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Transfer Hydrogenation of Ketones, Nitriles, and Esters Catalyzed by a Half-Sandwich Complex of Ruthenium

Sun-Hwa Lee and Georgii I. Nikonov*[a]

Half-sandwich complexes $[Cp(PiPr_3)Ru(CH_3CN)_2]PF_6$ (**1**; Cp = cyclopentadienyl) and $[Cp^*(phen)Ru(CH_3CN)]PF_6$ (**2**; Cp* = pentamethylcyclopentadienyl, phen = phenanthroline) catalyse the transfer hydrogenation of ketones to alcohols, aldimines to amines, and nitriles to imines under mild conditions. In the latter process, the imine products come from the coupling of the amines formed initially with acetone derived from the reducing solvent (isopropanol). Among functionally substituted nitriles, the aldo and keto groups are reduced concomitantly with the cyano group, whereas ester and amido groups are tolerated. Amides and alkyl esters are not reduced under these conditions even upon heating to 70 °C. However, phenylbenzoates and trifluoroacetates are reduced to alcohols. Kinetic studies on the reduction of acetophenone in isopropanol established that the reaction is first order in both the substrate and the alcohol. Stoichiometric mechanistic studies showed the formation of a hydride species. A hydride mechanism was proposed to account for these observations.

Introduction

Catalytic transfer hydrogenation (TH) is employed widely for the reduction of unsaturated organic molecules.[1] In this method, alcohols,[1,2] formates,[2,3] aminoboranes[4] and some reduced heterocycles[2,5,6] are used as the source of one or more equivalents of hydrogen that is transferred to the substrate usually with the assistance of a catalyst. TH avoids the high pressures usually required for catalytic hydrogenation but often requires elevated temperatures. The usual substrates for TH are ketones and, to a lesser extent, imines.[2,3a,7] Other substrates have been studied much less, and the highly efficient bifunctional Noyori/Ikariya systems are inactive towards such potentially sensitive functional groups as ester, sulfone, nitro, quinoline etc.[1a,e,8] Nevertheless, the TH of some challenging substrates has been reported. Thus, Elsevier et al. demonstrated the Pd-catalysed semi-hydrogenation of alkynes by HCO_2H/NEt_3.[3a] The reduction of nitro compounds to amines by formates and alcohols was reported by the groups of Beller, Williams, Sarkar and Gowda.[4,9,10] The TH of heteroaromatics has gained attention in the context of the preparation of biologically active molecules.[11] In contrast, nitriles are not typical substrates for TH and are actually often used as solvents for these reactions. Only a few and generally low-yielding examples of nitrile TH to primary amines are known,[4,10,12] with the notable exception of the report of Beller and co-workers on the $[Ru(p\text{-cymene})Cl_2]_2$/1,4-bis(diphenylphosphino)butane (DPPB) system that catalyses the reduction of aromatic and aliphatic nitriles by 2-butanol at 120 °C.[13] Beller and co-workers also found that if the catalyst is changed to $RuCl_2(PPh_3)_3$ the synthesis of secondary amines is allowed because of a concomitant reductive amination of acetone, derived from isopropanol, with the primary amine formed at the TH stage.[14] To the best of our knowledge, no example of the TH of esters to either alcohols or aldehydes has been reported to date.

Recently, we have shown the application of half-sandwich complexes of Ru for the chemoselective hydrosilylation of nitriles,[15] pyridines,[16] acid chlorides[17] and secondary amides[18] and we have provided some insights into the mechanism of these reactions.[16,19] Analysis of the current mechanistic proposals for TH suggested that our Ru systems can also be efficient catalysts for TH.[1] Therefore, we attempted to verify this hypothesis, and the results of our studies are reported here, which includes the coupling of nitriles with isopropanol to give imines and the first observation of the TH of esters to alcohols.

Results and Discussion

Initially, a series of half-sandwich complexes of Ru, $[Cp(PiPr_3)Ru(CH_3CN)_2]PF_6$ (**1**; Cp = cyclopentadienyl), $[Cp^*(phen)Ru(CH_3CN)]PF_6$ (**2**; Cp* = pentamethylcyclopentadienyl, phen = phenanthroline), $[Cp^*(PiPr_3)Ru(CH_3CN)]PF_6$ (**3**) and $Cp(PiPr_3)RuH_3$ (**4**), were screened as catalysts for the TH of various ketones and imines in isopropanol in the presence of a base (KO*t*Bu).[20] To our delight, catalytic activity was observed at room temperature, and the cationic complex **1** showed the best results. In the case of acetophenone, both good conversion and a high isolated yield (82%) of 1-phenylethanol were achieved in only 70 min (Table 1, entry 1). We found that ketones that bear both electron-donating and -withdrawing groups, such as methoxy, amino and chloro groups, can be reduced into the corresponding secondary alcohols with good to high yields (entries 2–4). Even a sterically hindered substrate, such as benzophenone,

[a] Dr. S.-H. Lee, Dr. G. I. Nikonov
Chemistry Department, Brock Univeristy
500 Glenridge Avenue, St. Catharines, ON L2S 3A1 (Canada)
E-mail: gnikonov@brocku.ca

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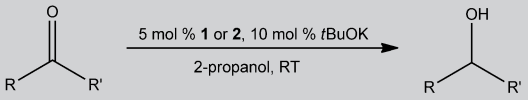
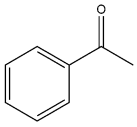
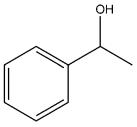
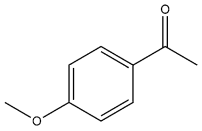
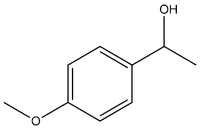
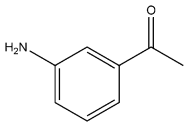
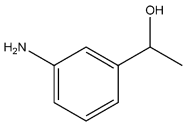
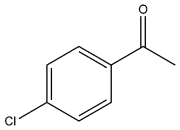
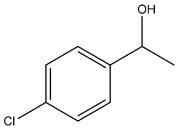
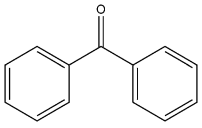
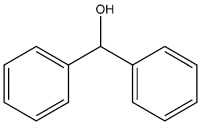
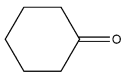
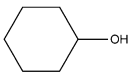
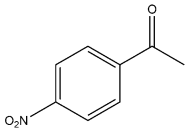
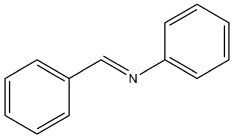
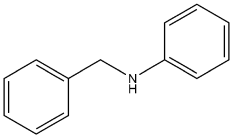
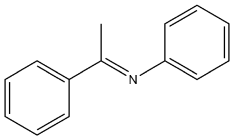
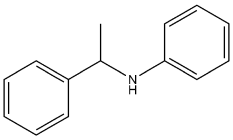
Table 1. Transfer hydrogenation of ketones and imines catalysed by **1** and **2**.[a]



