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Transfer Hydrogenation of Nitriles, Olefins, and *N*-Heterocycles Catalyzed by an *N*-Heterocyclic Carbene-Supported Half-Sandwich Complex of Ruthenium

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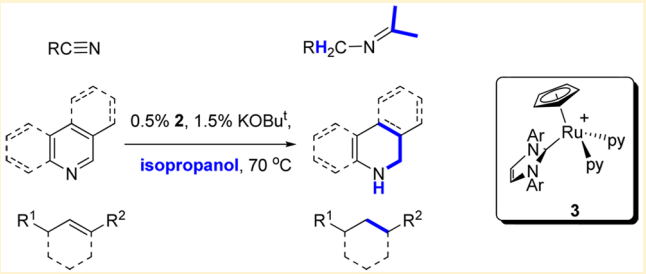
Supporting Information

ABSTRACT: In the presence of $KOBu^t$, *N*-heterocyclic carbene-supported half-sandwich complex $[Cp(IPr)Ru(pyr)_2][PF_6]$ (**3**) (IPr = 1,3-bis(2,6-diisopropylphenyl)imidazol-2-ylidene) catalyzes transfer hydrogenation (TH) of nitriles, activated *N*-heterocycles, olefins, and conjugated olefins in isopropanol at the catalyst loading of 0.5%. The TH of nitriles leads to imines, produced as a result of coupling of the initially formed amines with acetone (produced from isopropanol), and showed good chemoselectivity. Reduction of *N*-heterocycles occurs for activated polycyclic substrates (e.g., quinoline) and takes place exclusively in the heterocycle. The TH also works well for linear and cyclic olefins but fails for trisubstituted substrates. However, the C═C bond of *α*,*β*-unsaturated esters, amides, and acids is easily reduced even for trisubstituted species, such as isovaleriates. Mechanistic studies suggest that the active species in these catalytic reactions is the trihydride $Cp(IPr)RuH_3$ (**5**), which can catalyze these reactions in the absence of any base. Kinetic studies are consistent with a classical inner sphere hydride-based mechanism of TH.



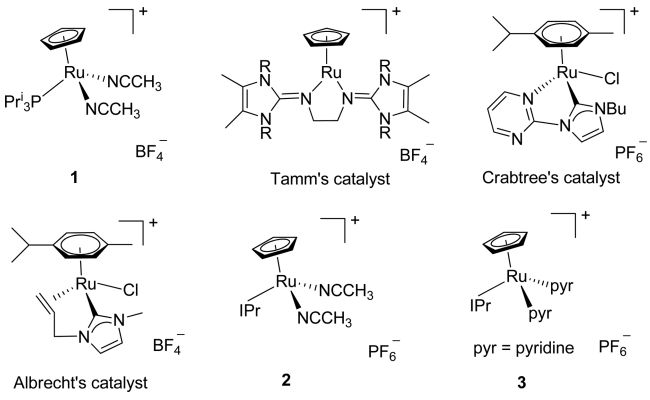
INTRODUCTION

Transfer hydrogenation (TH) from alcohols and formates has emerged as a powerful method for the conversion of unsaturated organic molecules into value added products.[1] TH offers certain advantages over other reduction methods due to the easy operational setup, low toxicity of reactants and byproducts (e.g., acetone for isopropanol and CO_2 for formates), and much reduced flammability in comparison with pressurized hydrogen or main-group metal hydrides. The asymmetric versions as well as the application of base metal catalysts have recently become available.[1a,j,k]

The prevailing substrates for catalytic TH are ketones and imines, whereas applications to other unsaturated systems are much less known. The TH of olefins is scarce[2−4] and, with a few exceptions,[3] is limited to activated substrates.[5] Unlike catalytic hydrogenation, the TH of heterocycles is much less developed and usually involves hydrogen transfer from dearomatized heterocycles, such as Hantzsch esters, which is very waste intensive.[6] The TH of nitrogen heterocycles by more benign reductants, such as alcohols[7] or formates,[8] is little studied but offers great potential for mild synthesis of biologically active molecules, such as tetrahydroquinolines.[9] The TH of nitriles has been known since 1982, but the yields and/or substrate scope were rather limited.[2i,10] In 2013, the Beller group disclosed the reduction of aromatic and aliphatic nitriles to amines by 2-butanol at 120 °C catalyzed by $[Ru(p\text{-cymene})Cl_2]_2$/DPPB (DPPB = 1,4-bis(diphenylphosphino)-butane).[11] The same workers showed that the related catalyst $RuCl_2(PPh_3)_3$ catalyzes tandem TH/alkylation of nitriles to secondary amines by isopropanol (IPA) at 120 °C.[12] Both these Ru-catalyzed processes require elevated temperatures and the catalyst load of 1−2%.[13]

