Catalytic (De)Hydrogenation

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From Esters to Alcohols and Back with Ruthenium and Osmium Catalysts**

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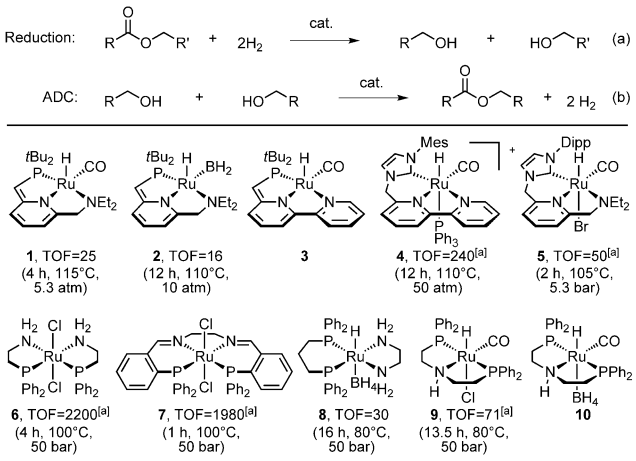
Hydrogenation is an attractive "green" method for the reduction of esters.[1–4] The reaction shown in Scheme 1 a is mildly exergonic, for example, formation of ethanol from



Scheme 1. Hydrogenation of esters and dehydrogenation of alcohols. [a] Under basic conditions. Dipp = 2,6-Diisopropylphenyl, Mes = 2,4,6-trimethylphenyl, S/M = molar ratio of substrate to metal, TOF = turnover frequency per hour for hydrogenation of PhCOOR (R = Me, Et).

ethyl acetate is favored by circa −5 kcal mol^{-1}.[5a] The reverse process of acceptorless dehydrogenative coupling (ADC, Scheme 1 b) is feasible in an open system, because H_2 gas is sparcely soluble and can be efficiently expelled under reflux conditions. Well-defined catalysts for reactions shown in Scheme 1 have been developed in the past five years. Milstein's complex **1**, which was reported in 2005, gives symmetrical esters from primary alcohols upon heating to more than 100 °C.[6] All Milstein-type complexes **1**–**5**[1,4a] and Noyori-type catalysts **6**-**10**[2,3] are active in ester hydrogenation (Scheme 1). These catalysts employ ligand cooperativity by pyridine aromatization/dearomatization in **1**–**5** and cleavage/formation of N–H bonds in **6**–**10**.[1e,2a,3c]

A meaningful comparison of the efficiency of these catalysts is currently problematic because of significant differences in the employed reaction temperatures and pressures. Available data for hydrogenation of benzoates (PhCOOR, R = Me, Et) serve to highlight the impressive performance of catalysts **6** and **7**, although a major drawback of these systems is the need for 5–10 mol % NaOMe. Hydrogenation of alkyl alkanoates proceeded slower compared to benzoates, for example, a turnover frequency (TOF) of 690 for methyl octanoate versus 2200 for methyl benzoate was reported for catalyst **6**.[2b,c]

Little is known about selectivity and functional-group tolerance of the existing ester hydrogenation catalysts. Testing of complexes **1**, **2**, **4**, and **5** was restricted to unfunctionalized aliphatic and aromatic esters. Catalyst **3** performed well for hydrogenation of methyl formate (TOF = 534 in 8 h) and dimethyl carbonate (TOF = 314 in 14 h) at 110 °C and $p(H_2)$ = 50 bar.[1b] Only complex **7** was studied with alkyl alkenoates and showed an excellent C=O/C=C selectivity, except for substrates with terminal C=C bonds, that is, methyl 10-undecanoate and the α,β-unsaturated methyl cinnamate.[2] Hydrogenation of *cis* alkenoates (common in plant oils) and their stability with respect to *cis*/*trans* isomerization under catalytic conditions have not been reported.