Entry	Substrate	Product	**1** *t* [h], conversion [%]	**2** *t* [h], conversion [%]
1			70 min, 90 (82)[b]	4.5, 92
2			2, 75 (72)[b]	48, 75
3			3, 95 (67)[b]	29, 97
4			3.5, 98 (86)[b]	24, 97
5			100 min, 97 (60)[b]	7, 95
6			1, 99	4.5, 99
7		–	NR[c]	–
8			22, 88 (34)[b]	35 min, 99
9			24, 32	–

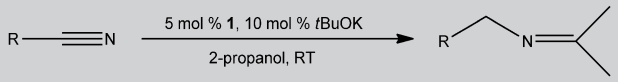
[a] 5 mol% Ru catalyst, 10 mol% *t*BuOK, 0.1 mmol substrate, isopropanol (0.5 mL), room temperature. [b] Isolated yield [%], 1 mmol substrate. [c] Fast decomposition of the catalyst. NR = No reaction.

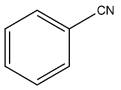
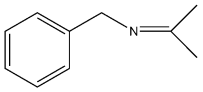
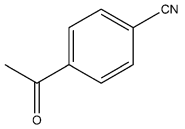
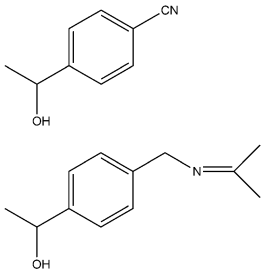
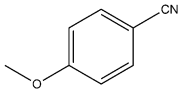
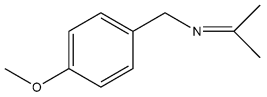
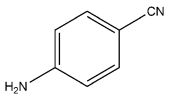
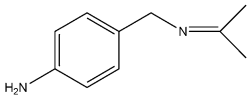
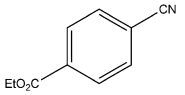
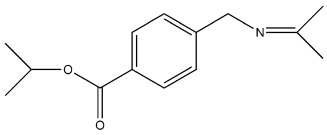
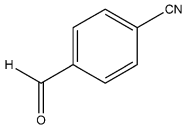
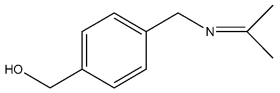
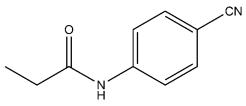
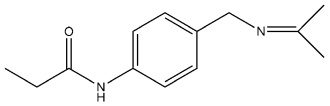
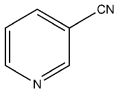
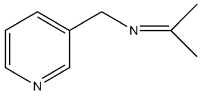
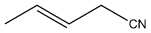
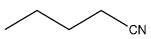
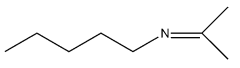
can be hydrogenated in a relatively short time (entry 5) as well as alkyl ketones (entry 6). However, the attempted reduction of an aryl ketone that bears the sensitive nitro group resulted in the rapid decomposition of the catalyst (entry 7). We also observed catalytic TH of an aldimine and a ketimine to secondary amines (entries 7 and 8), whereas attempts to react PhCH=NTs, PhCH=NC(O)Ph and *p*-$CH_3OC_6H_4C(CH_3)$=NPh failed to produce the desired amines. The latter example of an acetophenone-derived ketimine that has a strong donating group in the phenyl ring suggests that sufficient electrophilic activation of the imine group is required for the success of TH.

Given the previous success in the application of **1** for the chemoselective hydrosilylation of nitriles[15] and its activity in the TH of ketones, we were interested if this catalytic system could be applied to the reduction of nitriles. To our delight, NMR test reactions with benzonitrile showed that **1** catalyses the transformation of this substrate in isopropanol to *N*-phenyl *N*-isopropylidene effectively under very mild conditions (Table 2, entry 1). We believe that this product is obtained from the TH of nitrile to amine followed by in situ coupling with the alcohol-derived coproduct, acetone, to furnish the imine. In contrast, **2** was inactive in this reaction even at elevated temperatures (70 °C), whereas **3** and **4** showed comparable activity only upon heating to 70 °C. Our research was in progress when Beller and co-workers reported the first general protocols for the Ru-catalysed TH of nitriles to primary amines[13] and to alkylated secondary amines,[14] in which the latter products stem from a domino sequence of reduction, coupling with ketone and hydrogenation. However, both processes require a high temperature (120 °C).

We then examined the substrate scope of this new catalytic reaction. In all cases imine products derived from the coupling with acetone were observed in NMR tube reactions. Given the instability of imines, in preparative-scale reactions the products were hydrolysed and precipitated with dry HCl in the form of ammonium salts. Benzonitrile, which bears a *para*-acetyl substituent, initially showed a fast reduction of the keto group (30 min) and was reduced fully after 18 h (Table 2, entry 2). The reaction of electron-rich 4-methoxybenzonitrile also produced the desired imine in high yield after 18 h (entry 3), whereas the related TH of *para*-amino benzonitrile was achieved in only 3 h (entry 4). Similar to the previous observation by Beller et al.,[14] the ester group of ethyl 4-cyanobenzoate was not reduced but underwent transesterification with isopropanol, whereas the cyano moiety was transformed into the imino group (entry 5). If 4-cyanobenzaldehyde was used as the substrate, full conversion was achieved in 24 h. However, the reaction produced a mixture of several compounds, and the fully

Table 2. TH of nitriles to imines.[a]