We have recently reported that the half-sandwich complex $[Cp(^iPr_3P)Ru(NCCH_3)_2][BF_4]$ (**1**, Chart 1) catalyzes chemoselective reduction of nitriles and heterocycles by using silanes as reducing reagents.[14] More recently we found that the same complex **1** catalyzes room temperature reduction of nitriles by a

Chart 1. Structures of Half-Sandwich Complexes of Ruthenium



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much cheaper reagent, IPA. The products of this reaction were imines formed by the *in situ* coupling of the intermediate amine with acetone produced as a result of hydrogen transfer from IPA.[15] Several important functionalities were tolerated in this process but the catalyst load was relatively high (5%). Another ruthenium half-sandwich catalyst for the TH of ketones supported by a diimine ligand has been recently reported by Tamm et al.[16] The Crabtree group showed that a pyrimidyl-substituted *N*-heterocyclic carbene (NHC) complex of Ru [(η^6-cymene)(N-C)RuCl][PF_6] catalyzes the TH of acetophenone, cyclohexanone, and *N*-benzylideneaniline.[17] Albrecht et al. studied several half-sandwich Ru catalysts supported by NHCs and showed their ability to reduce PhCN and conjugated olefins.[3d] In light of these literature precedents and as part of our interest in the chemistry of half-sandwich complexes of Ru supported by NHCs,[18] we became interested in the catalytic activity of the related complex [Cp(IPr)Ru($NCCH_3$)$_2$][PF_6] (**2**, IPr = 1,3-bis(2,6-diisopropylphenyl)imidazol-2-ylidene). Here we report an improved TH of nitriles by IPA catalyzed by NHC-supported complexes and the application of this catalytic system to the reduction of heterocycles and olefins.

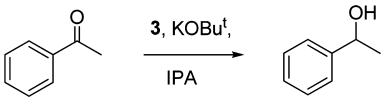
RESULTS AND DISCUSSION

Catalyst Optimization. The preparation of complexes [Cp(IPr)Ru($NCCH_3$)$_2$][PF_6] (**2**) and [Cp(IPr)Ru(pyr)$_2$][PF_6] (**3**, pyr = pyridine) has been recently reported.[18] The activity of **2**, **3**, and the commercially available compound [CpRu($NCCH_3$)$_3$]PF_6 (**4**) was tested in the TH of ketones and nitriles in isopropanol (IPA) at 70 °C in the presence of a base (KO^tBu). Acetophenone (Table 1) and benzonitrile (Table 2) were chosen as the test substrates to determine optimized reaction conditions. Complex **3** showed the superior catalytic activity in comparison with **2** and **4** (Table S1). Some catalyst turnover was observed for both substrates at room temperature (entry 1 in both Tables 1 and 2), but further optimization of the reduction of acetophenone determined the best conditions to be 0.05% catalyst load at 80 °C (Table 1, entry 7). In the case of benzonitrile, a comparable activity was reached at the 0.5% load (Table 2, entry 6). Although the TH of ketone by **3** is significantly improved in comparison with the catalyst **1**, it still falls short of the benchmark Noyori's catalyst [(η^6-arene)Ru(diamido)],[19] Baratta's catalyst [RuCl(κ^3-CNN)(dppb)] (5 min at 0.005 mol%),[20] and Stradiotto's catalyst [(η^6-cymene)Ru(κ^2-P,N)(Cl)] (5 min at 0.05 mol%).[21] We next optimized the amount of base ($KOBu^t$) and observed a saturation behavior at loads greater than 3 equiv (Table S2).

Transfer Hydrogenation of Nitriles. With the optimized conditions in hand (0.5 mol% catalyst, 1.5 mol% $KOBu^t$), complex **3** was then applied to the catalytic TH of a series of substituted nitriles (Table 3). Reactions of functionalized benzonitriles bearing the methoxy, amino, and ester groups in the 4-position proceeded chemoselectively, giving the corresponding imine derivatives in good to excellent yields (entries 2, 3, and 4).

