Transfer Hydrogenation and Hydrogenation of Commercial-Grade Aldehydes to Primary Alcohols Catalyzed by 2-(Aminomethyl)pyridine and Pincer Benzo[h]quinoline Ruthenium Complexes

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Transfer Hydrogenation and Hydrogenation of Commercial-Grade Aldehydes to Primary Alcohols Catalyzed by Ampy and Pincer Benzo[*h*]quinoline Ruthenium Complexes

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Abstract: Chemoselective reduction of commercial-grade aldehydes (97-99%) to primary alcohols is achieved with *cis*-[$RuCl_2$(ampy)(PP)] (ampy = 2-(aminomethyl)pyridine; PP = dppb, dppf) and pincer [RuCl(CNN^R)(PP)] (PP = dppp, dppb, dppf; $HCNN^R$ = 4-substituted-2-aminomethyl-benzo[*h*]quinoline, R = Me, Ph) complexes, via transfer hydrogenation and hydrogenation reactions. Aromatic, conjugated and aliphatic aldehydes are quantitatively converted to the corresponding alcohols using 2-propanol with potassium carbonate, at S/C up to 100000 via transfer hydrogenation, whereas aldehyde hydrogenation (5-20 atm of H_2) is efficiently achieved in MeOH in the presence of KO*t*Bu at S/C up to 40000.

Keywords: aldehydes • ligands • hydrogenation • hydrogen transfer • ruthenium

Introduction

Metal catalyzed hydrogenation (HY)[1] and transfer hydrogenation (TH)[2] of carbonyl compounds, with particular regard to ketones, are widely accepted as cost efficient routes in the industry for the synthesis of alcohols.[3] The HY and TH procedures, which involve H_2 and 2-propanol or formic acid as hydrogen sources, have a lower environmental impact and an easier work-up with respect to the classical reduction involving $NaBH_4$ or boranes still employed in industry.[4] In the last decades great attention has been devoted to the development of chiral ruthenium catalysts based on well-designed ligands for the synthesis of optically active alcohols, via asymmetric reduction of ketones.[1] In addition to the Noyori type TH and HY ruthenium catalysts,[5] showing an arene or a diphosphane in combination with a bidentate nitrogen ligand with a NH function, a new generation of highly active pincer ruthenium catalysts, containing neutral or anionic tridentate ligands, have been reported.[6] These systems have been found active in several organic reactions including alcohol dehydrogenation,[7] ester and amide hydrogenation,[8] as well as borrowing hydrogen

transformations.[9] In the last decade, we developed highly active and productive Ru and Os catalysts for the TH and HY of carbonyl compounds, displaying substituted 2-(aminomethyl)pyridines ligands and the progress in this area has been recently reviewed.[10] The commercially available *cis*-[$RuCl_2$(ampy)(PP)] (ampy = 2-(aminomethyl)pyridine; PP = dppb **1**,[11] dppf **2**[12]) and pincer [RuCl(CNN)(dppb)] (**3**)[13] are practical catalysts for ketone reduction, as well as for other organic transformations, including dehydrogenation, deuteration and isomerization of alcohols (Figure 1).[12, 14]

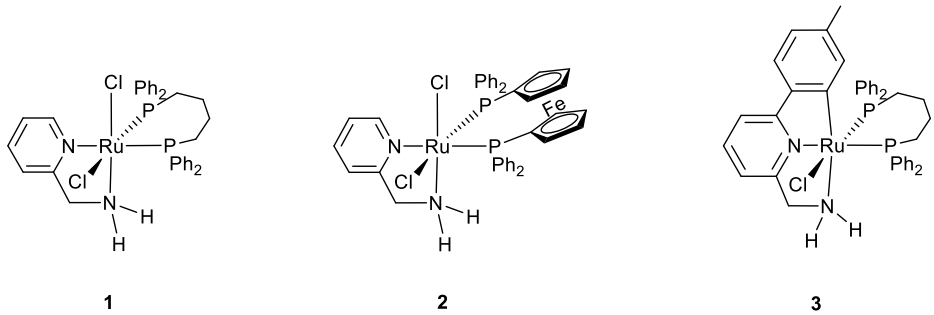
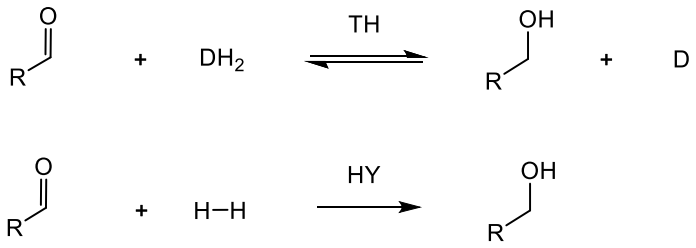


Figure 1. Ampy and CNN pincer ruthenium catalysts.

Conversely, for the reduction of simple aldehydes to primary alcohols, $NaBH_4$ remains the preferred reagent in industry.[3,15] Several heterogeneous catalysts, such as those based on Pd/C, are used in the HY of aromatic aldehydes to benzyl alcohols, and particular attention has been devoted to avoid the over reduction to methylarenes.[16] Furthermore, heterogeneous catalysts display low tolerance to several aromatic substituents, including nitro and halide groups which are easily hydrogenated. As regards the reduction of conjugated aldehydes, the chemoselective HY of cinnamaldehyde at C=O, without reduction of the C=C bond, has been a challenging target for heterogeneous catalysts for decades.[17] By contrast to ketone reduction, the number of catalysts for the TH and HY of aldehydes is much lower and the catalysis is usually performed with a S/C $\leq 10^3$ to achieve complete conversion of the substrate (Scheme 1).[1,2,18]

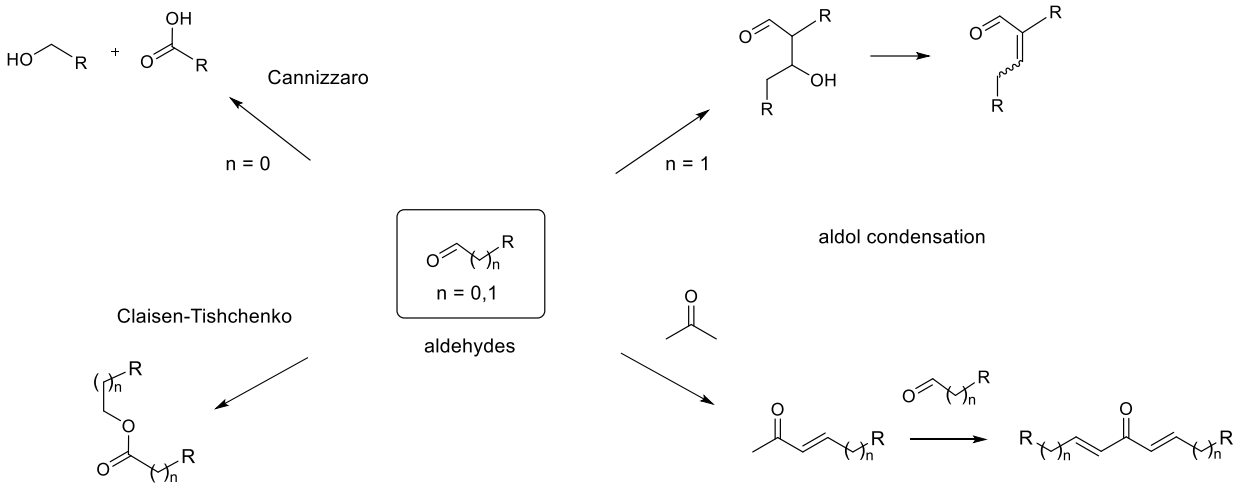


Scheme 1. Transfer hydrogenation and hydrogenation of aldehydes.