Catalysts **8** and **10** have been successfully tested with chiral esters of α-amino, α-hydroxy, β-amino, and β-hydroxy acids.[3] Good conversions and retention of the *ee* values were observed by using 0.1–1 mol % catalyst without base at 80 °C and $p(H_2)$ = 50 bar. Complex **9** is exceptionally active for hydrogenation of methyl (*R*)-lactate at 27 °C when used with 12 mol % of NaOMe.[3d]

Herein we report new Ru and Os catalysts capable of efficient reduction of esters under neutral conditions. This research is based upon our recent work with $[MH_2(CO)(HN(C_2H_4PiPr_2)_2)]$ complexes (M = Ru, Os), which are catalysts for transfer dehydrogenation of ethanol to ethyl acetate at room temperature and for acceptorless dehydrogenation of primary alcohols (Scheme 1 b) at temperatures above 120 °C.[5b] Use of 0.05 mol % $[RuH_2(CO)(HN(C_2H_4PiPr_2)_2)]$ gave a turnover frequency of 90 for hydrogenation of methyl benzoate after 18 hours at 100 °C with $p(H_2)$ = 50 bar. We thought that replacement of the PNHP*i*Pr ligand by a hemilabile NNHP*i*Pr system could facilitate the hydrogenation, by analogy with the Milstein's NNP complex **1**, which is more efficient than its PNP analogue.[1a]

The NNHP*i*Pr = $PyCH_2NHC_2H_4PiPr_2$ (Py = 2-pyridyl) ligand is easily assembled by condensation of the commercially available picolinaldehyde and 2-(diisopropylphosphino)ethanamine, followed by reduction with DIBAL. The

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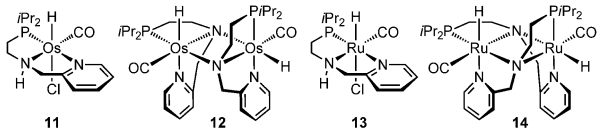
hydrido carbonyl chlorides [MHCl(CO)(NNHP*i*Pr)] (M = Os (**11**), Ru (**13**); Scheme 2) were prepared from the readily available [MHCl(CO)($AsPh_3$)$_3$] precursors by ligand meta-



Scheme 2. Complexes used in this communication.

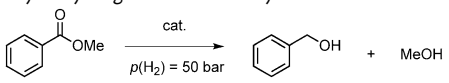
thesis. Treatment of complexes **11** and **13** with *t*BuOK afforded unusual dimers [MH(CO)(NNP*i*Pr)]$_2$ (M = Os (**12**), Ru (**14**); Scheme 2), presumably via intermediate 16-e amido species [MH(CO)(NNP*i*Pr)], which is analogous to the known [OsH(CO)(PNP*i*Pr)].[5b] Characterization of new complexes **11**–**14** was accomplished by a combination of spectroscopic methods and X-ray crystallography.

Dimers **12** and **14** have similar structures, however, they differ by the arrangements of the NNP*i*Pr ligands, which are spanning the Ru centers in **14**, but coordinate individual Os centers in **12**. These dimers are lacking symmetry and produce characteristic 1:1 hydride and phosphorus NMR resonances at room temperature. In the temperature range of 40 to 80 °C, a second minor 1:1 pattern appears in the hydride region and in the ^{31}P NMR spectra of **12** and **14** because of slow isomerization. No resonances of mononuclear species were seen even at 80 °C, as well as no saturation transfer between the hydrides, thus suggesting significant thermal and kinetic stability of **12** and **14** in solution.

Exposing **12** and **14** to 2-propanol or H_2 (1 atm) failed to produce [MH_2(CO)(NNHP*i*Pr)]. We obtained *trans*-[OsH_2(CO)(NNHP*i*Pr)] (**15**) by treating **11** with Li(Et_3BH) in THF. Characterization of the product in common solvents was hampered by the lack of solubility (in C_6D_6 and [D_8]THF) or rapid decomposition (in CD_3CN, CD_2Cl_2, and ethanol). Surprisingly, **15** is soluble and stable in [D_6]DMSO, in which the ^{1}H, ^{13}C, and ^{31}P NMR spectra are fully consistent with the *trans*-dihydride structure analogous to the related *trans*-[OsH_2(CO)(PNHP*i*Pr)] complex.[5b] Experimental and computational details for complexes **11**–**15** are provided in the Supporting Information.

