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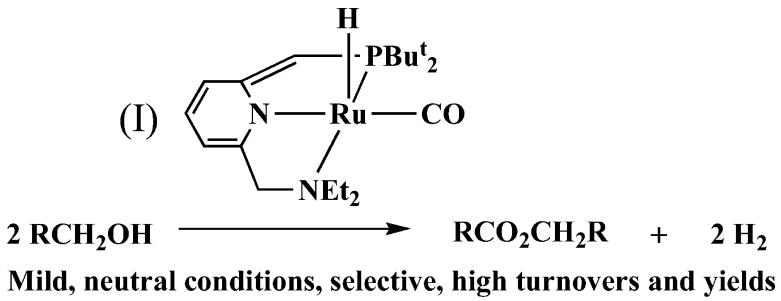

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Facile Conversion of Alcohols into Esters and Dihydrogen Catalyzed by New Ruthenium Complexes

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Esterification is one of the most fundamental and important reactions in organic synthesis.[1] Although several methods have been exploited and developed,[1] the search for new environmentally friendly, atom-efficient methods which avoid the use of large amounts of condensing reagents and activators has attracted much interest.[2] An attractive approach is the direct catalytic transformation of alcohols to esters, without the use of the corresponding acid or acid-derivative. In particular, dehydrogenative coupling of alcohols to esters with the evolution of H_2 is an attractive goal. As opposed to the normal esterification of an acid and alcohol, in which an equilibrium mixture is generated, the evolved hydrogen (valuable by itself) would shift the equilibrium to completion (eq 1). However relevant reports are limited to a few nonselective heterogeneous reactions[3] or homogeneous systems which utilize sacrificial hydrogen acceptors.[4,5] In general, homogeneous systems capable of thermally catalyzing acceptorless dehydrogenation of alcohols are relatively rare.[4,6−11] Moreover, most of these systems also require an additional acid or base and are not effective for dehydrogenation of primary mono-alcohols to the corresponding esters,[12] with the exception of two systems, reported by Murahashi[4] and by Shvo[11] (vide infra). We reported recently the Ru-catalyzed acceptorless dehydrogenation of secondary alcohols to ketones.[13] We now report the design of novel ruthenium complexes which efficiently and selectively catalyze dehydrogenation of primary alcohols to esters and H_2 in high turnover numbers under relatively mild, neutral conditions.

$$2RCH_2OH \xrightarrow[R=alkyl,aryl]{catalyst,\Delta} RCO_2CH_2R + 2H_2 \qquad (1)$$

Addition of the ligand ^{i}Pr-PNP (2,6-bis-(di-*iso*-propylphosphinomethyl)pyridine) to $RuHCl(PPh_3)_3(CO)$ in THF resulted in formation of the fully characterized [$RuHCl(^i$Pr-PNP)(CO)][14] **1** in 91% yield (Scheme 1). $^{31}P\{^1H\}$ NMR of **1** shows a singlet at 73.6 ppm, while the hydride ligand exhibits a triplet at −14.59 ppm (J_{PH} = 18.0 Hz) in the ^1H NMR. Complex **1** catalyzes alcohol dehydrogenative esterification in the presence of base. Thus, heating a solution containing 0.1 mol % (each) of **1** and KOH in 1-hexanol (157 °C) under argon flow resulted after 24 h in 67.2% conversion of the alcohol to hexyl hexanoate and H_2. A small amount of *n*-hexanal was also formed (Table 1, entry 1). No reaction took place in absence of a base.

Aiming at improving the catalytic activity, it was of interest to us to prepare a complex analogous to the coordinatively saturated **1**, but having a potentially "hemilabile" amine "arm". Complex **2** was obtained in 90% yield by reaction of $RuHCl(CO)(PPh_3)_3$ with the new ligand PNN (2-(di-*tert*-butylphosphinomethyl)-6-diethylaminomethyl)pyridine.[14] $^{31}P\{^1H\}$ NMR of **2** shows a singlet at 108.7 ppm, while the ^1H NMR of **2** exhibits the hydride ligand as a doublet at −15.25 ppm (J_{PH} = 27.5 Hz). A single-crystal X-ray diffraction study of **2** (Scheme 1) indicates a distorted octahedral geometry around the Ru(II) center, with the CO ligand coordinated trans to the pyridinic nitrogen atom and the hydride trans to the chloride.