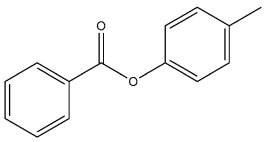
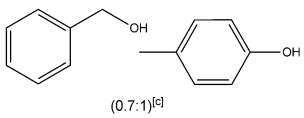
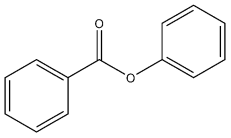
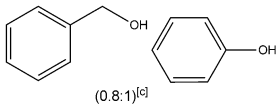
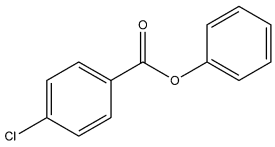
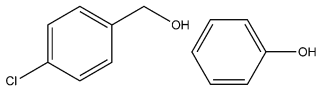
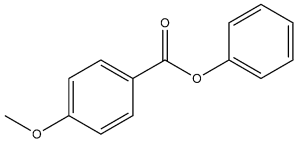
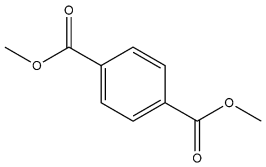
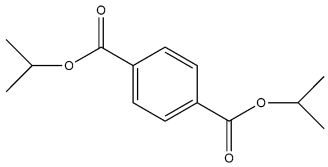
Entry	Substrate	Product	t [h]	Conversion [%]
1			5.5	99 (71)[b]
2			0.5 18	99 99 (63)[b]
3			18	99 (65)[b]
4			3	99 (91)[b]
5			18	99 (62)[b]
6			24	52
7			24	99 (91)[b]
8			72	93[c,d] (79)[b]
9		–	–	NR
10		–	–	NR[e]
11			48	99

[a] 5 mol% 1, 10 mol% *t*BuOK, 0.1 mmol substrate, isopropanol (0.5 mL), room temperature. [b] Isolated yields of ammonium salt after hydrolysis of imine. [c] 70 °C. [d] 85% in 2 d. [e] 86 °C.

reduced product was obtained in only 52% NMR yield (entry 6). Benzonitrile, which has an amide group, was reduced selectively under these conditions to the corresponding imine in high yield, which did not affect the amido functionality (entry 7). The reduction of nicotinonitrile was also achieved, although a much longer reaction time (three days) and higher temperature (70 °C) were required (entry 8). However, alkyl nitriles that bear a double bond, both conjugated (entry 9) and non-conjugated (entry 10), did not give the reduction products, presumably because the chelating 1,3-azobutadiene unit poisons the catalyst and because (*E*)-pent-3-enenitrile (entry 10) can isomerise into a conjugated system in the presence of a base. A similar problem has been noted previously in the hydrosilylation of conjugated unsaturated nitriles by **1**.[15] However, valeronitrile was reduced to amine, which then coupled with the acetone formed in situ to give the imine (entry 11). Further reduction to imine (cf. entries 8 and 9 in Table 1) does not occur because of catalyst decomposition.

The catalytic hydrogenation of esters is an area of active research.[21] Although hydrogen is the most attractive reducing agent from an economic point of view, most of the known catalysts for ester hydrogenation operate at high hydrogen pressure (up to 50 atm) and elevated temperatures (up to 100 °C), and therefore, require the use of special equipment. In this regard, TH offers certain advantages in terms of safety and operational simplicity. To the best of our knowledge, there have been no reports on the TH of esters by alcohols, and therefore, we became interested in the application of **1** in this reaction. Similar to the reduction of ethyl 4-cyanobenzoate (Table 2, entry 5), we subjected alkyl esters to catalytic TH conditions, which resulted only in transesterification even upon heating to 70 °C.[20] However, to our delight, the attempted TH of phenyl benzoates led to the reduction to benzyl alcohols (Table 3). The reduction of 4-methylphenyl benzoate was achieved at room temperature to give a mixture of benzyl alcohol and *p*-cresol as major products (Table 3, entry 1). The formation of *p*-cresol was monitored to show full conversion after three days. Interestingly, at this point the ratio of benzyl alcohol and *p*-cresol was 0.7:1 instead of the theoretical ratio of 1:1, which indicates that there must be (an)other, yet unaccounted for byproduct(s) of this reaction. Phenyl benzoate was converted into benzyl alcohol in a moderate yield (entry 2). In this case, the reaction takes place at 70 °C but stops after one day. Partial reduction of phenyl 4-chlorobenzoate was also achieved after one day, but no further conversion was observed after monitoring for three days (entry 3). However, a phenyl benzoate derivative that has an

Table 3. Reactions of esters with isopropanol mediated by **1**.[a]

Entry	Substrate	Product	*t* [h]	Yield [%][b]
1		 (0.7:1)[c]	24	48
2		 (0.8:1)[c]	24	45[d]
3		 (0.5:1)[c]	24	15[d]
4		–	72	NR[e]
5			20 min	100

[a] 5 mol% **1**, 10 mol% *t*BuOK, 0.1 mmol substrate, isopropanol (0.5 mL), room temperature. [b] NMR yield was calculated based on the formation of phenol derivatives. [c] The ratio of benzyl alcohol and phenol derivatives in isopropanol solution observed by ^{1}H NMR spectroscopy. [d] 70 °C. [e] 84 °C.

electron-donating methoxy group was not reduced even after an extended period of time and heating to 84 °C (entry 4).

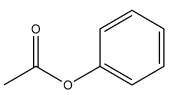
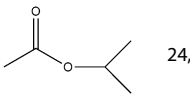
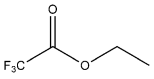
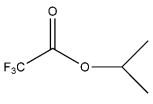
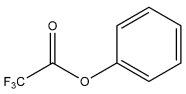
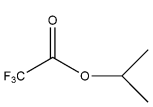
The realisation of the TH of phenyl benzoates but the lack of reduction for alkyl esters suggests that this catalytic process requires substrates that are activated electrophilically. We believe that the difference between the phenyl and alkyl esters can be then attributed to the difference in electronegativity between the sp^2- and sp^3-hybridised carbon atoms in the phenyl and alkyl esters, respectively, and/or to the mesomeric conjugation of the phenyl π system with the p orbital of the ester oxygen atom, which reduces the π donation from the ester oxygen atom to the carbonyl group and thus increases its electrophilicity.

To test this hypothesis, activated acetates were studied. In the case of phenyl acetate, a mixture of the transesterification and reduction products, isopropylacetate (67%) and ethanol (13%), respectively, was obtained after one day at room temperature (Table 4, entry 1). We then tried to enhance this mediocre activity by introducing electron-withdrawing groups in the alkyl chain. Indeed, both ethyl and phenyl trifluoroacetates showed significant reactivity. Under our catalytic conditions both substrates underwent rapid transesterification followed by the production of the reduction product, 2,2,2-trifluoroethanol (entries 2 and 3).