A stoichiometric reaction of dihydride **15** and methyl benzoate in [D_8]THF immediately produced methanol, benzyl alcohol, and a mixture of the isomers of **12**. The catalytic activity of complexes **11**–**14** under $p(H_2) = 50$ bar was first tested in a series of experiments with methyl benzoate (Table 1). The ultimate performance was observed with ruthenium dimer **14**, which gave 18000 turnovers in 17 hours at 100 °C by using 0.005 mol% (50 ppm) of the catalyst without base. Thus, this complex is one order of magnitude more efficient than [RuH_2(CO)(PNHP*i*Pr)], which was mentioned above. At 80 °C, complex **14** gave TOF = 1470 (Table 1, entry 11), which is 20 times faster than the hydrogenation rate reported[3c] for [RuHCl(CO)-(PNHPPh)] with 5 mol% NaOMe (catalyst **9**, Scheme 1). The efficiency of **14** increases markedly from 40 to 100 °C, yet a high conversion was achieved even at 40 °C by using only

Table 1: Catalytic hydrogenation of methyl benzoate.[a]



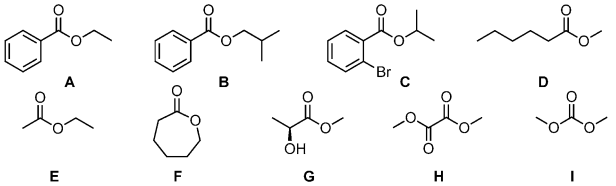
Entry	Cat.	Ester/Metal[b]	*T* [°C]	*t* [h]	Conv. [%]
1	**11**[c]	2000	100	1.5	100
2	**12**	2000	40	22	28
3	**12**	2000	60	7	82
4	**12**	2000	80	2.2	76
5	**12**	2000	100	1.5	99
6	**12**	3000	100	3	100
7	**12**	10000[d]	100	19	80
8	**13**[c]	2000	100	1.7	100
9	**14**	2000	40	17	82
10	**14**	2000	60	2.2	71
11	**14**	2000	80	1.2	88
12	**14**	2000	100	1	99
13	**14**	10000	100	14	100
14	**14**	20000	100	17	90

[a] PhCOOMe (20 mmol) in THF (7 mL) was hydrogenated in a 75 mL Parr pressure vessel. [b] Molar ratio of substrate to metal. [c] With *t*BuOK (1 mol%). [d] With PhCOOMe (120 mmol) in a 300 mL vessel.

0.05 mol% of the catalyst (Table 1, entry 9). Osmium dimer **12** is also an efficient catalyst for hydrogenation of methyl benzoate, however, at a slower rate compared to **14**. The chlorides **11** and **13** are similarly active in the presence of *t*BuOK.