Reactions of aromatic nitriles bearing more reactive carbonyl groups, such as acetyl and aldehyde groups, first resulted in selective reduction of the C=O bond followed by the TH of the C≡N bond (entries 1 and 5). A pyridyl-substituted nitrile was also successfully reduced (entry 6). As for catalyst **1**, the nitro substituent in the aromatic ring suppressed the catalytic activity (entry 13), resulting in a low yield of the imine product. Moreover, the more challenging aliphatic nitriles were also reduced but the yields dropped significantly, and longer reaction times were required to complete the reactions (entries 7−11). Longer chain and branched aliphatic nitriles are more

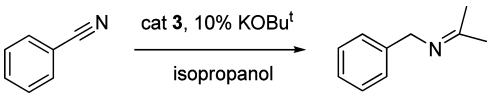
Table 1. Optimization of Catalytic Conditions for the 3-Catalyzed Transfer Hydrogenation of Acetophenone



entry	%C	B:C[a]	temp (°C)	yield[b] (%)	time
1	1	2:1	RT	83	17h
2	1	10:1	RT	67	7h20m
3	0.05	10:1	RT	<10	24h
4	0.1	10:1	40	40	20h
5	0.1	10:1	70	76	3h
6	0.05	10:1	70	83	7h
7	0.05	10:1	80	82	1h20m

[a]B = base $KOBu^t$, C = catalyst **3**. [b]NMR yield.

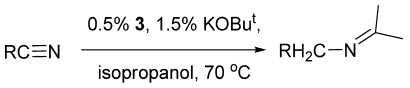
Table 2. Optimization of Catalytic Conditions for the 3-Catalyzed Transfer Hydrogenation of Benzonitrile



entry	%C[a]	temp (°C)	yield[b] (%)	time
1	0.05	70	63	4h50m
2	0.1	80	99	1h50m
3	0.1	RT	<10	24h
4	0.5	50	87	8h50m
5	0.5	60	93	5h10m
6	0.5	70	94	2h15m

[a]C = catalyst **3**. [b]NMR yield.

Table 3. 3-Catalyzed Transfer Hydrogenation of Nitriles



entry	product	yield[c] (%)	time
1	4-MeCH(OH)$C_6H_4CH_2N$=CMe_2	97	45m
2	4-(MeO)$C_6H_4CH_2N$=CMe_2	98 (57)	50m
3	4-(H_2N)$C_6H_4CH_2N$=CMe_2	87 (68)	90m
4	4-(EtO_2C)$C_6H_4CH_2N$=CMe_2	90	195m
5	4-($HOCH_2$)$C_6H_4CH_2N$=CMe_2	97	120m
6	NC_5H_4-3-CH_2N=CMe_2	95	165m
7	$Me(CH_2)_5CH_2N$=CMe_2	59	48h
8[a]	Me_3CCH_2N=CMe_2	32	48h
9[a]	$MeCH_2CH_2N$=CMe_2	98	48h
10[a]	$Me(CH_2)_2CH_2N$=CMe_2	99 (83)	48h
11[a]	$Me(CH_2)_3CH_2N$=CMe_2	87 (73)[d]	48h
12[b]	$C_6H_4CH_2N$=CMe_2	83	120m
13	3-NO_2-C_6H_4-CH_2N=CMe_2	35[e]	48h
14	HC≡C-$(CH_2)_4N$=CMe_2	24	48h

[a]At 90 °C. [b]1% **5** was used as a catalyst without added base. [c]NMR yield, isolated yield of ammonium salt after treatment with HCl in parentheses. [d]Isolated yield of amine after aqueous workup with NaOH. [e]Catalyst was deactivated upon the disappearance of tris-hydride peak, and color of sample turned black.

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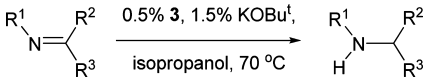
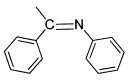
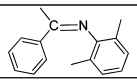
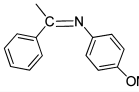
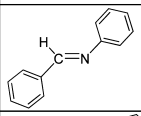
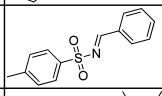
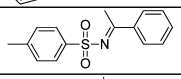
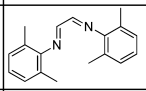
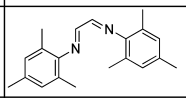
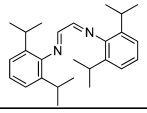
difficult to hydrogenate (entries 7 and 8). And elevated temperature (90 °C) is required to complete the reaction.

Transfer Hydrogenation of Imines. Given the activity of **3** in the TH of the C≡N triple bond, we became interested in the application of this catalyst to other unsaturated nitrogen substrates. Unexpectedly, ketimines PhMeC═NPh, PhMeC═N(2,6-$Me_2C_6H_3$), and (p-$MeOC_6H_4$)MeC═NPh were reduced only in trace amounts (<5%) even after 48 h at 70 °C. The aldimine PhHC═NPh was converted to PhH_2C-NHPh in only 45% yield after 8 h at 90 °C at 1% catalyst load. However, an aldimine activated by a tosyl group was successfully reduced to amine at only 0.5% catalyst load (Table 4, entry 5). The