Cumulatively, these results indicate that: 1) TH is slower than transesterification and 2) the reduction is facilitated by the presence of accepting groups that enhance the electrophilicity of the substrate. Furthermore, our studies established that the reduction of inactive phenyl esters can take place only before the transesterification is complete. A strong electron-withdrawing group at the carbonyl centre, such as F_3C, can overcome the donating ability of an alkyl substituent at the ester oxygen atom (Table 4, entry 2). However, the reaction of dimethyl terephthalate (Table 3, entry 5) produced only the transesterification product, which suggests that the accepting effect of an ester group in the *para* position of a benzoate is not strong enough to compensate for the donating effect of an alkyl group at the oxygen atom. Overall, the success of ester reduction is the function of the electrophilicity at the carbonyl centre.

The observed reactivity of nitriles and ketones under mild conditions is very unusual, which suggests that a new mechanism may be involved. Previous studies on the catalytic reduction of nitriles and pyridines by silanes suggested the occurrence of an ionic hydrosilylation mechanism,[16,19] so we wondered if any analogy can be drawn with these previous studies. As our system does not have a cooperative or bifunctional ligand,[1f,22] we considered two possible reaction pathways. First, in the classical Meerwein–Ponn-

Table 4. TH of activated acetates.[a]

Entry	Substrate	Transesterification product	*t* [h], conversion [%]	Reduction product	*t* [h], conversion [%]
1			24, 67		24, 13
2			20 min, 100		24, 60
3			20 min, 100		24, 30

[a] 5 mol% **1**, 10 mol% *t*BuOK, 0.1 mmol substrate, isopropanol (0.5 mL), room temperature.

dorf–Verley reduction the hydride is transferred directly from a hydrogen donor to a hydrogen acceptor if both are attached to the same metal centre.[23] Second, the usual hydride mechanism implies the formation of a metal hydride species from alcohol, which then undergoes substrate insertion into the M–H bond.[24,25] To distinguish between these two possibilities, a stoichiometric reaction between **1**, base and isopropanol in a 1:1:1 ratio in $[D_5]$PhCl was studied at low temperature. A ruthenium hydride complex **5**, characterised by the hydride resonance at $\delta = -10.80$ (d, J(H–P) = 40.2 Hz) and presumably formed by a β-hydride elimination from an alkoxide intermediate, was observed by NMR spectroscopy at −15 °C, which thus lends some support to the hydride mechanism. The catalytic reduction of acetophenone was then studied by using the initial rate analysis. To this end, we performed the reactions under pseudo-first-order conditions (10- to 30-fold excess of alcohol relative to acetophenone) and monitored the disappearance of the Me resonance. Linearisation of the data in the plot of $-\ln([\text{ketone}]/[\text{ketone}]_0)$ versus time established the first-order dependence of the reaction rate on the substrate (Figure 1).

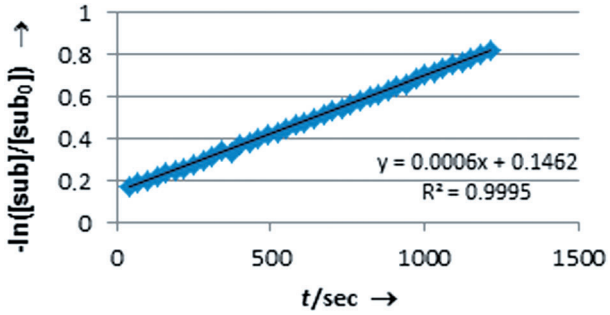
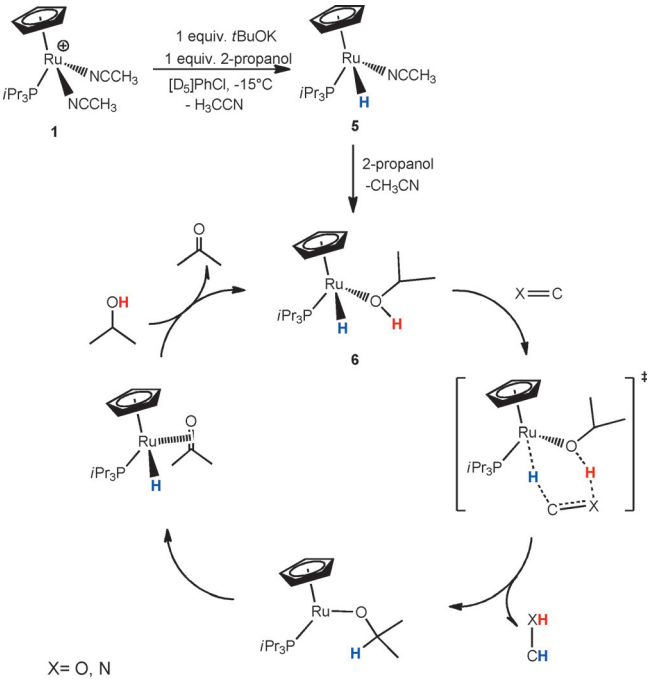


Figure 1. Kinetics of transfer hydrogenation of acetophenone in $[D_5]$PhCl at 22 °C in the presence of 25 equivalents of isopropanol.

A plot of the change of the effective rate constant k_{eff} against the amount of isopropanol used afforded a linear dependence, which indicates that the reaction is also first order in the alcohol.[20] Similarly, the amount of the Ru complex was varied from 4 to 7% with fixed amounts of the substrate and alcohol (in a 1:35 ratio), which resulted in a linear increase of the reaction rate, consistent with a catalytic reaction. Finally, the effect of acetonitrile was tested. The addition of 0.25–1 equivalents of $NCCH_3$ relative to **1** resulted in a decreased rate of reaction. The dependence of the effective rate constant on the nitrile concentration was then linearised in the plot of $1/k_{eff}$ versus $[NCCH_3]$, which suggests that nitrile dissociation is a step in the overall catalytic cycle. Altogether, these experiments result in the kinetic law rate = k[Ru][ketone][alcohol]/(constant+[nitrile]). However, this kinetic law does not allow us to underpin the exact sequence of mechanistic events, and in particular the order in which the alcohol and substrate add to the catalyst. Nevertheless, taken together with the outcome of the stoichiometric reactions and by analogy with the ionic mechanisms studied previously,[15,16] the reaction sequence shown in Scheme 1 can be suggested as a possible mechanistic scenario. This mechanistic proposal is consistent with the observed kinetics and, therefore, is a realistic working hypothesis.