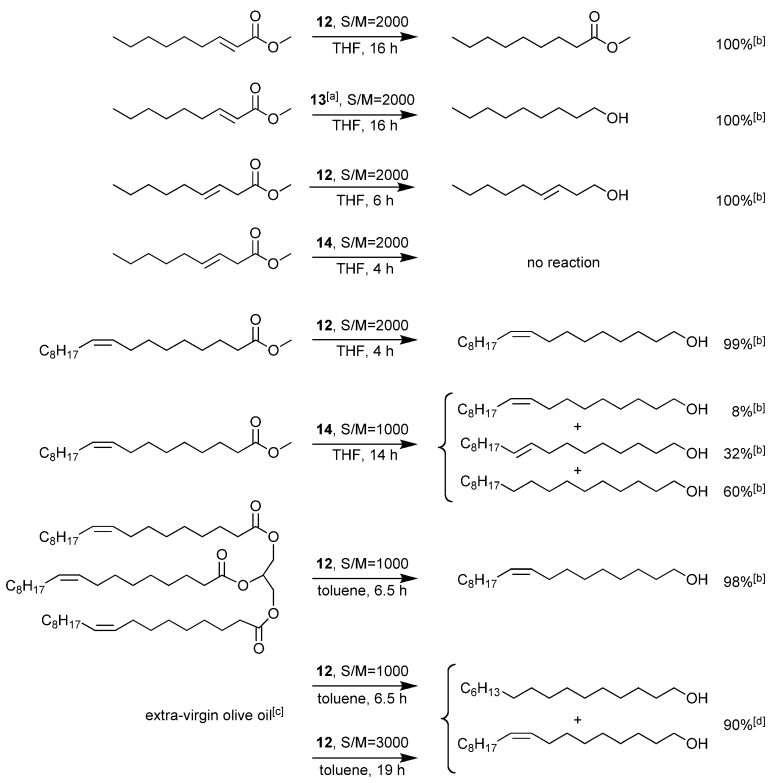
We further investigated hydrogenation of a group of carbonyl compounds (Table 2) and representative alkenoates (Scheme 3) at 100 °C, under $p(H_2) = 50$ bar. Catalyst **12** is equally active for hydrogenation of ethyl, *iso*-butyl, and methyl benzoates. However, hydrogenation of isopropyl 2-bromobenzoate was unsuccessful, apparently because of

Table 2: Catalytic hydrogenation of esters **A**–**I**.



Entry	Ester	Cat.	Ester/Metal[b]	*t* [h]	Conv. [%]
1	**A**	**12**	2000	1.6	99
2	**B**	**12**	2000	1.5	93
3	**C**	**12**	2000	17	0
4	**D**	**12**	2000	2	100
5[c]	**D**	**12**	3000	2.7	100
6	**D**	**14**	2000	1.5	93
7	**D**	**14**	10000	18	71
8	**E**	**12**	2000	3	100
9	**F**	**12**	2000	1.4	99
10	**F**	**14**	2000	5	67
11	**G**	**12**	2000	9	72
12	**H**	**12**	2000	23	0
13	**I**	**14**	2000	5.7	85

[a] Substrate (20 mmol) in THF (7 mL) was hydrogenated in a 75 mL pressure vessel at 100 °C and $p(H_2) = 50$ bar. [b] Molar ratio of substrate to metal. [c] Substrate (120 mmol) in a 300 mL vessel.



Scheme 3. Hydrogenation of alkenoates at 100 °C and $p(H_2) = 50$ bar, S/M = molar ratio of alkenoate groups to metal. [a] With *t*BuOK (0.5 mol %). [b] Conversion. [c] A mixture of triglycerides of oleic (ca. 85 %), linoleic (ca. 2–3 %), and palmitic acids as the main components in our samples. [d] Total yield of isolated alcohol mixture, containing approximately 85 % of oleyl alcohol.

catalyst deactivation. None of the catalysts shown in Scheme 1 have been tested with halogenated substrates, except **6**, which gave 88 % conversion for methyl 4-chlorobenzoate by using 0.05 mol % catalyst with 10 mol % NaOMe at 100 °C and $p(H_2) = 50$ bar.[2b,c]

Complexes **12** and **14** gave 100 % and 93 % reduction for methyl hexanoate in 2 and 1.5 hours, respectively. This compares favourably with the reduction of methyl octanoate with catalyst **6** (by using the same reaction temperature, pressure, and catalyst loading), for which 86 % conversion was reported after 2.5 hours of reaction in the presence of 10 mol % NaOMe.[2b,c] For ethyl acetate, the reduction with **12** was finished in three hours (Table 2, entry 8). The same reaction under $p(H_2) = 5$ bar required a 20 times higher catalyst loading to reach 96 % conversion in two hours with **5**[4a] and 86 % conversion in 12 hours with **1**,[1a] both at the slightly higher temperatures of 105 and 115 °C, respectively.