Table 4. 3-Catalyzed Transfer Hydrogenation of Imines



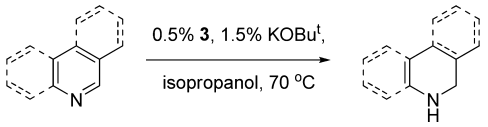
Entry	% cat	Substrate	Yield[a]	Time
1	5		5	48h
2	5		0	48h
3	5		<5	72h
4[b]	1		45	8h
5	0.5		99(88)	2h
6	5		82	16h
7	5		35	48h
8	5		23	48h
9	5		19	48h

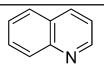
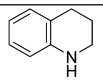
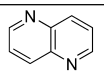
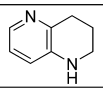
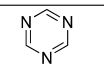
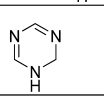
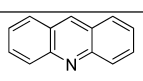
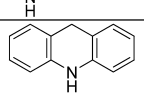
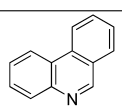
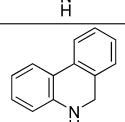
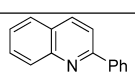
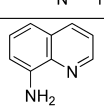
[a]NMR yields, isolated yield of amine in parentheses. [b]At 90 °C.

related activated ketimine derived from acetophenone was reduced to 82% yield in 16 h (entry 6). Interestingly, *N*-aryl dialdimines were also reduced but more sluggishly (entries 7−9) even at a higher catalyst loading (5%).

Transfer Hydrogenation of Heterocycles. The scope of substrates for TH was then extended to a range of *N*-heterocycles. We were delighted to see that quinoline and 1,5-napthyridine could be hydrogenated in good yields (Table 5, entries 1 and 2). As expected, less aromatically stabilized substrates, such as 1,3,5-triazine, acridine, and phenanthridine, can be easily reduced (entries 3−5). In contrast, bulkier substrates, such as 2-phenylquinoline (entry 6), and more electron rich substrates, such as 8-aminoquinoline (entry 7) were inert under these conditions. Unfortunately, no reactivity

Table 5. 3-Catalyzed Transfer Hydrogenation of Imines



Entry	Substrate	Product	Yield[a]	Time
1			62 (45)	6h
2			67	8h
3			60 (38)	75m
4			72	8h
5			58 (43)	8h
6		NR		8h
7		NR		8h

[a]NMR yields, isolated yields of amine in parentheses.

was observed for pyridine, isoquinoline, pyrimidine, pyrole, and imidazole.

Transfer Hydrogenation of Esters. In our previous work with the catalyst **1**, we observed partial TH of activated esters, such as phenyl acetates and trifluoroacetates, to alcohols.[15] But in all cases studied the main process was the transesterification of the substrate with IPA. Very similar results were obtained with the catalyst **3** (Table S3). For comparison, Albrecht et al. have previously observed only partial saponification of methyl benzoate under the action of an NHC-supported Ru complex under the TH conditions (IPA/KOH (aq)).[2i]

Transfer Hydrogenation of Olefins. In order to establish further the applicability of this catalytic system for the reduction of functionally loaded substrates, we tested catalyst **3** in the TH of C═C bonds. To our delight, several unfunctionalized olefins could be reduced well to the corresponding alkanes (Table 6). The yields are high for both linear and cyclic substrates (entries 1 and 2, respectively) but drop for trisubstituted olefins (entries 5 and 6). No reduction occurred for a tetrasubstituted olefin (entry 7). For styrene we observed formation of an insoluble gum at the bottom of NMR tube, suggesting formation of a polymer (entry 8). To the best of our knowledge, previously the catalytic TH of unactivated C═C bonds by IPA has been observed only for the complex [(η^6-cymene)(η^3-C═C-NHC)RuCl][BF_4] (where C═C-NHC is a chelating NHC with a pendant olefin group),[3d] for the catalysis by Ni nanoparticles,[3b] and in the tandem ring closure metathesis/TH reactions.[4] Attempted TH of alkynes was unsuccessful, as no reduction was observed after 48 h (entries 9 and 10).