In addition to iridium complexes,[19] the ruthenium Noyori system [(arene)RuCl(TsDpen)],[20] [$CpRu(PPh_3)$(PN)],[21] [$RuH_2(PPh_3)_4$],[22] [$RuCl_2(PTA)_4$],[23] [$RuCl_2$(*m*tppms)$_2]_2$,[24] [$RuCl_2(PO)_2$],[25]

$[RuCl_2(POP)(dmso)]$,[26] $[RuCl_2(PPh_3)(NNN)]$,[27] $[RuCl(PPh_3)_2(MeCN)_3][BPh_4]$,[28] $[RuCl_2(CO)_2(PS)]$ and Ru cluster carbonyl derivatives[29]catalyze the aldehyde TH using 2-propanol or formates as hydrogen donors which work at relatively low S/C ratio (100-1000). Complexes **2**[12] and **3**[30] were found active in the TH of aldehydes with NaO*i*Pr and K_2CO_3 as base. To achieve complete reduction, the aldehydes were distilled under inert atmosphere and rapidly used in TH, since commercial-grade substrates led to poor or no conversion.[30] It is worth noting that aldehydes are slowly reduced by alcohols in the presence of Group 1 alkoxides, hydroxide or carbonates, as well as Al alkoxides, via the Meerwein-Verley-Pondorf (MPV) reaction.[31] As regard HY, the Shvo type catalysts[32], arene[33] and phosphane based ruthenium complexes[34] were found active in the aldehyde reduction. Commercial grade aromatic aldehydes can be hydrogenated using the Will's tethered catalyst [(C3-teth-TsDpen)RuCl] in $MeOH/H_2O$,[35] with water shifting the acetal-aldehyde equilibrium to aldehyde. More recently Dupau et al. reported that $[Ru(O_2CR)_2(diamine)(PP)]$, bearing bulky carboxylates, are highly efficient catalysts for the reduction of redistilled commercially available aldehydes in alcoholic and nonprotic apolar solvents in neutral or slightly acidic conditions with S/C = 10^4-10^5, while ketones lead to very poor conversion.[36]

The comparison of the properties of the aldehydes vs. ketones may suggest that aldehydes can be more easily reduced to alcohols than ketones, on account of their higher redox potentials.[37] In addition, aldehydes have lower steric requirements, facilitating their approach to the metal center. However, in practice aldehydes are substrates difficult to be reduced selectively and the catalysis is affected by the substrate quality, nature and concentration of the base. Since TH and HY of the carbonyl compounds are usually carried out in basic conditions, to allow formation of the catalytically active metal-hydrides,[38] the control of the chemoselectivity is a delicate point. Aldehydes, displaying the formyl group, show a broader reactivity than ketones. Under basic conditions, aldehydes may undergo the Claisen-Tishchenko (dimerization)[39] and the Cannizzaro[40] reactions (Scheme 2).



Scheme 2. Base-mediated aldehyde reactions.

In addition to alkoxides and hydrides of the main group elements,[41] $[RuH_2(PPh_3)_4]$,[42] $[RuHCl(CO)(PPh_3)_3]$,[43] $[RuCl(SiMe_3)(CO)(PPh_3)_2]$,[44] $[(\eta^5\text{-}C_5Ph_4O)_2HRu_2H(CO)_4]$,[45] $[RuCl_2(p\text{-cymene})]_2$ / PR_3,[46] and also Os, Ir and Ni complexes catalyze the Claisen-Tishchenko reaction.[47] Aldehydes displaying reactive α-hydrogens can easily undergo aldol condensation in basic media.[48] It is worth noting that during the TH of aldehydes in 2-propanol, conjugated mono- and dienones can also be produced by cross coupling reactions between aldehyde and the formed acetone (vide infra) (Scheme 2). Furthermore, aldehydes can also undergo decarbonylation with Ru[49] and Os[47a] complexes, affording metal carbonyl derivatives and this reaction has been considered a deactivation pathway for Ir and Ru catalysts, resulting in a low S/C ratio.[19h,i,50] A strategy to achieve both high productivity and chemoselectivity in aldehyde reduction, entails the use of both fast and robust catalysts, which work in weak basic media. In addition, the development of catalysts that can work with a S/C ratio higher that 1000 to meet the industrial requirements and can be employed with commercial grade substrates and solvents is highly desirable for applications. Recently, we described that the easily accessible pincer complexes $[RuCl(CNN^R)(PP)]$ (**4**-**9**), based on 4-functionalized 2-aminomethyl-benzo[*h*]quinoline ligands ($HCNN^R$) prepared via a scalable synthesis, are highly productive catalysts for both TH and HY of ketones (Figure 2).[51a]

We report here the use of the ampy and the CNN^R pincer ruthenium complexes in the TH and HY of aldehydes of commercial-grade purity at S/C = 2000-100000. A comparison of the activity of the ampy and pincer complexes and the effect of the reaction parameters are also provided.

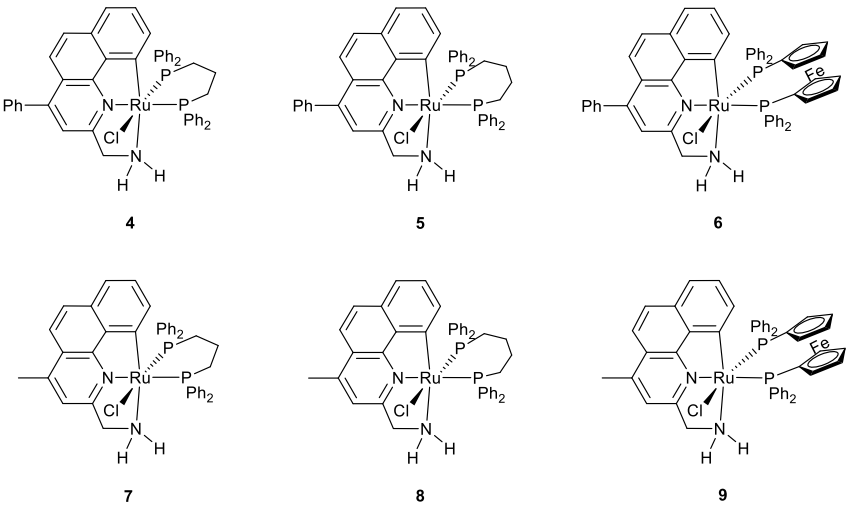
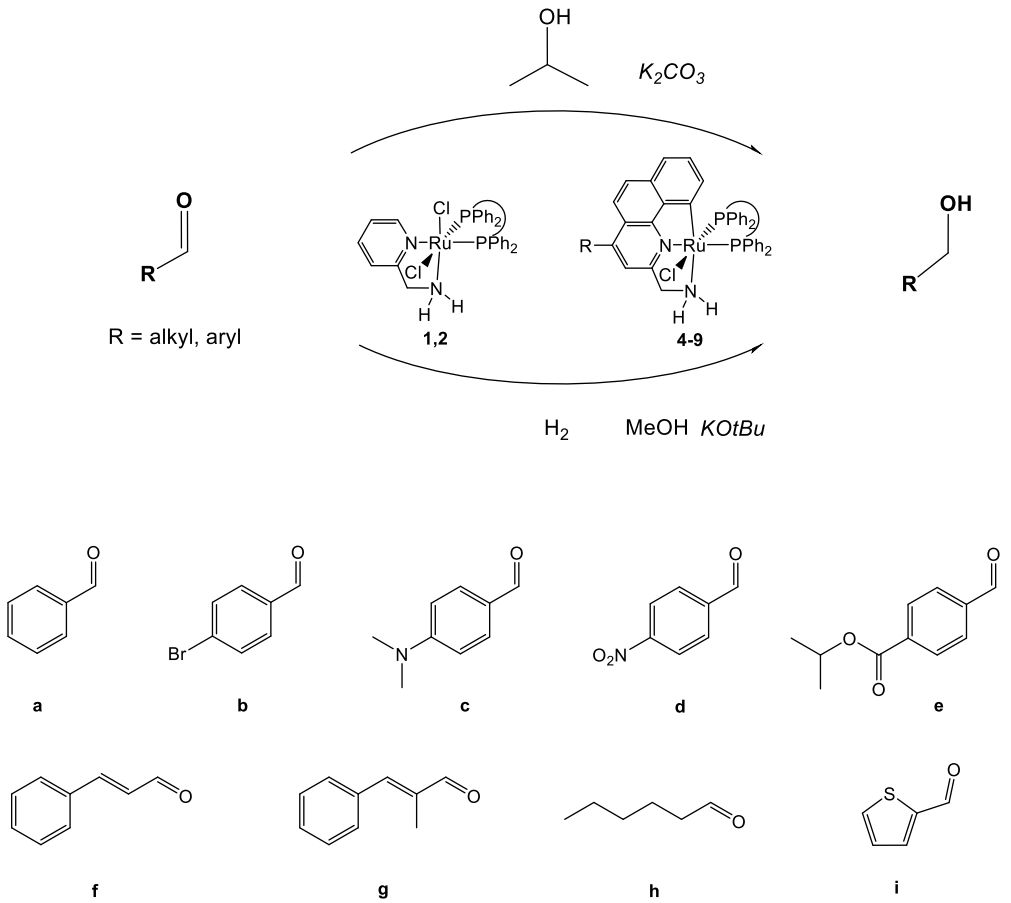


Figure 2. 4-Functionalized 2-aminomethyl-benzo[*h*]quinoline ruthenium complexes [RuCl(CNN^{R})(PP)] **4**-**9**.

Results and Discussion

Catalytic TH of aldehydes catalyzed by *cis*-[RuCl$_2$(ampy)(PP)] complexes 1, 2. The commercially available ampy complexes **1** and **2** were used in TH of several aldehydes of commercial-grade purity (Scheme 3).



Scheme 3. Transfer hydrogenation of aldehydes catalyzed by the ampy **1**, **2** and pincer **4-9** ruthenium complexes.