Scheme 1. Proposed hydride mechanism of TH by the pre-catalyst **1**.

According to this mechanistic proposal, the hydride species **5** undergoes displacement of the second nitrile molecule by the isopropanol solvent to generate a reactive hydride **6**. The latter Ru^{II} complex features a combination of a hydridic Ru–H bond and an O–H bond acidified by alcohol coordination to the Lewis acidic metal. In analogy with Noyori-type bifunctional catalysis,[1f,22d] an unsaturated X=C bond can be reduced by a synchronised proton transfer from the OH to the hard X end (O or N), which thus activates the substrate electrophilically, followed by hydride transfer to the carbon atom. The ruthenium alkoxide intermediate thus produced then undergoes a β-hydride shift, which completes the cycle after the dissociation of acetone.

The difference in reactivity between nitriles and esters then comes from the different basicity of the X atom. For the more basic nitrile, activation by forming a H bond with the OH group is significant, whereas sufficient electrophilic activation within the substrate is required for the less basic ester.

Conclusion

Ru complexes **1** and **2** catalyse the transfer hydrogenation of ketones, aldimines and nitriles under mild conditions. Aldehydes and ketones are more reactive than nitriles and are reduced first, whereas amides and alkyl esters are not hydrogenated even upon heating to 70 °C. However, more electrophilic phenyl benzoates and trifluoroacetates can be partially reduced to alcohols. Although the efficiency of this reaction is low, it is the first example of such a reductive transformation and serves as a proof of principle for further research in this

area. Mechanistic studies with acetophenone in isopropanol showed that the reaction is first order in both the substrate and the alcohol, whereas low-temperature NMR spectroscopy showed the formation of ruthenium hydride species, which suggests that a usual hydride mechanism can operate in these reactions.

Experimental Section

All manipulations were performed using conventional high-vacuum or nitrogen-line Schlenk techniques. Solvents were predried by using Grubbs-type purification columns and stored in ampoules equipped with a Teflon valve. Deuterated solvents were dried over sodium, potassium or CaH_2 as appropriate, distilled under reduced pressure and stored in ampoules with a Teflon valve. NMR samples were prepared in New Era tubes equipped with J. Young-type Teflon valves. NMR spectra were recorded by using Bruker DPX-300 (^{1}H, 300 MHz; ^{13}C, 75.4 MHz) and/or Bruker DPX-600 (^{1}H, 600 MHz; ^{13}C, 150.8 MHz) spectrometers at 298 K. ^{1}H and ^{13}C NMR spectra were referenced internally to residual protio-solvent (^{1}H) or solvent (^{13}C) resonances and are reported relative to tetramethylsilane ($\delta = 0$ ppm). Chemical shifts are quoted in δ [ppm], and coupling constants in Hertz. IR spectra were recorded by using a PerkinElmer 1600 FTIR spectrometer as Nujol mulls between NaCl windows. All chemicals were purchased from Sigma–Aldrich and Alfa Aesar and were used without further purification. $CDCl_3$, C_6D_6 and C_6D_5Cl were purchased from Cambridge Isotope Laboratories. These NMR solvents were dried over CaH_2 before use. 2-Propanol was dried over molecular sieves (4 Å) overnight and used without further purification. CH_3CN, Et_2O and hexane were dried by using a Grubbs-type solvent purification system supplied by Innovative Technology. Complexes **1**, **2**, **3** and **4** were prepared according to literature procedures.[16b,26–28]

General procedure for the reduction of ketones to alcohols

In a representative procedure, **1** (2.5 mol%) was added to a solution of $PhCOCH_3$ (120.2 μL, 1.0 mmol) and *t*BuOK (11.2 mg, 0.1 mmol) in isopropanol (4 mL). The progress of the reaction was monitored by NMR spectroscopy at RT. The alcohol $PhCH(OH)CH_3$ was obtained as the product. After the reaction was completed, H_2O was added to the reaction flask to deactivate the catalyst. Then the precipitate was removed by filtration, and the filtrate was dried under vacuum to give a brown oil. $PhCH(OH)CH_3$ was isolated by chromatography over silica using 3:1 hexane/ethyl acetate as the eluent to afford the product as a yellow oil (0.100 g, 82% yield). ^{1}H NMR ($CH_3CH(OH)CH_3$, $CDCl_3$): $\delta = 7.62$ (d, J(H–H) = 7.37 Hz, 2, Ph), 7.52 (t, J(H–H) = 7.37 Hz, 2, Ph), 7.43 (t, J(H–H) = 7.37 Hz, 1, Ph), 5.09 (q, 1, C*H*), 1.72 ppm (d, J(H–H) = 6.37 Hz, 3, CH_3); ^{1}H–^{13}C HSQC ($CH_3CH(OH)CH_3$, $CDCl_3$): $\delta = 128.1$ (s, *Ph*), 126.7 (s, *Ph*), 125.4 (s, *Ph*), 69.1 (s, $PhCH(OH)CH_3$), 25.1 ppm (s, $PhCH(OH)CH_3$).

General procedure for the reduction of imines to amines

In a representative procedure, **1** (2.5 mol%) was added to a solution of PhCH=NPh (183.3 mg, 1.0 mmol) and *t*BuOK (11.2 mg, 0.1 mmol) in isopropanol (4 mL). The progress of the reaction was monitored by NMR spectroscopy at RT. The amine $PhCH_2NHPh$ was obtained as a product. After the reaction was completed, the mixture was concentrated. Initially, a mixture of compounds $PhCH_2NHPh$ (93%) and benzaldehyde (7%) was isolated by chromatography over silica using 15:1 hexane/ethyl acetate (1% Et_3N) as the eluent. Benzaldehyde was removed under vacuum to afford the product $PhCH_2NHPh$ as a yellow oil (0.062 g, 34% yield). ^{1}H NMR ($CH_3CH(OH)CH_3$, $CDCl_3$): $\delta = 7.62$ (d, J(H–H) = 7.46 Hz, 2, *Ph*), 7.52 (t, J(H–H) = 7.90 Hz, 2, *Ph*), 7.43 (t, J(H–H) = 7.46 Hz, 1, *Ph*), 7.29 (t, J(H–H) = 7.46 Hz, 2, *Ph*), 6.91 (d, J(H–H) = 7.46 Hz, 2, *Ph*), 6.84 (d, J(H-H) = 7.46 Hz, 2, *Ph*), 4.58 ppm (d, J(H–H) = 5.82 Hz, 2, CH_2); ^{1}H–^{13}C HSQC ($CDCl_3$): $\delta = 129.5$ (s, *Ph*), 128.4 (s, *Ph*), 128.2 (s, *Ph*), 127.7 (s, *Ph*), 117.4 (s, *Ph*), 113.0 (s, *Ph*), 48.2 ppm ($PhCH_2$).