Given the relative inactivity of ester, amido, and carboxy groups in TH, we became interested in studying conjugated

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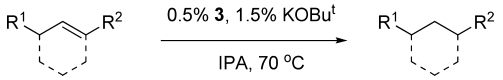
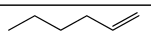
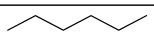
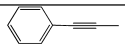
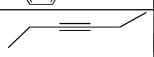
Table 6. 3-Catalyzed Transfer Hydrogenation of Olefins and Alkynes



Entry	Substrate	Product	Yield[d] (%)	Time
1			95	48h
2			78	48h
3[a]			82	48h
4[b]			82	48h
5			12	48h
6			8[c]	48h
7		NR		48h
8		Polystyrene gum[e]		48h
9		NR		48h
10		NR		48h

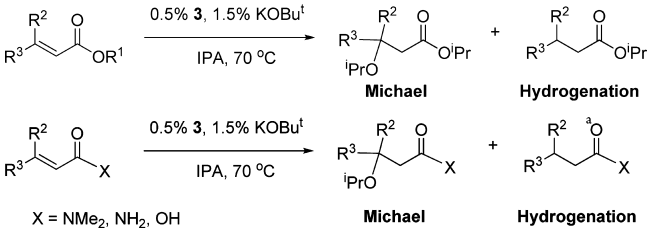
[a]Cp(IPr)RuH_3/^{t}BuOK was used as a catalyst. [b]Cp(IPr)RuH_3 was used as a catalyst without added base. [c]At 80 °C. [d]NMR yields. [e]Styrene polymerized.

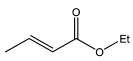
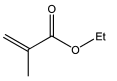
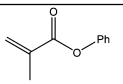
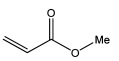
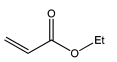
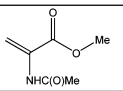
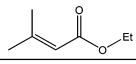
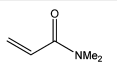
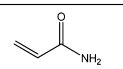
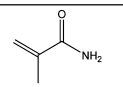
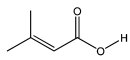
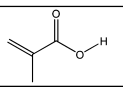
systems. Monitoring the reactions of α,β-unsaturated esters revealed fast (<20 min) formation of β-isopropoxy-substituted esters formed as a result of Michael addition of IPA. These compounds were formed as kinetic products because further heating at 70 °C resulted in a slow reduction of the ethereal moiety RH_2C-O-^{i}Pr to RH_2C-H (Table 7, entries 1−7). As could be expected, the ester part of both Michael and hydrogenation products contained the isopropoxy group instated as a result of concomitant transesterification. The hydrogenation process most likely occurs via a reversible dissociation of IPA (a retro-Michael reaction) followed by the TH of the re-formed C═C double bond. Analogous observations were made for the TH of enamides (entries 8−10). To our delight, 3,3-dimethylacrylic acid also could be reduced to the isovaleric acid (entry 11). In contrast, attempted reduction of methacrylic acid resulted in fast deactivation of the catalyst (entry 12). The reasons behind this divergent reactivity are not clear at the moment.

Mechanistic Studies. A careful inspection of the ^{1}H NMR spectra of different catalytic mixtures allowed for the observation that the trihydride Cp(IPr)RuH_3 (**5**) is the resting state of the catalyst. Indeed, complex **5** can be cleanly generated under the conditions of our catalytic mixtures, i.e., by the reaction of $[Cp(IPr)Ru(pyr)_2]^+$ (**3**) with 1 equiv of ^{t}BuOK in IPA. The trihydride **5** was synthesized on the preparative scale and isolated in 80% yield after recrystallization from a mixture of toluene/hexane (1:3). The ^{1}H NMR spectrum of **5** in C_6D_6 shows a typical hydride signal at −10.67 ppm as a time-averaged singlet for three hydrides and the Cp peak at 4.30 ppm (5H), in addition to the signals of the IPr ligand.[18]

The catalytic activity of trihydride **5** was tested in the TH of benzonitrile (Table 3, entry 12) and in the TH of cyclohexene (Table 6, entries 3 and 4). Interestingly, in both cases the reduction occurred without addition of any base and at reaction times well comparable with cases when ^{t}BuOK was employed

Table 7. 3-Catalyzed Transfer Hydrogenation of Conjugated Substrates



Entry	Substrate	Yield[a]	Time
1		20% M, 80% H ethyl butyrate (78%)[b]	8h
2		5% M, 95%H ethyl isobutyrate (82%)[b]	8h
3		15%M , 85%H	8h
4		11% M, 89% H methyl propionate (64%)[b]	8h
5		11% M, 89% H ethyl propionate (74%)[b]	16h
6		98%H	48h
7		7% M, 93% H	16h
8		98% H	8h
9		55% M, 45% H propionamide (43%)	48h
10		15% M, 85% H isobutyramide (58%)	48h
11[c]		99% H isopropyl isovaleri-ate[d]	72h
12		NR[e]	24h

[a]NMR yields, isolated yields in parentheses. [b]Isolated yields for ester obtained after transesterification with ethanol or methanol. [c]The catalyst was premixed with base in IPA prior to addition of the substrate. [d]After the TH, the isovaleric acid was converted to ester by acid-catalyzed esterification. [e]However, prior conversion of crotonic acid into isopropyl ester resulted in 65% isolated yield of isopropyl isobutyrate.