When benzaldehyde **a** (assay 99%) was refluxed in 2-propanol with complex **1** (S/C = 2000) and the weak base K_2CO_3 (5 mol%), 98% conversion was achieved in 1.75 h, affording 92% of benzyl alcohol (Table 1, entry 1). Complex **2** (S/C = 2000), bearing dppf in place of dppb, afforded 85% conversion of **a** with 74% of benzyl alcohol in 4 h, whereas with a S/C = 5000, only 49% of alcohol is obtained (entries 3, 4). It is worth noting that using freshly distilled **a**, complex **1** (S/C = 2000) with K_2CO_3 (5 mol%) gives 94% of benzyl alcohol in 1 h (entry 5), whereas complex **2** (S/C = 20000) in the presence of NaO*i*Pr (2 mol%) gives 95% conversion in 2 h.[12] Complex **1** (S/C = 2000) catalyzes the selective reduction of 4-bromobenzaldehyde **b** (assay 99%) to 4-bromobenzyl alcohol (>97%) in 30 min (entry 6).

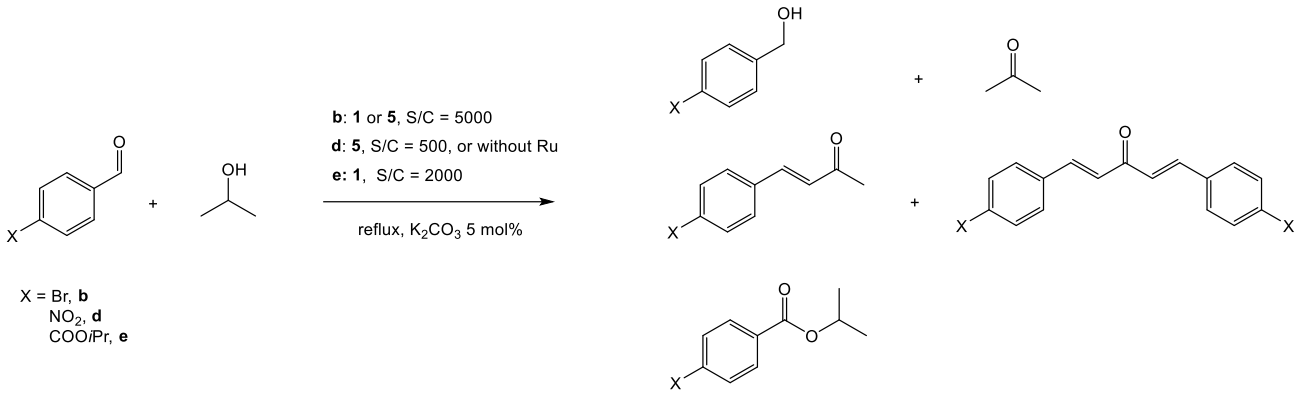
Table 1. TH of aldehydes (0.1 M) catalyzed by complexes **1**, **2** and K_2CO_3 (5 mol%) in 2-propanol at 82 °C.

Entry	Substrate	Complex	Loading [S/C]	Time [h]	Conv. [%][a]	Alcohol [%][a]	By-prds. [%][a]
1	**a**	**1**	2000	1.75	98	92	6

2	**a**	**1**	5000	5	43	39	4
3	**a**	**2**	2000	4	85	74	11
4	**a**	**2**	5000	5	59	49	10
5[b]	**a**	**1**	2000	1	95	>94	<1
6	**b**	**1**	2000	0.5	98	>97	<1
7	**b**	**1**	5000	1.5	92	70	22
8	**b**	**2**	2000	2.5	92	62	30
9	**c**	**1**	2000	0.5	98	>97	<1
10	**c**	**1**	5000	1	99	>98	<1
11	**c**	**1**	10000	4.5	95	89	6
12	**c**	**2**	2000	0.5	99	98	1
13	**c**	**2**	5000	4	52	49	3
14	**e**	**1**	2000	2	36	21	15
15	**e**	**2**	2000	2	42	28	14
16	**f**	**1**	2000	3	78	>77	<1
17	**f**	**1**	5000	3	11	>10	<1
18	**f**	**2**	2000	0.5	98	>97	<1
19	**f**	**2**	5000	4	52	50	2
20[c]	**f**	**2**	2000	0.5	95	>94	<1
21	**g**	**1**	2000	3.5	60	42	18
22	**g**	**2**	2000	3	98	93	5
23	**h**	**1**	2000	4	89	66	23
24	**h**	**2**	2000	4	95	29	66
25	**i**	**1**	2000	3	>99	70	30
26	**i**	**2**	2000	3	94	70	24

[a] The conversion and the amount of by-products were determined by GC analysis or by ^{1}H-NMR spectroscopy. [b] Substrate was distilled. [c] Substrate and 2-propanol were distilled and NaO^{i}Pr (2 mol%) was used as base (see ref. [12]).

By performing the reaction at S/**1** = 5000, almost full conversion was achieved in 1.5 h (92%), but with formation of 70 % of alcohol (entry 7), indicating that carrying out experiments at longer reaction time generally results into a decrease of selectivity. The NMR analysis of the product distribution revealed also the formation of (*E*)-4-(4-bromophenyl)but-3-en-2-one and (1*E*,4*E*)-1,5-bis(4-bromophenyl)penta-1,4-dien-3-one, in about 1/2 molar ratio, as outcome of the condensation between **b** and acetone formed during the TH (Scheme 4, see Supporting Information).



Scheme 4. Transfer hydrogenation of **b**, **d** and **e** in 2-propanol.

Complex **2** was found less active and selective than **1** for **b**, leading to 62% of alcohol (entry 8). The substrate 4-(dimethylamino)benzaldehyde **c** (assay 99%) is efficiently reduced with **1** at S/C = 5000 and 10000 affording 99 and 89% of 4-(dimethylamino)benzyl alcohol in 1 and 4.5 h, respectively (entries 10, 11). With **2** (S/C = 2000), 98% of alcohol was attained in 0.5 h, whereas at S/C = 5000 incomplete conversion was achieved (entries 12, 13). TH of isopropyl 4-formylbenzoate **e** with **1** and **2** (S/C = 2000) attained moderate conversion (36 and 42 %, entries 14 and 15), with formation of the aldol condensation dienone product with acetone (Schema 4, see Supporting Information), indicating that the presence of the carboxylate function inhibits the catalytic activity of **1**. Complexes **1** and **2** catalyze the chemoselective reduction of conjugated aldehydes. With **1** (S/C = 2000) *trans*-cinnamaldehyde **f** (assay 98%) has been converted to the corresponding allylic alcohol (77%) in 3 h, while **2** gave 97% in 0.5 h without reduction at the C=C bond (entries 16, 18). This result is similar to that obtained using freshly distilled **f** with **2** in the presence of NaO*i*Pr (entry 20).[12] At lower loading of **1** and **2** (S/C = 5000) incomplete conversion was observed (entries 17, 19). The TH of α-methylcinnamaldehyde **g** (assay 97%, predominantly *E*-isomer) with **1** gave 60% conversion with 42% of α-methylcinnamol, whereas with **2** chemoselective formation of alcohol (93%) was attained (entries 21, 22). Hexanal **h** (assay 98%) with **1** and **2** led to 1-hexanol (66 and 29%), with formation of aldol-condensation by-products (entries 23 and 24). TH of the heteroaromatic thiophene-2-carbaldehyde **i** (assay 98%) with **1** and **2** gave quantitative conversion in 3 h, affording 70% of 2-thienylmethanol with formation of enone and dienone side products in about 2/1 molar ratio (entries 25, 26, see Supporting Information).

These results indicate that the commercially available ampy complexes **1**, **2** can be employed in the TH of commercial grade aromatic and conjugated aldehydes at S/C = 2000-10000. For aromatic aldehydes chemoselective TH has been achieved using the dppb complex **1**. Conversely,

conjugated aldehydes can be selectively converted to allylic alcohols with the less basic dppf derivative **2**.

Catalytic TH of aldehydes catalyzed by the pincer [RuCl(PP)(CNN^R)] complexes 4-9. The easily accessible pincer complexes **4-9**, obtained from 4-functionalized 2-aminomethylbenzo[*h*]quinoline ligands,[51a] have been studied in TH of aldehydes of commercial-grade purity in basic 2-propanol. Benzaldehyde **a** (essay 99%) has been quantitatively and selectively reduced to benzyl alcohol (98-99%) with complexes **4-9** (S/C = 2000) in the presence of K_2CO_3 (5 mol%) within 1.25 – 6.5 h, the dppf catalysts **6**, **9** being more active than the dppp and dppb derivatives (Table 2, entries 1-6).

Table 2. TH of aromatic aldehydes (0.1 M) catalyzed by complexes **4-9** and K_2CO_3 (5 mol%) in 2-propanol at 82 °C.