We further investigated hydrogenation of ε-caprolactone, a substrate that is known to undergo ring opening polymerization (ROP) in the presence of *t*BuOK and similar bases.[7] Indeed, polymeric material was formed in an attempted reduction of ε-caprolactone with **13** in the presence of *t*BuOK. When catalyzed by **14** without base, the hydrogenation proceeded without polymerization, but stopped at 67 % conversion as if the catalyst was deactivated at that time. Rapid reduction of ε-caprolactone was achieved with osmium dimer **12** (Table 2, entry 9).

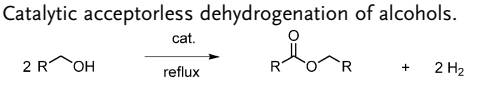
Substrates **G** and **I** are difficult to hydrogenate and require longer reaction times. The TOF of 160 for **G** (Table 2, entry 11) and 298 for **I** (entry 13) compare well with the best reported values under neutral conditions with catalysts **10** (TOF = 62 in 16 h at 80 °C)[3c] and **3** (TOF = 314 in 14 h at 110 °C).[1b] No hydrogenation of methyl oxalate (**H**) was observed with **12**; this substrate has not been studied with catalysts **1**–**10**.[8]

Activity and selectivity of complexes **12**–**14** were tested with substrates containing C=C bonds. The results show significant differences for ruthenium and osmium catalysts (Scheme 3). Hydrogenation of α,β-unsaturated methyl 2-nonenoate was not selective with **13** and afforded nonanol, which is not surprising with regard to the poor selectivity of **7** with methyl cinnamate.[2a] Unexpectedly, reduction of methyl 2-nonenoate with **12** quantitatively afforded methyl nonanoate. Such unusual selectivity and the lack of further conversion to nonanol in this case are puzzling. Osmium dimer **12** successfully catalyzed reduction of methyl 3-nonenoate to 3-nonenol, whereas ruthenium dimer **14** proved inactive in this reaction. Methyl oleate was hydrogenated with **12** with retention of the C=C bond to give (*Z*)-octadec-9-enol. The same reaction was very sluggish and required more catalyst with **12**; the reaction also lacked selectivity and afforded a mixture of octadecanol and (*E*)- and (*Z*)-octadec-9-enols.

We further tested osmium dimer **12** for reduction of glyceryl trioleate and a sample of domestic olive oil, which is a natural mixture of triglycerides of oleic (ca. 85 %), linoleic (ca. 2–3 %), and palmitic acids (main components). Hydrogenation of the trioleate quantitatively afforded neat (*Z*)-octadec-9-enol (oleyl alcohol) after aqueous washing, based on comparison of the ^1H and ^{13}C NMR spectra of the product with those of an authentic sample of the alcohol. A similar product containing mostly oleyl (85 %) and palmityl alcohols was obtained after hydrogenation of olive oil followed by aqueous washing. The reduction appeared close to quantitative, although we noted that the ^1H NMR spectra of the product were missing the characteristic C11-CH_2 resonance of linoleyl alcohol (expected at 2.77 ppm in $CDCl_3$). Hydrogenation of esters of polyunsaturated acids will need to be studied further.

We finally tested the activity of the NNHP*i*Pr catalysts for dehydrogenative coupling of alcohols. Two complexes were selected for this study, the ruthenium hydrido chloride **13** and osmium dimer **12** (Table 3). We found the catalytic activity of **12** particularly impressive in ethanol and propanol at 78° and 96 °C respectively, as conversions of these alcohols to ethyl acetate and propyl propionate with high yields have never been observed below 100 °C. The previously reported best ADC catalyst **1** was inactive for ethanol and propanol and required heating to more than 100 °C to produce esters from butanol and higher-boiling alcohols. The exceptional activity of **12** for ester synthesis naturally correlates with the excellent

Table 3: Catalytic acceptorless dehydrogenation of alcohols.