Scheme 1

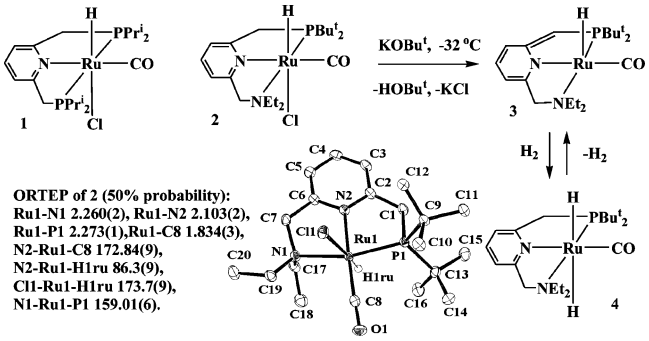

Table 1. Dehydrogenation of Primary Alcohols to Esters and H_2 Catalyzed by Complexes **1**, **2**, and **3**[a]

entry	cat.	KOH (equiv)	alcohol	temp. (°C)	time (h)	conv. (%)	yield (%) (ester)	yield (%) (aldehyde)
1	**1**	1	1-hexanol	157	24	70.6	67.2	2.8
2	**1**	0	1-hexanol	157	24	0	0	0
3	**2**	1	1-hexanol	157	24	90.4	90	0.3
4	**2**	0	1-hexanol	157	24	0	0	0
5	**2**	1	1-hexanol	115[b]	24	95	94.5	0.1
6	**2**	1	1-butanol	117	72	92.5	91.5	1
7	**2**	1	benzyl alcohol	115[b]	72	100	99.5	0
8	**3**	0	1-butanol	117	5	91	90	0.5
9	**3**	0	1-hexanol	157	2.5	91.5	91.4	0.1
10	**3**	0	1-hexanol	115[b]	6	99	99	0
11	**3**	0	benzyl alcohol	115[b]	4	93.2	92.1	1

[a] 0.01 mmol KOH, 0.01 mmol catalyst, and 10 mmol alcohol were heated neat under Ar flow. [b] 2 mL of toluene was added, and the solution was refluxed.

Complex **2** in the presence of 1 equiv of base is an efficient dehydrogenative esterification catalyst, exhibiting superior activity relative to that of **1**. Thus, upon heating a 0.1 mol % solution of complex **2** with KOH (1 equiv relative to Ru) in neat 1-hexanol at 157 °C under argon for 24 h, 91.5% hexyl hexanoate was formed accompanied by a trace of 1-hexanal (entry 3). The temperature can be lowered to 115 °C in refluxing toluene, resulting in 94.5% yield (945 turnovers) to the ester after the same period (entry 5). No reaction took place in the absence of base. Other alcohols react similarly. Thus, upon heating 1-butanol with 0.1 mol % of **2** and KOH (1 equiv) at 117 °C for 72 h, butyl butyrate was formed in 91.5% yield (entry 6). With benzyl alcohol at 115 °C in toluene, reaction follow-up indicated that 91% benzyl benzoate was formed after 6 h, with TOF reaching 333 h^{-1} at the level of 50% benzyl

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benzoate.[14] Formation of the ester became very slow after 6 h, perhaps because of retardation of the reaction by the high ester concentration. However, almost quantitative formation of benzyl benzoate was obtained (entry 7).

To further improve the reaction, we aimed at totally eliminating the need for a base. A possible role of the base is deprotonation of **2** to the corresponding Ru(0) complex. Exploring this possibility, **2** was treated with 1 equiv of KOBu^t at −32 °C. Interestingly, deprotonation of the benzylic phosphine "arm", rather then the hydride ligand, took place, resulting in the brown-red Ru(II) complex **3**[14] in 89% yield. $^{31}P\{^1H\}$ NMR of **3** shows a singlet at 94.7 ppm, representing an upfield shift of 14 ppm relative to complex **2**. The hydride ligand gives rise to a doublet at −26.45 ppm (J_{PH} = 25.5 Hz) in ^1H NMR. A one-proton singlet at 3.66 ppm in ^1H NMR and a doublet at 65.25 (J_{PC} = 50.3 Hz) in $^{13}C\{^1H\}$ NMR indicate formation of an anionic PNN system. The CO ligand absorbs at 1899 cm^{-1} in the IR spectrum.