Entry	Substrate	Complex	Loading [S/C]	Time [h]	Conv. [%][a]	Alcohol [%][a]	By-prds. [%][a]
1	**a**	**4**	2000	2	100	99	1
2	**a**[b]	**5**	2000	1.5	100	>99	<1
3	**a**	**6**	2000	1.25	99	98	1
4	**a**	**7**	2000	5	99	98	1
5	**a**	**8**	2000	5	99	98	1
6	**a**	**9**	2000	1.25	99	98	1
7	**b**	**4**	2000	0.5	98	78	20
8	**b**	**5**	2000	2	100	82	18
9	**b**	**5**	5000	3	66	36	19
10	**b**	**6**	2000	0.5	98	>97	<1
11	**b**	**7**	2000	3	67	44	23
12	**b**	**8**	2000	1	100	81	19
13	**b**	**9**	2000	0.5	>99	>98	<1
14	**c**	**4**	5000	1.5	95	>94	<1
15	**c**	**4**	10000	3	98	>97	<1
16	**c**	**5**	2000	0.5	98	>97	<1
17	**c**	**5**	5000	0.5	98	>97	<1
18	**c**	**5**	10000	1.5	97	>96	<1

19	**c**	**5**	20000	3	98	>97	<1
20	**c**	**5**	40000	7	>99	>99	<1
21	**c**	**5**	100000	20	>99	>99	<1
22	**c**	**6**	5000	1.5	92	>91	<1
23	**c**	**6**	10000	3	98	>97	<1
24	**c**	**7**	2000	2	98	>97	<1
25	**c**	**8**	2000	2	99	>98	<1
26	**c**	**9**	2000	2	98	>97	<1
27	**c**	none	--	10	-	-	-
28	**d**	**5**	2000	2	41	36	5
29	**d**	**5**	500	2	80	65	15[c]
30	**d**	none	--	2	31	17	14[d]
31	**e**	**4**	2000	5	52	>51	<1
32	**e**	**5**	2000	5	75	>74	<1
33	**e**	**6**	2000	0.75	95	>94	<1
34	**e**	**7**	2000	6	33	>32	<1
35	**e**	**8**	2000	5	53	>52	<1
36	**e**	**9**	2000	1	96	>95	<1

[a] The conversion and the amount of by-produtcs were determined by GC analysis or by ^{1}H-NMR spectroscopy. [b] By using distilled **a**, 97% of benzyl alcohol is formed in 35 min. [c] (1*E*,4*E*)-1,5-bis(4-nitrophenyl)penta-1,4-dien-3-one and *iso*-propyl 4-nitrobenzoate in 2 / 3 ratio. [d] Percentage of the saturated alcohol 3-phenylpropan-1-ol between brackets.

Notably, under the same conditions, but using distilled **a**, the pincer **5** (S/C = 2000) affords 97% of alcohol in 35 min, while with **3** quantitative conversion is achieved in 30 s.[30] The bromo aldehyde **b** was quantitatively converted with **4**-**6**, **8** and **9** (S/C = 2000) in a shorter time with respect to that required for **a**. High selectivity was achieved with the dppf complexes **6** and **9** leading to 98-99% of 4-bromobenzyl alcohol (entries 10, 13), whereas the dppp **4**, **7** and dppb **5**, **8** derivatives gave 44-82% of alcohol. The NMR analysis of the isolated products of the TH of **b** with **5** (S/C = 5000, entry 9) after 3 h, showed the formation of 4-bromobenzyl alcohol (36 %), (1*E*,4*E*)-1,5-bis(4-bromophenyl)penta-1,4-dien-3-one (18 %) in a 2/1 molar ratio, with a small amount of isopropyl 4-bromobenzoate (1%) (Scheme 4, see Supporting Information). The isopropyl benzoate is likely produced from **b** via cross-Claisen-Tischenko or Claisen-Tischenko reaction, followed by trans-esterification. These results indicate that at high S/C (≥ 5000) and longer reaction time, C-C coupling reactions compete significantly with TH resulting in low selectivity. Initial attempts to

inhibit the aldol condensation by fractional distillation of acetone (b.p. = 56 °C) failed.[52] The effect of substrate concentration has also been investigated. Since aldehydes show a higher reduction potential than ketones,[37] a higher substrate concentration could be employed in TH, with significant advantage for industrial applications. However, by increasing the concentration of **b** from 0.1 to 1 M (**b**/**5** = 10000, 5 mol% K_2CO_3) the conversion dropped from 69 to 33% (16 h), with formation of 37, 27 and 22 % of alcohol at 0.1, 0.2 and 1 M, respectively. Complexes **4**-**9** were found to efficiently catalyze the chemoselective TH of 4-(dimethylamino)benzaldehyde **c** (0.1 M) to alcohol. With **4** at S/C = 5000 and 10000, 4-(dimethylamino)benzyl alcohol was attained in 94 and 97% (1.5 and 3 h, respectively) (entries 14, 15), whereas with **5** 99% conversion was achieved at remarkably high S/C = 100000 in 20 h, with no erosion of the selectivity (entries 16-21). Without Ru catalyst and in the presence of K_2CO_3, no reduction occurred (entry 27). The strong electron-donating property of the dimethylamino group of **c** leads to a low electrophilic formyl functionality, hindering the C-C coupling reactions. On the other hand, the TH of *p*-nitrobenzaldehyde **d** with **5** (S/C = 2000) affords poor conversion (41% in 2 h) with 36% of alcohol (entry 28). The analysis of the products at S/**5** = 500, revealed the formation of 4-nitrobenzyl alcohol **A** (65 %), (1*E*,4*E*)-1,5-bis(4-nitrophenyl)penta-1,4-dien-3-one **B** (2%) and isopropyl 4-nitrobenzoate **C** (13%) (Scheme 4, entry 29). Without **5** and in the presence of K_2CO_3 (5 mol%), **d** undergoes 31% conversion in 2 h, with formation of **A**/**B**/**C** in about 6/2/3 molar ratio (entry 30, see Supporting Information). Thus, the ruthenium catalyzed TH of **d**, displaying a highly electrophilic formyl group, leads to the alcohol, via both Ru-hydride and K alkoxide species,[53] and products of condensation and Claisen-Tischenko reactions. By contrast to the ampy complexes **1**, **2**, the pincer **4**-**9** (S/C = 2000) promote the selective reduction of isopropyl 4-formylbenzoate **e** to alcohol (up to 95%). With the dppf derivatives **6** and **9**, the corresponding hydroxymethyl benzoate is obtained in 94 and 95% (entries 33, 36), whereas the dppp and dppb catalysts gave lower conversion. *Trans*-cinnamaldehyde **f** has been reduced to *trans*-3-phenyl-2-propen-1-ol with **4**-**9** (S/C = 5000-10000) with conversion in the range 52-98% in 0.5-6.5 h (Table 3, entries 1-12). Complex **5** at S/C = 10000 gave 84% of the allylic alcohol in the presence of small amount of 3-phenylpropan-1-ol (4%, entry 4). Since the pincer catalysts **4**-**9** show high activity for the C=O, but not for the C=C bond reduction, it is likely that the saturated alcohol is formed through an isomerization of the allylic alcohol to the saturated aldehyde.[12] Notably, with **1** and **2** the TH of **f** gave allylic alcohol with nearly no by-products (Table 1, entries 16-19).

Table 3. TH of conjugated and aliphatic aldehydes (0.1 M) catalyzed by complexes **4**-**9** and K_2CO_3 (5 mol%) in 2-propanol at 82 °C.

Entry	Substrate	Complex	Loading [S/C]	Time [h]	Conv. [%][a]	Alcohol [%][a]	By-prods. [%][a]
1	**f**	**4**	5000	1	99	89	10 (10)[b]
2	**f**	**4**	10000	6.5	68	59	9 (1)[b]
3	**f**	**5**	5000	1	99	90	9 (7)[b]
4	**f**	**5**	10000	6.5	98	84	14 (4)[b]
5	**f**	**6**	5000	0.5	96	77	19 (19)[b]
6	**f**	**6**	10000	4	98	80	18 (3)[b]
7	**f**	**7**	5000	4	93	73	20 (3)[b]
8	**f**	**7**	10000	4	96	77	19 (4)[b]
9	**f**	**8**	5000	4	93	73	20 (3)[b]
10	**f**	**8**	10000	4	96	77	19 (4)[b]
11	**f**	**9**	5000	1	98	84	14 (5)[b]
12	**f**	**9**	10000	4	57	44	13 (2)[b]
13	**g**	**4**	5000	0.25	95	>95	<1
14	**g**	**4**	10000	2.75	92	>91	<1
15	**g**	**5**	5000	0.25	92	>91	<1
16	**g**	**5**	10000	1.75	96	>95	<1
17	**g**	**6**	5000	0.25	97	>96	<1
18	**g**	**6**	10000	0.5	97	>96	<1
19	**g**	**6**	20000	2.75	96	>95	<1
20	**h**	**4**	2000	0.25	>99	>99	<1
21	**h**	**4**	5000	0.67	>99	>99	<1
22	**h**	**5**	2000	0.1	>99	>99	<1
23	**h**	**5**	5000	0.33	>99	>99	<1
24	**h**	**5**	10000	0.8	>99	>99	<1
25	**h**	**5**	20000	3	94	54	40
26	**h**	**6**	2000	0.15	>99	>99	<1
27	**h**	**6**	5000	0.33	>99	>99	<1
28	**h**	**6**	10000	1	>99	>99	<1

[a] The conversion and the amount of by-produtcs were determined by GC analysis or by ^{1}H-NMR spectroscopy. [b] Percentage of the saturated alcohol 3-phenylpropan-1-ol between brackets.