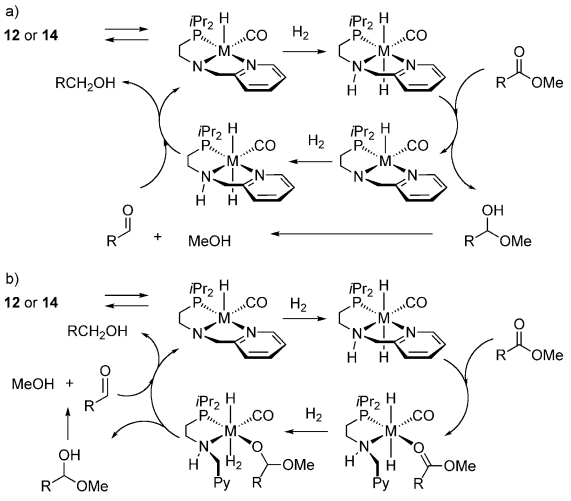


Entry	R[a]	*T* [°C]	Cat.	ROH/Metal[b]	*t* [h]	Conv. [%]
1	Me	78	**12**	1000	24	7
2	Me	78	**12**[c]	1000	8	61
3	Me	78	**12**[c,d]	1000	8	96
4	Me	78	**13**[d]	1000	7.5	30
5	Et	96	**12**	1000	8.5	86
6	Et	96	**13**[d]	1000	8	73
7	Pr	118	**12**	1000	3	93
8	Pr	118	**13**[d]	1000	3	78
9	*i*-Amyl	131	**12**	1000	3	86
10	*i*-Amyl	131	**13**[d]	1000	2.5	92
11	Hexyl	158	**12**	1000	1.3	97
12	Hexyl	158	**12**	4000	1.3	71
13	Hexyl	158	**13**[d]	1000	1	86

[a] Neat substrate (52 mmol). [b] Molar ratio of substrate to metal. [c] In toluene (3 mL). [d] With *t*BuOK (0.5 mol%).

activity of this catalyst for the reverse reaction, the reduction of esters under hydrogen pressure.

Both the Noyori-type outer-sphere and the classical inner-sphere hydrogenation mechanisms are possible with the NNHP*i*Pr complexes (Scheme 4). The superior activity of **12**



Scheme 4. Outer-sphere (a) and inner-sphere (b) hydrogenation. Py = pyridine.

versus $[RuH_2(CO)(PNHPiPr)]$ for hydrogenation of methylbenzoate suggests an important role of hemilability of the NNHP*i*Pr-coordinated catalysts. Continuing work in our group with XNHP ligands that are modified in order to disfavor dimerization and to enhance lability of the X group of the product complexes may shed more light on the mechanistic details of the reactions catalyzed by complexes **11**–**14**.

In conclusion, this communication presents outstanding versatile catalysts for reduction of esters and for dehydrogenative coupling of alcohols. Ruthenium dimer **14** has shown an unmatched efficiency under neutral conditions by giving 18000 turnovers in 17 hours for methyl benzoate and 7100 turnovers in 18 hours for methyl hexanoate. Osmium dimer **12** has proved to be a particularly useful catalyst for hydrogenation of esters with C=C bonds. To the best of our knowledge, complex **12** is the first homogenous catalyst efficient for hydrogenation of triglycerides, allowing production of fatty alcohols directly from olive oil. Complex **12** is also uniquely distinguished by effecting conversion of alcohols to esters, for example, ethanol into ethyl acetate, at temperatures below 100 °C.

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[8] Reduction of dimethyl oxalate to ethylene glycol was reported by using 0.2 mol% of a catalyst prepared from $[Ru(acac)_3]$ and $MeC(CH_2PPh_2)_3$. It took 16 hours at 120 °C and $p(H_2) = 80$ bar to achieve full conversion.[4h,j]