General procedure for the reduction of nitriles to imines

In a representative procedure, **1** (2.5 mol%) was added to a solution of PhCN (82.5 μL, 0.8 mmol) and *t*BuOK (4.48 mg, 0.04 mmol) in isopropanol (4 mL). The progress of the reaction was monitored by NMR spectroscopy at RT. The imine $PhCH_2N{=}C(CH_3)_2$ was obtained as the major product. ^{1}H NMR ($CH_3CH(OH)CH_3$): $\delta = 7.51$ (m, 5, Ph), 4.80 (s, 2, CH_2), 2.42 (s, 3, CH_3), 2.27 ppm (s, 3, CH_3); ^{1}H NMR (C_6D_6): $\delta = 7.57$ (d, J(H–H) = 6.89 Hz, 2, *Ph*), 7.35 (t, J(H–H) = 7.16 Hz, 2, *Ph*), 7.24 (t, J(H–H) = 7.42 Hz, 1, *Ph*), 4.41 (s, 2, $PhCH_2N$), 1.97 (s, 3, $NC(CH_3)_2$), 1.44 ppm (s, 3, $NC(CH_3)_2$); ^{1}H–^{13}C HSQC (C_6D_6): $\delta = 166.0$ (s, $NC(CH_3)_2$), 141.1 (s, *Ph*), 128.3 (s, *Ph*), 127.9 (s, *Ph*), 126.2 (s, *Ph*), 55.1 (s, $PhCH_2$), 28.7 (s, $NC(CH_3)_2$), 17.6 ppm (s, $NC(CH_3)_2$); IR (neat): υ (C=N) = 1666 cm^{-1}.

HCl (1 M, 1.8 mL) was added to a solution of $PhCH_2N{=}C(CH_3)_2$ and **1** in isopropanol. The mixture was stirred for 1 h after which the imine was hydrolysed. After the removal of volatiles under vacuum, a light pink solid was obtained. The solid was washed with hexane and dried. The ammonium salt $[PhCH_2NH_3]Cl$ was obtained as a pale yellow solid (0.081 g, 71% yield). ^{1}H NMR (D_2O): $\delta = 7.39$ (m, 5, *Ph*), 4.10 ppm (s, 2, $PhCH_2$); ^{1}H–^{13}C HSQC (D_2O): $\delta = 129.4$ (s, *Ph*), 43.3 ppm (s, $PhCH_2$); IR (neat): $\tilde{\nu} = 3391$ cm^{-1} (NH_3).

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Keywords: cyclopentadienyl ligands · hydrogenation · ketones · reaction mechanisms · ruthenium

[1] a) R. Noyori, S. Hashiguchi, *Acc. Chem. Res.* **1997**, *30*, 97–102; b) S. E. Clapham, A. Hadzovic, R. H. Morris, *Coord. Chem. Rev.* **2004**, *248*, 2201–2237; c) K.-H. Fujita, R. Yamaguchi, *Synlett* **2005**, *4*, 560–571; d) J. S. M. Samec, J. E. Bäckvall, P. G. Anderson, P. Brandt, *Chem. Soc. Rev.* **2006**, *35*, 237–248; e) S. Gladiali, E. Alberico, *Chem. Soc. Rev.* **2006**, *35*, 226–236; f) T. Ikariya, J. Blacker, *Acc. Chem. Res.* **2007**, *40*, 1300–1308; g) W. Baratta, P. Rigo, *Eur. J. Inorg. Chem.* **2008**, 4041–4053; h) R. H. Morris, *Chem. Soc. Rev.* **2009**, *38*, 2282–2291; i) R. Malacea, R. Poli, E. Manoury, *Coord. Chem. Rev.* **2010**, *254*, 729–752; j) P. E. Sues, K. Z. Demmans, R. H. Morris, *Dalton Trans.* **2014**, *43*, 7650–7667.

[2] S. Fukuzumi, T. Suenobu, *Dalton Trans.* **2013**, *42*, 18–28.

[3] For selected examples, see: a) P. Hauwert, R. Boerleider, S. Warsink, J. J. Weigand, C. J. Elsevier, *J. Am. Chem. Soc.* **2010**, *132*, 16900–16910; b) S. Wu, X. Li, A. Zanotti-Gerosa, A. Pettman, J. Liu, A. J. Mills, J. Xiao, *Chem. Eur. J.* **2008**, *14*, 2209–2222; c) J. Canivet, L. Karmazin-Brelot, G. Süss-Fink, *J. Organomet. Chem.* **2005**, *690*, 3202–3211.

[4] For example, see: T. D. Nixon, M. K. Whittlesey, J. M. J. Williams, *Tetrahedron Lett.* **2011**, *52*, 6652–6654.

[5] For an example of TH from benzothiazoline, see: Y. Shibata, M. Yamanaka, *J. Org. Chem.* **2013**, *78*, 3731–3736.

[6] For selected reviews and further examples of reductions by Hantzsch esters, see: a) S. G. Ouellet, A. M. Walji, D. W. C. MacMillan, *Acc. Chem. Res.* **2007**, *40*, 1327–1339; b) T. Marcelli in *Enantioselective Organocata-*

lyzed Reactions I: Enantioselective Oxidation, Reduction, Functionalization and Desymmetrization, ch. 2 (Ed.: R. Mahrwald), Springer, Berlin, **2011**; c) X. F. Cai, M. W. Chen, Z. S. Ye, R. N. Guo, L. Shi, Y. Q. Li, Y. G. Zhou, *Chem. Asian J.* **2013**, *8*, 1381 – 1385.

[7] For selected examples, see: a) S. Kuhl, R. Schneider, Y. Fort, *Organometallics* **2003**, *22*, 4184 – 4186; b) T. Privalov, J. S. M. Samec, J. E. Bäckvall, *Organometallics* **2007**, *26*, 2840 – 2848; c) S. Zhou, S. Fleischer, K. Junge, S. Das, D. Addis, M. Beller, *Angew. Chem. Int. Ed.* **2010**, *49*, 8121 – 8125; *Angew. Chem.* **2010**, *122*, 8298 – 8302.