The substrate α-methylcinnamaldehyde **g** was promptly reduced to α-methylcinnamol (92-97%) with **4-6** (S/C = 5000-20000) in a shorter time (0.25-2.75 h) with respect to **f**, without hydrogenation of the C=C bond (Table 3, entries 13-19). The aliphatic aldehyde **h** was rapidly and selectively reduced to 1-hexanol (>99%) by **4-6** (S/C = 2000-10000) in 6 min – 1 h (entries 20-24, 26-28). At higher S/**5** = 20000, 94% conversion is achieved in 3 h, but with lower selectivity due to the formation of condensation products (entry 25, see Supporting Information).

These results indicate that for aromatic and aliphatic aldehydes the pincer complexes **4-9** are superior with respect to the ampy **1**, **2**, affording high selectivity at high S/C ratio (2000 – 100000) and in a shorter time. The pincer complexes **6** and **9** bearing dppf gave generally better results compared to the catalysts with the more basic dppp and dppb phosphanes. The presence of the orthometallated CNN terdentate ligand makes these complexes[51] thermally more stable and catalytically more productive compared to the related ampy catalysts. As regards α,β-unsaturated aldehydes, high selectivity toward the formation of the allylic alcohol has been achieved with the ampy dppf **2** derivative. Aldol condensation with acetone and Claisen - Tischenko side reactions were observed mainly for aromatic aldehydes with electron-withdrawing groups, while those with electron-donating groups gave chemoselective TH to alcohols.

Catalytic HY of aldehydes catalyzed by *cis*-[RuCl$_2$(ampy)(PP)] complexes 1, 2 and pincer [RuCl(PP)(CNN^R)] complexes 4-6. The Ru derivatives **1**, **2** and **4-6** in the presence of KO*t*Bu were found active in the hydrogenation (5-20 atm of H_2) of aromatic, conjugated and aliphatic aldehydes of commercial-grade purity (98-99%) using methanol as solvent and with S/C up to 40000 (Scheme 3). The ampy **2** complex (S/C = 2000), bearing dppf phosphane, catalyzed the quantitative HY of benzaldehyde **a** (2 M) into benzyl alcohol (98%) in 16 h at 50 °C in the presence of 2 mol% of KO*t*Bu (Table 4, entry 3), whereas the dppb derivative **1** shows poor activity (entries 1, 2). Notably, with distilled **a**, complex **2** (S/C = 5000) afforded benzyl alcohol in 10 min.[12] The pincer complexes **4-6** were found more active than the ampy **1**, **2**, leading to quantitative conversion at higher S/C ratio. The HY of **a** with the dppp complex **4** (S/C = 10000 and 20000) gave selective reduction to benzyl alcohol (97, 99%) in 8 h (entries 4, 5). In a gram scale reaction, 5 g of **a** (3.3 M) was converted to alcohol (92 %, 20 h) in a Parr autoclave (20 atm of H_2) at **S**/**4** = 25000 (entry 6). With complex **5** (S/C = 20000) 98% of alcohol is obtained in 16 h (entry 8), while the less basic dppf derivative **6** was found less active than **4**, **5**, affording 60% of alcohol (entry 9). Interestingly, with complex **4** and under 5 atm of H_2, the electron-rich aldehyde **c** is quantitatively and chemoselectively reduced to 4-(dimethylamino)benzyl alcohol (>97%) at high S/C = 10000-40000 in 1-22 h (entries 10-12).

Table 4. HY aldehydes (2 M) catalyzed by complexes **1**, **2** and **4**-**6** with KO*t*Bu (2 mol%) in methanol at 50 °C (Biotage® Endeavor).

Entry	Substrate	Complex	Loading [S/C]	P (H_2) [atm]	Time [h]	Conv. [%][a]	Alcohol [%][a]	By-prds. [%][a]
1	**a**	**1**	1000	10	3	35	33	2
2	**a**	**1**	2000	10	8	22	7	15
3	**a**	**2**	2000	10	16	100	98	2
4	**a**	**4**	10000	10	8	100	97	3
5	**a**	**4**	20000	10	8	100	99	1
6	**a**[b]	**4**	25000	20	20	92	92	0
7	**a**	**5**	10000	10	16	98	98	2
8	**a**	**5**	20000	10	16	99	98	1
9	**a**	**6**	10000	13	16	63	60	3
10	**c**[c,d]	**4**	10000	5	1	100	>99	<1
11	**c**[c,d]	**4**	20000	5	7	98	>97	<1
12	**c**[c,d]	**4**	40000	5	22	98	>97	<1
13	**f**	**1**	1000	10	3	95	87	8
14	**f**	**2**	2000	10	8	98	89	9
15	**f**	**4**	10000	10	8	99	89	10
16	**f**	**4**	20000	10	8	96	75	21
17	**f**	**5**	10000	10	8	99	90	11
18	**f**	**6**	10000	10	8	80	20	60
19	**g**[c]	**4**	15000	5	24	100	>99	<1
20	**h**[c,d]	**4**	5000	5	1.5	99	90	9
21	**i**[c,d]	**4**	10000	5	1	100	99	1
22	**i**[c]	**4**	5000	5	0.66	100	95	5

[a] Conversion and product distribution were determined by GC analysis or by ^{1}H-NMR spectroscopy. [b] [S] = 3.3 M, 5 g-scale reaction in a Parr autoclave. [c] Parr autoclave. [d] [S] = 1 M.

Cinnamaldehyde **f** was hydrogenated with the ampy derivatives **1**, **2** (S/C = 1000 and 2000) to cinnamol (87, 89%, respectively) in 3 and 8 h (entries 13, 14). Conversely, the pincer dppp and dppb complexes **4** and **5** gave 89 and 90% of alcohol at higher S/C (10000) (entries 15, 17). As for the substrate **a**, the less basic dppf derivative **6** was found less actives than **4** and **5**, leading to poor

selectivity in the reduction of **f** (entry 18). Complex **4** catalyzes the highly chemoselective HY of α-methylcinnamaldehyde **g** (S/C = 15000), attaining the unsaturated alcohol (>99%) in 24 h (entry 19). With **4**, hexanal **h** (S/C = 5000) is promptly reduced to 1-hexanol with good selectivity (90 %, entry 20) in 1.5 h. In addition, thiophene-2-carbaldehyde **i** (1 M) is selectively transformed to 2-thienylmethanol (99%) with a S/**4** = 10000 (1 h), while at higher substrate concentration (2 M) 95% of alcohol was formed (entries 21, 22). The influence of the solvent in the HY of **a** has been investigated for the pincer complexes **4**-**6**. With **4** (S/C = 10000) under 13 atm of H_2 in MeOH, **a** is converted to alcohol (96%) in 16 h at 50 °C with 2 mol% of KO*t*Bu (Table 5, entry 1).

Table 5. Effect of the solvent in the HY of benzaldehyde **a** (2 M) catalyzed by **4**-**6** (S/C = 10000) with 2 mol% of KO*t*Bu, under 13 atm of H_2 in 16 h at 50 °C (Biotage® Endeavor).

Entry	Complex	Solvent	Conv. [%][b]	Alcohol [%][b]	By-prds. [%][b]
1	**4**	MeOH	100	96	4
2	**4**	MeOH/EtOH = 3/1	100	93	7
3	**4**	MeOH/EtOH = 1/1	100	88	12
4	**4**	MeOH/EtOH = 1/3	100	86	11
5	**4**	EtOH	79	58	21
6	**4**	Toluene[a]	11	10	1
7	**5**	MeOH	100	98	2
8	**5**	MeOH/EtOH = 3/1	100	97	3
9	**5**	MeOH/EtOH = 1/1	100	97	3
10	**5**	MeOH/EtOH = 1/3	90	80	10
11	**5**	EtOH	100	82	18
12	**5**	Toluene[a]	6	6	0
13	**6**	MeOH	63	60	3
14	**6**	MeOH/EtOH = 3/1	23	19	4
15	**6**	MeOH/EtOH = 1/1	23	18	5
16	**6**	MeOH/EtOH = 1/3	19	16	3
17	**6**	EtOH	29	18	11

[a] The reaction was run for 32 h. [b] Conversion was determined by GC analysis or by ^{1}H-NMR spectroscopy.

