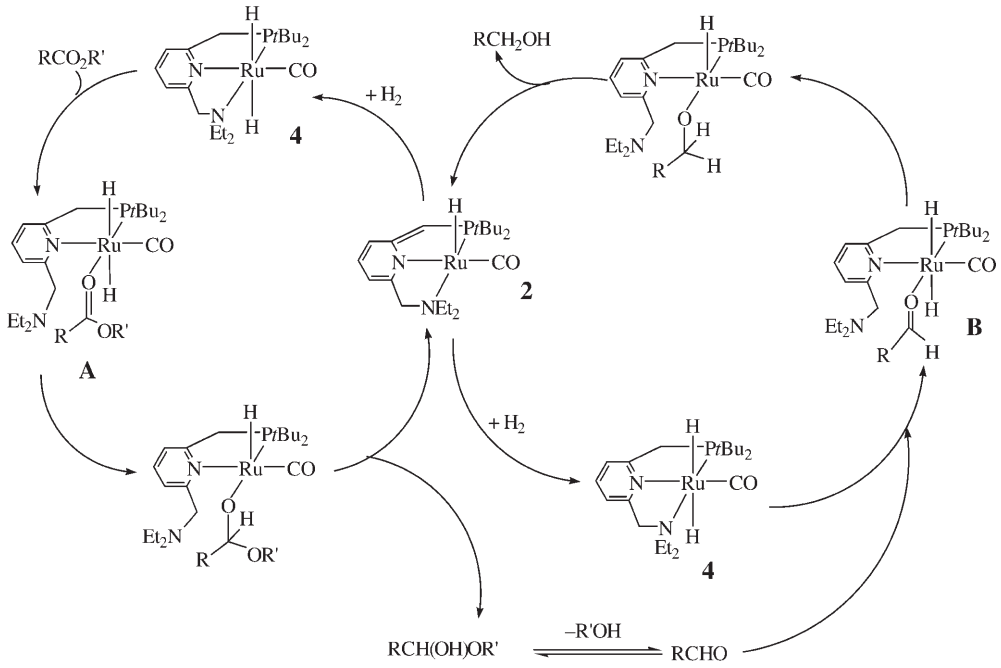
A possible cycle for catalysis of ester hydrogenation by **2** is presented in Scheme 2. Initially, dihydrogen addition to complex **2** results in aromatization, to form the coordinatively saturated, *trans* dihydride complexes **4**, as experimentally observed. Dissociation of the amine "arm" can provide a site for ester coordination to the ruthenium center, to give the intermediate **A**. A hydride ligand subsequently transfers to the carbonyl group of the ester, followed by O–H elimination of a hemiacetal and regeneration of complex **2**. The hemiacetal is in equilibrium with the aldehyde, which is readily hydrogenated following a similar catalytic cycle via intermediate **B** to form the corresponding alcohol.[12] The much lower catalytic activity of complex **1** is attributable to the difficulty in opening the chelate ring to provide a coordination site for ester coordination, to generate an intermediate analogous to **A**, possibly indicating the importance of ligand hemilability for ester hydrogenation. This mechanism differs significantly from the ones outlined for ruthenium-catalyzed ketone hydrogenation, in which binding of the ketone to the metal is not required and hydrogenation takes place by a concerted hydride/proton transfer.[13]

In conclusion, non-activated aromatic and aliphatic esters can be effectively hydrogenated to the corresponding alcohols under relatively mild, neutral conditions using a (PNN)ruthenium hydride complex as catalyst. This reaction involves an unusual aromatization/dearomatization sequence. The analogous PNP complex is much less active, suggesting that

Table 1: Hydrogenation of esters catalyzed by **1** and **2**.[a]

Entry	Ester	cat.	*t* [h]	*T* [°C]	Conversion [%]	Products (yield [%])[b]
1	ethyl benzoate	**1**	16	115	7.5	benzyl alcohol (7); ethanol (7.5)[c]
2	ethyl benzoate	**1**	16	140	12	benzyl alcohol (11.5); ethanol (12)[c]
3	ethyl benzoate	**2**	4	115	99.2	benzyl alcohol (96); ethanol (99)[c]
4	hexyl hexanoate	**2**	5	115	82.2	1-hexanol (82.2)
5	benzyl benzoate	**2**	7	115	98.5	benzyl alcohol (98)
6	methyl benzoate	**2**	4	115	100	benzyl alcohol (97); methanol (100)[c]
7	ethyl butyrate	**2**	4	115	100	1-butanol (98); ethanol (98.6)
8	ethyl acetate	**2**	12	115	86	ethanol (85.6)
9	*tert*-butyl acetate	**2**	24	115	10.5	ethanol (10.5); *tert*-butanol (10.5)
10	dimethyl terephthalate	**2**	5	115	100	1,4-dimethanolbenzene (97); methanol (100)

[a] Reaction conditions: ester (2 mmol); catalyst (0.02 mmol); H_2 (5.3 atm); dioxane (2 mL). [b] Percentage of maximum possible amount of each of the product alcohols; determined by GC. [c] A trace of benzyl benzoate was also formed: 0.3% (entries 1 and 2); 1% (entries 3 and 6).



Scheme 2.

pincer ligand hemilability[14] and ester coordination are part of the reaction mechanism, although other mechanisms might also be possible. The mechanism and scope of this reaction are being investigated.

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