[8] T. Zweifel, J. V. Naubron, T. Büttner, T. Ott, H. Grützmacher, *Angew. Chem. Int. Ed.* **2008**, *47*, 3245 – 3249; *Angew. Chem.* **2008**, *120*, 3289 – 3293.

[9] a) R. V. Jagadeesh, G. Wienhöfer, F. A. Westerhaus, A. E. Surkus, H. Junge, K. Junge, M. Beller, *Chem. Eur. J.* **2011**, *17*, 14375 – 14379; b) G. Wienhöfer, I. Sorribes, A. Boddien, F. Westerhaus, K. Junge, H. Junge, R. Llusar, M. Beller, *J. Am. Chem. Soc.* **2011**, *133*, 12875 – 12879; c) S. Hohloch, L. Suntrup, B. Sarkar, *Organometallics* **2013**, *32*, 7376 – 7385.

[10] S. Gowda, D. C. Gowda, *Tetrahedron* **2002**, *58*, 2211 – 2213.

[11] For example: a) J. Wu, W. Tang, A. Pettman, J. Xiao, *Adv. Synth. Catal.* **2013**, *355*, 35 – 40; b) M. Rueping, A. P. Antonchick, *Angew. Chem. Int. Ed.* **2007**, *46*, 4562 – 4565; *Angew. Chem.* **2007**, *119*, 4646 – 4649; c) X. F. Tu, L. Z. Gong, *Angew. Chem. Int. Ed.* **2012**, *51*, 11346 – 11349; *Angew. Chem.* **2012**, *124*, 11508 – 11511; d) M. Rueping, A. P. Antonchick, T. Theissmann, *Angew. Chem.* **2006**, *118*, 3765 – 3768; *Angew. Chem. Int. Ed.* **2006**, *45*, 3683 – 3686; e) M. Rueping, F. Tato, F. R. Schoepke, *Chem. Eur. J.* **2010**, *16*, 2688 – 2691; f) Q. S. Guo, D. M. Du, J. Xu, *Angew. Chem. Int. Ed.* **2008**, *47*, 759 – 762; *Angew. Chem.* **2008**, *120*, 771 – 774; g) C. Wang, C. Li, X. Wu, A. Pettman, J. Xiao, *Angew. Chem. Int. Ed.* **2009**, *48*, 6524 – 6528; *Angew. Chem.* **2009**, *121*, 6646 – 6650; h) A. Ferry, J. Stemper, A. Marinetti, A. Voituriez, X. Guinchard, *Eur. J. Org. Chem.* **2014**, 188 – 193; i) K. Fujita, C. Kitatsuji, S. Furukawa, R. Yamaguchi, *Tetrahedron Lett.* **2004**, *45*, 3215 – 3217.

[12] a) G. R. Brown, A. J. Foubister, *Synthesis* **1982**, 1036 – 1037; b) S. Horn, C. Gandolfi, M. Albrecht, *Eur. J. Inorg. Chem.* **2011**, 2863 – 2868; c) E. Mizushima, M. Yamaguchi, T. Yamagishi, *J. Mol. Catal. A* **1999**, *148*, 69 – 75; d) R. C. Mebane, D. R. Jensen, K. R. Rickerd, B. H. Gross, *Synth. Commun.* **2003**, *33*, 3373 – 3379.

[13] S. Werkmeister, C. Bornschein, K. Junge, M. Beller, *Chem. Eur. J.* **2013**, *19*, 4437 – 4440.

[14] a) S. Werkmeister, C. Bornschein, K. Junge, M. Beller, *Eur. J. Org. Chem.* **2013**, 3671 – 3674; b) Beller and co-workers also reported TH from HCO_2H/NEt_3 catalysed by Pd/C: M. Vilches-Herrera, S. Werkmeister, K. Junge, A. Börner, M. Beller, *Catal. Sci. Technol.* **2014**, *4*, 629.

[15] D. V. Gutsulyak, G. I. Nikonov, *Angew. Chem. Int. Ed.* **2010**, *49*, 7553 – 7556; *Angew. Chem.* **2010**, *122*, 7715 – 7718.

[16] a) D. V. Gutsulyak, G. I. Nikonov, *Angew. Chem. Int. Ed.* **2011**, *50*, 1384 – 1387; *Angew. Chem.* **2011**, *123*, 1420 – 1423; b) S. H. Lee, D. V. Gutsulyak, G. I. Nikonov, *Organometallics* **2013**, *32*, 4457 – 4464.

[17] D. V. Gutsulyak, G. I. Nikonov, *Adv. Synth. Catal.* **2012**, *354*, 607 – 611.

[18] S. H. Lee, G. I. Nikonov, *Dalton Trans.* **2014**, *43*, 8888 – 8893.

[19] D. V. Gutsulyak, S. F. Vyboishchikov, G. I. Nikonov, *J. Am. Chem. Soc.* **2010**, *132*, 5950 – 5951.

[20] For details see the Supporting Information.