Using MeOH/EtOH mixtures, complete conversion was observed, but with a decrease of selectivity (93 – 86%, entries 2-4), whereas in EtOH both lower conversion (79%) and selectivity (58% of alcohol) were attained (entry 5). In toluene, **4** displays poor activity with formation of only 10% of alcohol after 32 h (entry 6). A similar behavior has been observed with complex **5**, methanol being the solvent of choice, leading to 98% of alcohol in 16 h (entry 7), with 6% conversion in toluene (entry 12). Finally, the dppf derivative **6** was found less active, with 60 and 18% of alcohol in MeOH and EtOH, respectively (entries 13, 17). These data indicate that in the HY of aldehydes with the pincer complexes[13b] the alcohol media plays a crucial role, methanol being the solvent of choice. The use of KO*t*Bu in methanol results in the formation of the weaker base KOMe, which is involved in the formation of the catalytically active Ru-hydride species from dihydrogen, via Ru-alkoxide-amide species.[13b] The comparison of the activity of the ampy and pincer complexes in HY shows that while the ampy dppf **2** is more active than the dppb **1**, for the pincer complexes a reverse behavior is observed, the dppp and dppb **4** and **5** complexes being superior than the dppf derivative **6**.

Conclusion

In conclusion, we have demonstrated that the easily accessible ampy complexes *cis*-[$RuCl_2$(ampy)(PP)] (**1**, **2**) and the pincer complexes [RuCl(CNN^R)(PP)] (**4**-**9**) are highly active catalysts for the reduction of commercial-grade (97-99%) aromatic, aliphatic and conjugated aldehydes to their corresponding primary alcohols via both transfer hydrogenation (TH) with 2-propanol and hydrogenation (HY) (5-20 atm of H_2) in MeOH. The pincer catalysts **4**-**9** display generally higher productivity with respect to the ampy derivatives **1**, **2** for both TH (S/C up to 100000) and HY (S/C up to 40000) of aromatic and aliphatic aldehydes. Conversely, the ampy complexes **1**, **2** were found more efficient for the chemoselective reduction of unsaturated aldehydes, thus indicating that the best performance in term of selectivity and productivity can be achieved by a correct matching of the substrate and catalyst. For both ampy and pincer complexes the type of the diphosphine strongly affects the aldehyde TH and HY reactions. On account of the formation of acetone in the TH, cross aldol-condensation side-products may form during the catalysis, depending on the electrophilic character of the formyl group. The ability of the pincer complexes to catalyze the reduction of not distilled substrates at high S/C ratio makes these ruthenium catalysts suitable systems for applications in the reduction of industrially relevant aldehydes. Further studies are currently in progress to extend the use of ampy and pincer ruthenium catalysts in other organic transformations.

Experimental Section

General: All reactions were carried out under an argon atmosphere using standard Schlenk techniques. The aldehydes **a** (99%), **f** (98%), **g** (97%), **h** (98%) were purchased from Alfa Aesar, **b** (99%), **d**, (98%), from Aldrich, **c** (99%) from Merck and used without further purification, whereas **e** was prepared from 4-formylbenzoic acid.[54] The solvent methanol (100%), ethanol (99.7%), toluene (99%) were from VWR, while 2-propanol (99.7%) was from Alfa Aesar and used as received. All other chemicals were from Aldrich and Alfa Aesar. Complexes **1**, **2** were obtained by Alfa Aeser, whereas the pincer **4**-**9** were prepared according to the literature procedure.[51a] NMR measurements were recorded on a Bruker AC 200, chemical shifts, in ppm, are relative to TMS for ^{1}H and $^{13}C\{^{1}H\}$, whereas the GC analyses were performed with a Varian GP-3380 gas chromatograph with a MEGADEX-ETTBDMS-β column of 25 m of length, internal diameter 0.25 mm, column pressure 5 psi, H_2 as carrier gas and flame ionization detector (FID). The injector and detector temperature was 250 °C. Program used: initial T =150°C ramped to 190 °C at 3 °C min^{-1} and then to 220 °C at 20 °C min^{-1}. The hydrogenation experiments were carried out with a Biotage® Endeavor and a Parr autoclave.

Procedure for the TH of aldehydes. The selected aldehyde (1 mmol), K_2CO_3 (6.9 mg; 0.05 mmol) and 2-propanol (8 ml) were introduced in a Schlenk, subjected to three vacuum-argon cycles and the system was put in an oil bath at 90 °C. From a 250 μM solution of the ruthenium complex in 2-propanol, 2 ml (0.5 μmol of Ru) were added to the refluxing mixture to reach a final volume of 10 ml. The reaction was sampled by removing an aliquot of the reaction mixture, adding diethyl ether (1/1 in volume) and after filtration over a short silica pad, the conversion was determined by GC analysis. For solid and high boiling compounds, the solvent was evaporated by gently heating under vacuum, the crude mixture was dissolved in $CDCl_3$ and analyzed by ^{1}H-NMR spectroscopy; S/C = 2000, K_2CO_3 5 mol%.

Procedure for the HY of aldehydes. In a 10 mL glass tube, the selected ruthenium catalyst (0.001 mmol) and aldehyde (10 mmol) were dissolved in 4 ml of MeOH and 0.2 ml of a 1.0 M solution of KO*t*Bu (0.2 mmol) in *tert*-butanol were added. The tube was put in an Endeavour apparatus, the system filled and vented under stirring four times with nitrogen, then four times with hydrogen (without stirring) and finally charged to the desired hydrogen pressure. The system was kept at 50 °C for the proper time and the reaction was sampled by removing an aliquot of the reaction mixture (approximately 0.5 ml), followed by addition of MeOH (1.5 ml) and water (150 μl). After filtration over a short silica pad, the conversion was determined by GC analysis; S/C = 10000, KO*t*Bu 2 mol%, aldehyde 2 M.

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References and notes

[1] a) M. Yoshimura, S. Tanaka, M. Kitamura, *Tetrahedron Lett.* **2014**, *55*, 3635; b) G. Shang, W. Li, X. Zhang, *Catalytic Asymmetric Synthesis*, 3rd ed. (Ed.: I. Ojima), John Wiley & Sons, Hoboken, 2010; Chapter 7; c) *The Handbook of Homogeneous Hydrogenation*, *Vols. 1-3* (Eds. J. G. de Vries, C. J. Elsevier) Wiley-VCH: Weinheim, 2007; d) *Transition Metals for Organic Synthesis*, 2nd ed. (Eds. M. Beller, C. Bolm) Wiley-VCH: Weinheim, 2004, p. 29; e) *Asymmetric Catalysis on Industrial Scale* (Eds. H.-U. Blaser, E. Schmidt) Wiley-VCH, Weinheim, 2004.

[2] a) D. Wang, D. Astruc, *Chem. Rev.* **2015**, *115*, 6621; b) F. Foubelo, C. Nájera, M. Yus, *Tetrahedron: Asymmetry* **2015**, *26*, 769; c) J. Ito, H. Nishiyama, *Tetrahedron Lett.* **2014**, *55*, 3133; d) R. H. Morris, *Chem. Soc. Rev.* **2009**, *38*, 2282; e) W. Baratta, P. Rigo, *Eur. J. Inorg. Chem.* **2008**, 4041; f) C. Wang, X. Wu, J. Xiao, *Chem. Asian J.* **2008**, *3*, 1750; g) T. Ikariya, A. J. Blacker, *Acc. Chem. Res.* **2007**, *40*, 1300; h) J. S. M. Samec, J. E. Bäckvall, P. G. Andersson, P. Brandt, *Chem. Soc. Rev.* **2006**, *35*, 237.

[3] J. Magano, J. R. Dunetz, *Org. Process Res. Dev.* **2012**, *16*, 1156.

[4] a) M. V. N. de Souza, T. R. A. Vasconcelos, *Appl. Organomet. Chem.* **2006**, 20, 798; b) E. R. Burkhardt, K. Matos, *Chem. Rev.* **2006**, 106, 2617.

[5] a) K. J. Haack, S. Hashiguchi, A. Fujii, T. Ikariya, R. Noyori, *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 285, b) H. Doucet, T. Ohkuma, K. Murata, T. Yokozawa, M. Kozawa, E. Katayama, A. F. England, T. Ikariya, R. Noyori, *Angew. Chem. Int. Ed*. **1998**, *37*, 1703.

[6] a) H. A. Younus, W. Su, N. Ahmad, S. Chen, F. Verpoort, *Adv. Synth. Catal.* **2015**, *357*, 283; b) C. Gunanathan, D. Milstein, *Chem. Rev.* **2014**, *114*, 12024; c) H. A. Younus, N. Ahmad, W. Su, F. Verpoort, *Coord. Chem. Rev.* **2014**, *276*, 112; d) S. Schneider, J. Meiners, B. Askevold, *Eur. J. Inorg. Chem.* **2012**, 412; e) J. M. Serrano-Becerra, D. Morales-Morales, *Curr. Org. Synth.* **2009**, *6*, 169; f) D. Benito-Garagorri, K. Kirchner, *Acc. Chem. Res.* **2008**, *41*, 201.