(e.g., Table 2, entry 6 vs Table 3, entry 12). These observations suggested that the role of base is solely to convert the precursor **3** into complex **5** which is the true catalyst.

To get more insight into the nature of this catalytic system, kinetic studies using the initial rate analysis were carried out. *p*-Methoxybenzonitrile was chosen as the substrate because it allows for the monitoring of the MeO signal by ^{1}H NMR. Complex **5** was employed as the catalyst to suppress any effect of the catalyst generation stage. Nevertheless, we chose to use some additional base to mimic the actual catalytic conditions better. The reaction rates were measured in chlorobenzene with the catalyst/base ratio 1:3 and by using a large but controlled

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Organometallics XXXX, XXX, XXX−XXX

amount of IPA (the range 10−40 equiv). A first-order dependence of the reaction rate on the concentration of substrate was observed (Figures S8−12). Plotting the reaction rate vs the amount of IPA revealed a saturation behavior at large concentrations of the alcohol (Figure 1). This kinetic

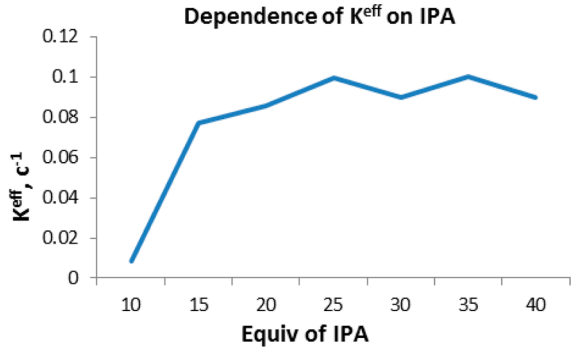


Figure 1. Dependence of the **5**-catalyzed transfer hydrogenation on the amount of IPA.

behavior suggests the occurrence of a pre-equilibrium involving the substrate. To elucidate the effect of base, the kinetic measurements were repeated under the pseudo-first-order conditions (15 equiv of IPA relative to substrate) for varying amounts of ^{t}BuOK. In contrast to the results of the initial tests with the catalyst **2**, increasing the amount of base had a detrimental effect on catalysis (Figure S13). This experiment confirms our conclusion that in the case of TH of benzonitrile the base plays no other role in catalysis but converts the precatalyst **2** into the true catalyst **5** (vide supra). All together these kinetic data agree with a classical hydride mechanism of TH (Figure 2).[22] The key steps 2, 3, and 4 of this cycle have

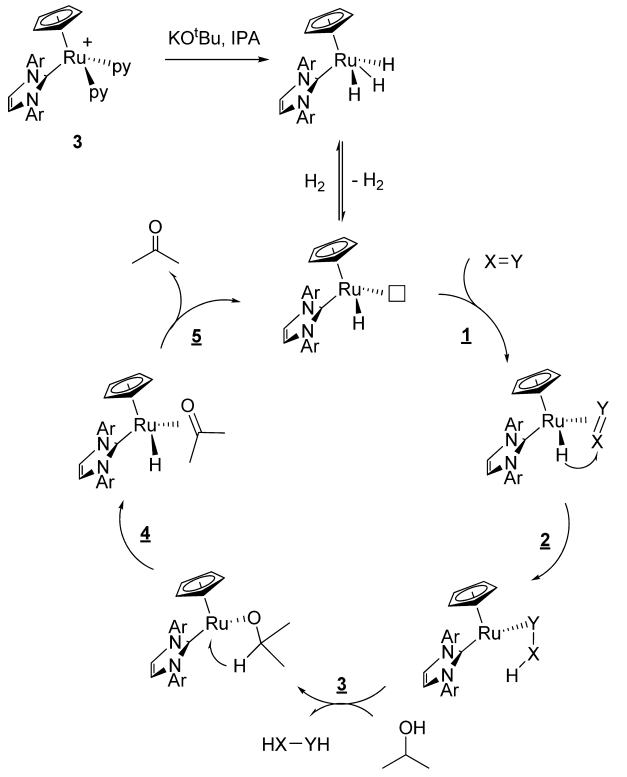
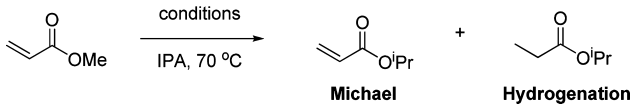


Figure 2. Proposed mechanism for **3**-catalyzed transfer hydrogenation.