Transition-metal complexes with an anionic PNP ligand ($C_5H_3N(CHPPh_2)(CH_2PPh_2)$) were reported.[15]

In an unusual observation, reaction of complex **3** with excess dihydrogen resulted in aromatization, yielding the *trans*-dihydride complex **4**, which was fully characterized.[14] $^{31}P\{^1H\}$ NMR of **4** shows a singlet at 124.9 ppm, downfield shifted by 30 ppm relative to complex **3**. The two magnetically equivalent hydride ligands give rise to a doublet at −4.06 ppm (J_{PH} = 17.0 Hz) in ^1H NMR. A doublet (2H) at 3.12 ppm (J_{PH} = 8.5 Hz) and a singlet (2H) at 3.83 ppm for the two benzylic methylene groups in ^1H NMR, respectively, indicate the presence of a regular aromatic PNN system. Significantly, **4** slowly loses H_2 at room temperature to regenerate complex **3** (Scheme 1).

Complex **3** is the best homogeneous catalyst for acceptorless dehydrogenative esterification of alcohols. When used as catalyst without any base, ester yields of over 90% (TON > 900) were obtained from the alcohols in relatively short reaction times (Table **1**, entries 8−11). This reaction provides a convenient method for the synthesis of esters because of its high efficiency, simplicity, and facile isolation of the desired products. Murahashi et al reported that heating $Ru(H)_2(PPh_3)_4$ with 1-butanol at 180 °C in toluene (sealed tube) resulted in 40 turnovers of butyl butyrate after 24 h.[4] For direct comparison with our system, 0.1 mol % $Ru(H)_2(PPh_3)_4$ was refluxed in 1-butanol at 117 °C for 72 h under argon atmosphere, resulting only in 2% butyraldehyde and no formation of ester, while the reaction catalyzed by **3** gave 90% of the ester after 5 h under the same conditions. Heating the Shvo catalyst η^4-$Ph_4C_4CO)Ru(CO)_3$ with 1000 equiv of benzyl alcohol in toluene at 115 °C for 24 h resulted in 2% benzaldehyde; no ester was observed, although this complex catalyzes ester formation at higher temperatures.[11]

Dehydrogenation of primary alcohols to esters may, in principle, proceed by dehydrogenation to the aldehyde followed by (a) hemiacetal formation from the aldehyde and alcohol followed by its dehydrogenation to the ester[4,16] or (b) a Tischenko-type disproportionation involving the aldehyde.[17] When complex **3** was heated with 100 equiv of benzaldehyde in toluene at 115 °C for 12 h, no benzyl benzonate was formed. On the other hand, heating complex **3** with 100 equiv each of benzaldehyde and benzyl alcohol in toluene at 115 °C for 12 h resulted in formation of benzyl benzonate in 100% yield, indicating that the hemiacetal pathway is likely to be operative.

Although further studies are required, a novel mechanism involving aromatization/dearomatization and amine arm hemilability seems plausible. Upon reaction of **3** with the alcohol, an aromatic, coordinatively saturated alkoxy hydride complex may be generated. Amine "arm" opening would enable the β-H elimination process, followed by aldehyde elimination to give complex **4**. Dihydrogen loss from **4** regenerates **3**, as described above. Mechanistic studies are now underway.

In conclusion, new Ru(II) hydride complexes based on electron-rich PNP and PNN ligands catalyze alcohol dehydrogenation to esters. Catalyst design has resulted in the novel complex **3** which is an outstanding catalyst for the acceptorless dehydrogenation of primary alcohols to esters under mild, neutral conditions, providing an environmentally benign method for the direct synthesis of esters from alcohols.

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Supporting Information Available: Experimental procedures and characterization of the PNN ligand and complexes **1**−**3**, procedure for catalytic reactions. X-ray data for complex **2** in CIF format. This material is available free of charge via the Internet at http://pubs.acs.org.

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