[7] a) K-N. T. Tseng, J. W. Kampf, N. K. Szymczak, *ACS Catalysis* **2015**, *5*, 5468; b) S. Muthaiah, S. H. Hong, *Adv. Synth. Catal.* **2012**, *354*, 3045; c) T. C. Johnson, D. J. Morris, M. Wills, *Chem. Soc. Rev.* **2010**, *39*, 81; d) G. E. Dobereiner, R. H. Crabtree, *Chem. Rev.* **2010**, *110*, 681; e) J. Zhang, M. Gandelman, L. J. W. Shimon, D. Milstein, *Dalton Trans.* **2007**, 107.

[8] a) N. T. Fairweather, M. S. Gibson, H. Guan, *Organometallics* **2015**, *34*, 335; b) S. Werkmeister, K. Junge, M. Beller, *Org. Process Res. Dev.* **2014**, *18*, 289; c) A. P. Dub, T. Ikarya, *ACS Catal.* **2012**, *2*, 1718; d) E. Balaraman, C. Gunanathan, J. Zhang L. J. W. Shimon, D. Milstein, *Nature Chem.* **2011**, *3*, 609; e) E. Fogler, E. Balaraman, Y. Ben-David, G. Leitus, L. J. W. Shimon, D. Milstein, *Organometallics* **2011**, *30*, 3826.

[9] a) J. Leonard, A. J. Blacker, S. P. Marsden, M. F. Jones, K. R. Mulholland, R. Newton, *Org. Process Res. Dev.* **2015**, *19*, 1400; b) D. Spasyuk, C. Vicent, D.G. Gusev, *J. Am. Chem. Soc.* **2015**, *137*, 3743; c) E. J. Derrah, M. Hanauer, P. N. Plessow, M. Schelwies, M. K. da Silva, T. Schaub, *Organometallics* **2015**, *34*, 1872; d) A. J. A. Watson, B. N. Atkinson, A. C. Maxwell, J. M. J. Williams, *Adv. Synth. Catal.* **2013**, *355*, 734; e) J. R. Zbieg, E. L. McInturff, M. J. Krische, *Org. Lett.* **2010**, *12*, 2514; f) A. Denichoux, T. Fukuyama, T. Doi, J. Horiguchi, I. Ryu, *Org. Lett.* **2010**, *12*, 1.

[10] a) G. Chelucci, S. Baldino, W. Baratta, *Coord. Chem. Rev.* **2015**, *300*, 29; b) G. Chelucci, S. Baldino, W. Baratta, *Acc. Chem. Res.* **2015**, *48*, 363.

[11] W. Baratta, E. Herdtweck, K. Siega, M. Toniutti, P. Rigo, *Organometallics* **2005**, *24*, 1660.

[12] E. Putignano, G. Bossi, P. Rigo, W. Baratta, *Organometallics* **2012**, *31*, 1133.

[13] a) W. Baratta, G. Chelucci, S. Gladiali, K. Siega, M. Toniutti, M. Zanette, E. Zangrando, P. Rigo, *Angew. Chem. Int. Ed.* **2005**, *44*, 6214; b) W. Baratta, S. Baldino, M. J. Calhorda, P. J. Costa, G. Esposito, E. Herdtweck, S. Magnolia, C. Mealli, A. Messaoudi, S. A. Mason, L. F. Veiros, *Chem. Eur. J.* **2014**, *20*, 13603.

[14] a) W. Baratta, G. Bossi, E. Putignano, P. Rigo, *Chem. Eur. J.*, **2011**, *17*, 3474; b) G. Bossi, E. Putignano, P. Rigo, W. Baratta, *Dalton Trans.* **2011**, *40*, 8986.

[15] J. Seyden-Penne, *Reductions by the Alumino- and Borohydrides in Organic Synthesis*, VCH, New York, 1991.

[16] S. Nishimura, *Handbook of Heterogeneous Catalytic Hydrogenation for Organic Synthesis*, Wiley-VCH: New York. 2001. 700 pp.. ISBN 0-471-39698-2.

[17] a) H. Chen, D. A. Cullen, J. Z. Larese, *J. Phys. Chem C* **2015** *119*, 28885; b) H. Liu, Z. Li, Y. Li, *Ind. Eng. Chem. Res* **2015**, *54*, 1487; c) L. J. Malobela, J. Heveling, W. G. Augustyn, L. M. Cele, *Ind. Eng. Chem. Res* **2014**, *53*, 13910; d) J. Hajek, N. Kumar, T Salmi, D. Yu. Murzin, H. Karhu , J. Vayrynen, L Cerveny, I. Paseka, *Ind. Eng. Chem. Res.* **2003**, *42*, 295; e) G. Neri, L. Bonaccorsi, L. Mercadante, S. Galvagno, *Ind. Eng. Chem. Res* **1997** *36* , 3554.

[18] a) M. L. Clarke, G. J. Roff, *Handbook of Homogeneous Hydrogenation*, Vol. 1 (Eds.: J. G. de Vries, C. J. Elsevier), Wiley-VCH, Weinheim, 2007, pp. 413; b) L. A. Saudan, *Acc. Chem. Res.* **2007**, *40*, 1309.

[19] a) J. R. Miecznikowski, R. H. Crabtree, *Organometallics* **2004**, *23*, 629; b) Y.-M. He, Q.-H. Fan, *ChemCatChem.* **2015**, *7*, 398; c) D. Talwar, X. Wu, O. Saidi, N. Poyatos Salguero, J. Xiao, *Chem. Eur. J.* **2014**, *20*, 12835; d) Y. Wei, D. Xue, Q. Lei, C. Wang, J. Xiao, *Green Chem.* **2013**, *15*, 629; e) M. V. Jiménez, J. Fernández-Tornos, J. J. Pérez-Torrente, F. J. Modrego, S. Winterle, C. Cunchillos, F. J. Lahoz, L. A. Oro, *Organometallics* **2011**, *30*, 5493; f) Y. Himeda, N. Onozawa-Komatsuzaki, S. Miyazawa, H. Sugihara, T. Hirose, K. Kasuga, *Chem. Eur. J.* **2008**, *14*, 11076; g) X. Wu, C. Corcoran, S. Yang, J. Xiao, *ChemSusChem*. **2008**, *1*, 71; h) X. Wu, J. Liu, X. Li, A. Zanotti-Gerosa, F. Hancock, D. Vinci, J. Ruan, J. Xiao, *Angew. Chem. Int. Ed.* **2006**, *45*, 6718; i) C. M. Beck, S. E. Rathmill, Y. J. Park, J. Chen, R. H. Crabtree, L. M. Liable-Sands, A. L. Rheingold, *Organometallics* **1999**, *18*, 5311.

[20] a) J. W. Faller, A. R. Lavoie, *Organometallics* **2002**, *21*, 3493; b) I. Yamada, R. Noyori, *Org. Lett.* **2000**, *2*, 3425.

[21] P. Kumar, A. K. Singh, S. Sharma, D. S. Pandey, *J. Organomet. Chem.* **2009**, *694*, 3643.

[22] H. Imai, T. Nishiguchi, K. Fukuzumi, *J. Org. Chem.* **1976**, *41*, 665.

[23] D. J. Darensbourg, F. Joo, M. Kannisto, A. Katho, J. H. Reibenspies, *Organometallics* **1992**, *11*, 1990.

[24] I. Szatmári, G. Papp, F. Joó, Á. Kathó, *Catal. Today* **2015**, *247*, 14.

[25] S. Sabata, J. Vcelak, J. Hetflejs, *Collect. Czech. Chem. Commun.* **1995**, *60*, 127.

[26] A. N. Kharat, A. Bakhoda, B. T. Jahromi, *Inorg. Chem. Commun.* **2011**, *14*, 1161.

[27] M. Zhao, Z. Yu, S. Yan, Y. Li, *Tetrahedron Lett*. **2009**, *50*, 4624.

[28] S. Naskar, M. Bhattacharjee, *J. Organomet. Chem.* **2005**, *690*, 5006.

[29] a) B. Deb, P. P. Sarmah, D. K. Dutta, *Eur. J. Inorg. Chem.* **2010**, 1710; b) B. Deb, B. J. Borah, B. J. Sarmah, B. Das, D. K. Dutta, *Inorg. Chem. Commun.* **2009**, *12*, 868; c) S. Bhaduri, K. Sharma, D. Mukesh, *J. Chem. Soc., Dalton Trans*, **1992**, 77; d) S. Bhaduri, K. Sharma, *J. Chem. Soc. Chem. Commun.* **1988**, 173.

[30] W. Baratta, K. Siega, P. Rigo, *Adv. Synth. Catal.* **2007**, 349, 1633.

[31] MPV reductions see: a) A. L. Wilds, *Org. React.* **1944**, *2*, 178; b) B. Verley, *Bull. Soc. Chim. Fr.* **1925**, *37*, 537; c) B. Verley, *Bull. Soc. Chim. Fr.* **1927**, *41*, 788; d) W. Pondorff, *Angew. Chem.* **1926**, *39*, 138. For reviews on MPV see: a) J. S. Cha, *Org. Process Res. Dev.* **2006**, *10*, 1032; b) C. R. Graves, E. J. Campbell, S. T. Nguyen, *Tetrahedron: Asymmetry* **2005**, *16*, 3460.