been previously studied by Nolan et al. in a combined experimental and theoretical study of alcohol racemization catalyzed by the related complex Cp*(NHC)RuCl.[23] It is interesting to compare the mechanistic proposal of Figure 2 with our previous studies on the phosphine catalyst **1**. In that case we also observed the formation of a hydride species, which however was different from the known trihydride Cp(^{i}Pr$_3$P)-RuH$_3$ and whose exact nature remained unclear. The main difference is that for **1** we observed the first-order kinetics in IPA in the range of 10−30 equiv of IPA, which prevented us from drawing a reliable conclusion about the exact sequence of mechanistic events. The reason for the different mechanistic behavior of the catalysts **1** and **5** likely lies in their structural features. In the phosphine species **1**, the substituents at the phosphorus center are oriented backward, thus creating a more open space around the ruthenium atom. In the NHC complexes **3** and **5**, the bulky Ar groups at nitrogen look forward, toward the positions occupied by the pyridine and hydride ligands, respectively. This structural difference, on one hand, hampers the coordination of bulkier substrates to ruthenium atom but, on the other hand, facilitates ligand dissociation from **3** (e.g., pyridine) and insertion reactions (step 2 in Figure 2).

Further experiments, however, revealed that the effect of base can be substrate sensitive. Thus, screening various catalytic conditions for the TH of methyl acrylate showed that the cationic complexes **4** and [CpRu(pyr)$_3$]PF$_6$ (**4a**) show comparable (Table 8, entries 1 and 2) but reduced activity in

Table 8. Transfer Hydrogenation of Methyl Acrylate under Different Conditions



entry	conditions	yield[a]	time
1	**4** + 3KOtBu	85% M, 15% H	72h
2	**4a** + 3KOtBu	85% M, 15% H	72h
3	**3** + 3KOtBu	17% M, 83% H	16h
4	Cp(IPr)RuH$_3$	18% H	24h
5	Cp(IPr)RuH$_3$ + KOtBu	98% H	24h
6	Cp(IPr)RuH$_3$ + 3KOtBu	11% M, 89% H	8h
7	KOtBu	99% M, 0% H	20m
8	no catalyst + no base	0% M, 0% H	24h

[a]NMR yield.

comparison with the NHC-supported complex [Cp(IPr)Ru-(pyr)$_2$]$^+$ (**3**) (Table 8, entry 3). The trihydride Cp(IPr)RuH$_3$ (**5**) taken alone can mediate the reduction too but its activity is significantly increased upon addition of KOBu^{t} (entries 4−6). On the other hand, a control experiment showed that the base alone does not catalyze this reaction (entry 7). The latter fact is of significance because Ouali et al. have previously reported that simple bases can catalyze TH of ketones in the absence of any transition metal.[24]

CONCLUSIONS

The NHC-supported half-sandwich complexes [Cp(IPr)Ru-(NCCH$_3$)$_2$][PF$_6$] (**2**) and [Cp(IPr)Ru(pyr)$_2$][PF$_6$] (**3**) are effective catalysts for the transfer hydrogenation of nitriles and actually perform this reaction much better (at lower catalyst load and faster rates) than the isolobal phosphine complex

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$[Cp(^iPr_3P)Ru(NCCH_3)_2][BF_4]$. Complex **3** also catalyzes the TH of activated heterocycles (including quinoline) and cyclic and acyclic olefins. In the latter case, good results were obtained for mono- and bis(substituted) olefins but the yield drops significantly for a tri(substituted) system. In the case of activated olefins (conjugated esters, amides, and acids) the TH works well for mono-, bis-, and tri(substituted) C=C bonds. Mechanistic studies showed that the resting state in this catalysis is the trihydride $Cp(IPr)RuH_3$ (**5**) which can catalyze the reduction of nitriles without any additional base and that the external base actually has a detrimental effect on catalysis. Therefore, the role of base in the **3**-catalyzed reaction is merely to effect the conversion of the precatalyst into a reactive hydride. However, the efficiency of reduction increases in the presence of a base when methyl acrylate was used as substrate. The reason for this discrepancy is not yet understood. Kinetic studies for the **5**-catalyzed TH of 4-methoxybenzonitrile suggested a classical hydride mechanism of reduction based on substrate coordination to a metal hydride complex, migratory insertion, and release of the product after a metathesis with IPA.