[21] a) H. T. Teunissen, C. J. Elsevier, *Chem. Commun.* **1997**, 667 – 668; b) H. T. Teunissen, C. J. Elsevier, *Chem. Commun.* **1998**, 1367 – 1368; c) K. Nomura, H. Ogura, Y. Imanishi, *J. Mol. Catal. A* **2002**, *178*, 105 – 114; d) M. C. van Engelen, H. T. Teunissen, J. G. de Vries, C. J. Elsevier, *J. Mol. Catal. A* **2003**, *206*, 185 – 192; e) J. Zhang, G. Leitus, Y. Ben-David, D. Milstein, *Angew. Chem. Int. Ed.* **2006**, *45*, 1113 – 1115; *Angew. Chem.* **2006**, *118*, 1131 – 1133; f) L. A. Saudan, C. M. Saudan, C. Debieux, P. Wyss, *Angew. Chem. Int. Ed.* **2007**, *46*, 7473 – 7476; *Angew. Chem.* **2007**, *119*, 7617 – 7620; g) M. L. Clarke, M. B. Díaz-Valenzuela, A. M. Z. Slawin, *Organometallics* **2007**, *26*, 16 – 19; h) W. W. N. O, A. J. Lough, R. H. Morris, *Chem. Commun.* **2010**, *46*, 8240 – 8242; i) W. Kuriyama, Y. Ino, O. Ogata, N. Sayo, T. Saito, *Adv. Synth. Catal.* **2010**, *352*, 92 – 96; j) Y. Ino, W. Kuriyama, O. Ogata, T. Matsumoto, *Top. Catal.* **2010**, *53*, 1019 – 1024; k) M. Ito, T. Ootsuka, R. Watari, A. Shiibashi, A. Himizu, T. Ikariya, *J. Am. Chem. Soc.* **2011**, *133*, 4240 – 4242; l) Y. N. Sun, C. Koehler, R. Tan, V. T. Annibale, D. Song, *Chem. Commun.* **2011**, *47*, 8349 – 8351; m) M. J. Hanton, S. Tin, B. J. Boardman, P. Miller, *J. Mol. Catal. A* **2011**, *346*, 70 – 78; n) F. Stempfle, D. Quinzler, I. Heckler, S. Mecking, *Macromolecules* **2011**, *44*, 4159 – 4166; o) E. Fogler, E. Balaraman, Y. Ben-David, G. Leitus, L. J. W. Shimon, D. Milstein, *Organometallics* **2011**, *30*, 3826 – 3833; p) J. Zhang, E. Balaraman, G. Leitus, D. Milstein, *Organometallics* **2011**, *30*, 5716 – 5724; q) D. Spasyuk, S. Smith, D. G. Gusev, *Angew. Chem. Int. Ed.* **2012**, *51*, 2772 – 2775; *Angew. Chem.* **2012**, *124*, 2826 – 2829; r) M. L. Clarke, *Catal. Sci. Technol.* **2012**, *2*, 2418 – 2423; s) K. Junge, B. Wendt, F. A. Westerhaus, A. Spannenberg, H. Jiao, M. Beller, *Chem. Eur. J.* **2012**, *18*, 9011 – 9018; t) I. Carpenter, S. C. Eckelmann, M. T. Kuntz, J. A. Fuentes, M. B. France, M. L. Clarke, *Dalton Trans.* **2012**, *41*, 10136 – 10140; u) A. Acosta-Ramirez, M. Bertoli, D. G. Gusev, M. Schlaf, *Green Chem.* **2012**, *14*, 1178 – 1188; v) W. Kuriyama, T. Matsumoto, O. Ogata, Y. Ino, K. Aoki, S. Tanaka, K. Ishida, T. Kobayashi, N. Sayo, T. Saito, *Org. Process Res. Dev.* **2012**, *16*, 166 – 171; w) D. Lazzari, M. C. Cassani, M. Bertola, F. C. Moreno, D. Torrente, *RSC Adv.* **2013**, *3*, 15582 – 15584; x) T. Zell, Y. Ben-David, D. Milstein, *Angew. Chem. Int. Ed.* **2014**, *53*, 4685 – 4689; *Angew. Chem.* **2014**, *126*, 4773 – 4777; y) W. W. N. O, R. H. Morris, *ACS Catal.* **2013**, *3*, 32 – 40; z) S. Chakraborty, H. Dai, P. Bhattacharya, N. T. Fairweather, M. S. Gibson, J. A. Krause, H. Guan, *J. Am. Chem. Soc.* **2014**, *136*, 7869 – 7872.

[22] a) C. Gunanathan, D. Milstein, *Acc. Chem. Res.* **2011**, *44*, 588; b) H. Grützmacher, *Angew. Chem. Int. Ed.* **2008**, *47*, 1814 – 1818; *Angew. Chem.* **2008**, *120*, 1838 – 1842; c) R. Noyori, T. Ohkuma, *Angew. Chem. Int. Ed.* **2001**, *40*, 40 – 73; *Angew. Chem.* **2001**, *113*, 40 – 75.

[23] a) H. Meerwein, R. Schmidt, *Justus Liebigs Ann. Chem.* **1925**, *444*, 221 – 238; b) W. Ponndorf, *Angew. Chem.* **1926**, *39*, 138 – 143; c) A. Verley, *Bull. Soc. Chim. Fr.* **1925**, *37*, 871 – 874; d) J. S. Cha, *Org. Process Res. Dev.* **2006**, *10*, 1032 – 1053.

[24] a) S. Chakraborty, H. Guan, *Dalton Trans.* **2010**, *39*, 7427 – 7436; b) J. E. Bäckvall, *J. Organomet. Chem.* **2002**, *652*, 105 – 111.

[25] The involvement of ruthenium hydrides in TH by alcohols and deoxygenation of alcohols is well documented, see Refs. [1d,1g] and: P. Ghosh, P. J. Fagan, W. J. Marshall, E. Hauptman, R. M. Bullock, *Inorg. Chem.* **2009**, *48*, 6490 – 6500.

[26] A. L. Osipov, D. V. Gutsulyak, L. G. Kuzmina, J. A. K. Howard, D. A. Lemenovskii, G. Süss-Fink, G. I. Nikonov, *J. Organomet. Chem.* **2007**, *692*, 5081 – 5085.

[27] a) B. Steinmetz, A. W. Schenk, *Organometallics* **1999**, *18*, 943 – 946; b) B. M. Trost, C. M. Older, *Organometallics* **2002**, *21*, 2544 – 2546.

[28] A. L. Osipov, S. F. Vyboishchikov, K. Y. Dorogov, L. G. Kuzmina, J. A. K. Howard, D. A. Lemenovskii, G. I. Nikonov, *Chem. Commun.* **2005**, 3349 – 3351.

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*S.-H. Lee, G. I. Nikonov**

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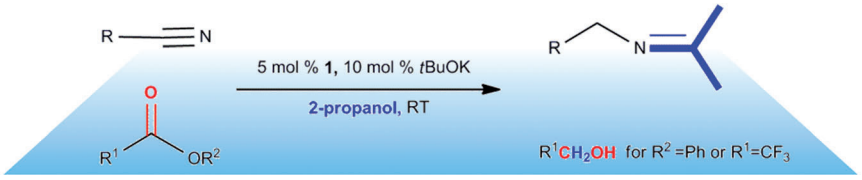
Transfer Hydrogenation of Ketones, Nitriles, and Esters Catalyzed by a Half-Sandwich Complex of Ruthenium



Scope out the scope: Half-sandwich complexes of Ru catalyze the transfer hydrogenation of ketones to alcohols, aldimines to amines, and nitriles to imines under mild conditions. In the latter process, the imine products come from coupling of the amines formed initially with acetone derived from the reducing solvent (isopropanol).