[32] a) C. P. Casey, H. Guan, *Organometallics* **2012**, *31*, 2631; b) C. P. Casey, S. E. Beetner, J. B. Johnson, *J. Am. Chem. Soc.* **2008**, *130*, 2285; c) Y. Blum, D. Czarkie, Y. Rahamin, Y. Shvo, *Organometallics* **1985**, *4*, 1459.

[33] A. B. Chaplin,P. J. Dyson, *Organometallics* **2007**, *26*, 4357.

[34] a) T. Miyada, E. H. Kwan, M. Yamashita, *Organometallics* **2014**, *33*, 6760; b) I. Warad, H. Al-Hussain, R. Al-Far, R. Mahfouz, B. Hammouti, T. Ben Hadda, *Spectrochim. Acta A* **2012**, *95*, 374; c) L. G. Melean, M. Rodriguez, A. González, B. González, M. Rosales, P. J. Baricelli, *Catal. Lett.* **2011**, *141*, 709; d) S. Jiménez, J. A. López, M. A. Ciriano, C. Tejel, A. Martínez, R. A. Sánchez-Delgado, *Organometallics* **2009**, *28*, 3193.

[35] K. E. Jolley, A. Zanotti-Gerosa, F. Hancock, A. Dyke, D. M. Grainger, J. A. Medlock, H. G. Nedden, J. J. M. Le Paih, S. J. Roseblade, A. Seger, V. Sivakumar, I. Prokes, D. J. Morris, M. Wills, *Adv. Synth. Catal.* **2012**, *354*, 2545.

[36] a) P. Dupau, L. Bonomo, L. Kermorvan, *Angew. Chem. Int. Ed.* **2013**, *125*, 11557; b) L. Bonomo, L. Kermorvan, P. Dupau, *ChemCatChem.* **2015**, *7*, 907.

[37] H. Adkins, R. M. Elofson, A. G. Rossow, C. C. Robinson, *J. Am. Chem. Soc.* **1949**, *71*, 3622.

[38] a) S. E. Clapham, A. Hadzovic, R. H. Morris, *Coord. Chem .Rev.* **2004**, *248*, 2201; b) P. Espinet, A. C. Albéniz, *Fundamentals of Molecular Catalysis, Current Methods in Inorganic Chemistry, Vol. 3* (Eds. H. Kurosawa, A. Yamamoto) Elsevier: Amsterdam, 2003, Chap. 6, p. 328; c) *Recent Advances in Hydride Chemistry* (Eds. M. Peruzzini, R. Poli) Elsevier: Amsterdam, 2001.

[39] a) A. M. P. Koskinen, A. O. Kataja, Organic Reactions, **2015**, DOI: 10.1002/0471264180.or086.02; b) T. Werner, J. Koch, *Eur. J. Org. Chem.* **2010**, 6904; c) K. Ekoue-Kovi, C. Wolf, *Chem. Eur. J.* **2008**, *14*, 6302; d) T. Seki, T. Nakajo, M. Onaka, *Chem.*

Lett. **2006**, *35*, 824; e) R. Mahrwald, *Curr. Org. Chem.* **2003**, *7*, 1713; f) O. L. Toermaenkangas, A. M. P. Koskinen, *Recent. Res. Devel. Org. Chem.* **2001**, *5*, 115; g) L. Claisen, *Chem. Ber.* **1887**, *20*, 646.

[40] T. A. Geissman, *Org. React.* **1944**, *2*, 94.

[41] a) S. P Curran, S. J. Connon, *Org. Lett.* **2012**, *14*, 1074; b) B. M. Day, N. E. Mansfield, M. P. Coles, P. B. Hitchcock, *Chem. Commun.* **2011**, *47*, 4995; c) L. Cronin, F. Manoni, C. J. O'Connor, S. J. Connon, *Angew. Chem. Int. Ed.* **2010**, *49*, 3045; d) T. Werner, J. Koch, *Eur. J. Org. Chem.* **2010**, 6904; e) M. R. Crimmin, A. G. M. Barrett, M. S. Hill, P. A. Procopiou, *Org. Lett.* **2007**, *9*, 331.

[42] a) S.-I. Murahashi, T. Naota, K. Ito, Y. Maeda, H. Taki, *J. Org. Chem*. **1987**, *52*, 4319; b) T. Ito, H. Horino, Y. Koshiro, A. Yamamoto, *Bull. Chem. Soc. Jpn.* **1982** , *55*, 504; c) H. Horino, T. Ito, A. Yamamoto, *Chem. Lett.* **1978**, 17.

[43] S. Omura, T. Fukuyama, Y. Murakami, H. Okamoto, I. Ryu, *Chem. Commun.* **2009**, 6741.

[44] A. Sorkau, K. Schwarzer, C. Wagner, E. Poetsch, D. Steinborn, *J. Mol. Catal. A* **2004**, *224*, 105.

[45] N. Menashe, Y. Shvo, *Organometallics* **1991**, *10*, 3885.

[46] M.-O. Simon, S. Darses, *Adv. Synth. Catal.* **2010**, *352*, 305.

[47] B. Liu, F. Hu, B-F Shi, *ACS Catalysis* **2015**, *5*, 1863. Osmium: a) P. Barrio, M. A. Esteruelas, E. Onate, *Organometallics* **2004**, *23*, 1340; iridium: b) C. Tejel, M. A. Ciriano, V. Passarelli, *Chem. Eur. J.* **2011**, *17*, 91; c) T. Suzuki, T;Yamada, T. Matsuo, K. Watanabe, T. Katoh, *Synlett* **2005**, 1450; d) T. Suzuki, T. Yamada, K. Watanabe, T. Katoh, *Bioorg. Med. Chem. Lett.* **2005**, 15, 2583; e) S. H. Bergens, D. P. Fairlie, B. Bosnich, *Organometallics* **1990**, *9*, 566; nickel: f) S. Ogoshi, Y. Hoshimoto, M. Ohashi, *Chem. Commun.* **2010**, *46*, 3354; g) Y. Hoshimoto,M. Ohashi, S. Ogoshi, *J. Am. Chem. Soc.* **2011**, *133*, 4668.

[48] M. B. Smith, J. March, *Advanced Organic Chemistry*, 5th ed.; New York: Wiley Interscience, 2001, p. 1218.

[49] a) P. D. Bolton, M. Grellier, N. Vautravers, L. Vendier, S. Sabo-Etienne, *Organometallics*, **2008**, *27*, 5088; b) W. Baratta, A. Del Zotto, G. Esposito, A. Sechi, M. Toniutti, E. Zangrando, P. Rigo, *Organometallics* **2004**, *23*, 6264; c) J. N. III Coalter, J. C. Huffman, K. G. Caulton, *Organometallics* **2000**, *19*, 3569.

[50] L. A. Saudan, C. M. Saudan, C. Debieux, P. Wyss, *Angew. Chem., Int. Ed.* **2007**, *46*, 7473.

[51] a) S. Facchetti, V. Jurcik, S. Baldino, S. Giboulot, H. G. Nedden, A. Zanotti-Gerosa, A. Blackaby, R. Bryan, A. Boogaard, D. B. McLaren, E. Moya, S. Reynolds, K. S. Sandham, P. Martinuzzi, W. Baratta, O*rganometallics*, **2016**, *35*, 277; b) W. Baratta, L. Fanfoni, S.

Magnolia, K. Siega, P. Rigo, *Eur. J. Inorg. Chem.* **2010**, 1419; c) W. Baratta, M. Ballico, S. Baldino, G. Chelucci, E. Herdtweck, K. Siega, S. Magnolia, P. Rigo, *Chem. Eur. J.* **2008**, *14*, 9148.

[52] The separation of acetone and 2-propanol is a key operation in industrial biocatalysis. See: J. Tao, G. Q. Lin, A. Liese, *Biocatalysis for the Pharmaceutical Industry: Discovery, Development, and Manufacturing,* Wiley **2009**, Chapter 4.

[53] a) C. F. de Graauw, J. A. Peters, H. Bekkum, J. Huskens, *Synthesis* **1994**, 1007; b) D. Wang, C. Deraedt, J. Ruiz, D. Astruc, *J. Mol. Cat. A* **2015**, *400*, 14.

[54] Compound **e** was prepared following the procedure for the synthesis of a *t*Bu ester (see Supporting Information): S. E. Bode, D. Drochner, M. Müller, *Angew. Chem. Int. Ed.* **2007**, *46*, 5916.

Graphical abstract

Transfer Hydrogenation and Hydrogenation of Commercial-Grade Aldehydes to Primary Alcohols Catalyzed by Ampy and Benzo[*h*]quinoline Pincer Ruthenium Complexes

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Ruthenium ampy and benzo[*h*]quinoline pincer complexes efficiently catalyze the reduction of commercial-grade aldehydes to alcohols via transfer hydrogenation with 2-propanol and hydrogenation with H_2 at S/C up to 100000.