EXPERIMENTAL SECTION

General Details. All manipulations were carried out, using conventional inert atmosphere glovebox and Schlenk techniques. Solvents were dried by Grubbs-type columns, except for THF which was distilled from a sodium benzophenone ketyl solution. NMR spectra were obtained with Bruker DPX-400 and Bruker DPX-600 instruments (^1H, 400 and 600 MHz; ^{13}C, 100.6 and 151 MHz). The ^1H and $^{13}C\{^1H\}$ NMR spectra of isolated organic products were recorded in $CDCl_3$. Complexes $[Cp(IPr)Ru(NCCH_3)_2][PF_6]$ (**2**), $[Cp(IPr)Ru(pyr)_2][PF_6]$ (**3**), $[CpRu(pyr)_3][PF_6]$ (**4a**), $[CpRu(NCCH_3)_3][PF_6]$ (**4**), and $Cp(IPr)RuH_3$ (**5**) were prepared as previously described.[18,25]

General Procedure for the Reduction of Nitriles. Stock solutions of catalysts **1**, **2**, **3**, **4**, and **5** in IPA and $KOBu^t$ in IPA were prepared separately before use. In a glovebox, a 10 mL, flame-dried Schlenk tube equipped with a magnetic stirring bar was charged with **3** (0.5 mol%), nitrile (0.8 mmol) and $KOBu^t$ (1.5 mol%) in IPA (4 mL). The Schlenk flask was brought out of the glovebox and equipped with a condenser under N_2 atmosphere. The progress of the reaction was monitored by NMR spectroscopy at 70 °C. The imine $RCH_2N{=}C(CH_3)_2$ was obtained as the major product. After the reaction was completed, the resulting solution was treated with aqueous HCl (1 M, 1.8 mL). Then the mixture was stirred for 1 h at room temperature to ensure the complete hydrolysis of imine. After the removal of volatiles under vacuum, 5 mL fresh water was added into solid residue to extract ammonium salts. The water solution of ammonium salts was then recrystallized with (1 mL) addition of hexane (5:1 v/v) to yield corresponding ammonium microcrystal salts, which are analytically clean, as confirmed by NMR. The ammonium salt $[RCH_2NH_3]Cl$ was obtained as a pale yellow or brownish solid, depending on the nitrile used. The ammonium salt was converted to amine by treatment with a 3 M NaOH solution (3 mL) in a 2 × 10 mL mixture of diethyl ether and water (2:1 v/v). The organic phase was separated and dried over $MgSO_4$.

General Procedure for the Reduction of *N*-Heterocycles. In a glovebox, a 10 mL flame-dried Schlenk tube equipped with a magnetic stirring bar was charged with **3** (0.5 mol%), *N*-heterocycle (0.8 mmol), and $KOBu^t$ (1.5 mol%) in IPA (4 mL). The Schlenk flask was brought out of the glovebox, equipped with a condenser under N_2 atmosphere and heated to 70 °C. The progress of the reaction was monitored by NMR spectroscopy and TLC. The reaction was stopped when the highest amount of the partially hydrogenated product was observed. After the removal of volatiles under vacuum, hexane was used to extract the product and the remaining substrate from the solid residue. The product was then isolated by chromatography on silica gel, using a mixture of hexane and ethyl acetate (4:1).

General Procedure for the Reduction of Olefins. In a glovebox, a 10 mL flame-dried Schlenk tube equipped with a magnetic stirring bar was charged with **3** (0.5 mol%), olefin (0.8 mmol), and $KOBu^t$ (1.5 mol%) in IPA (4 mL). The Schlenk flask was brought out of the glovebox, equipped with a condenser under N_2 atmosphere and heated to 70 °C. The progress of the reaction was monitored by NMR spectroscopy and TLC. The reaction was stopped when the highest amount of the hydrogenated products was observed. Then the reaction mixture was treated by two portions of a 10 mL mixture of diethyl ether and water (2:1 v/v). The organic phase was separated and dried over $MgSO_4$. In the case of ester substrates, the initially formed mixture of the starting ester (methyl or ethyl), reduced ester, and their isopropyl analogues, formed by the transesterification in IPA, was converted into the ethyl or methyl ester by transesterification with corresponding alcohol. For example, to convert a mixture of isopropyl butyrate and ethyl butyrate into ethyl butyrate, excess amount of ethanol was added with a drop of H_2SO_4, and the mixture was refluxed for 2 h, followed by a standard workup.

Dependence of the Reaction Rate on Isopropanol. In a glovebox, seven NMR samples were prepared each containing 0.5 mol % (0.527 mmol) of $Cp(IPr)RuH_3$ (**5**, from a stock solution in IPA), 1.5 mol% of $KOBu^t$ (1.577 mmol, from a stock solution in PhCl), *p*-methoxybenzonitrile (105.1 mmol), and an additional amount of IPA with the total amount of IPA in the range of 10−40 equiv with respect to *p*-methoxybenzonitrile (250 μL, 105.1 mmol). For each sample, a timer was started when the sample was placed inside a Bruker DPX-600 NMR spectrometer preheated to 70 °C, and ^1H NMR spectra were obtained every 5 min for 1.5 h. The rate of the reaction was determined from the decrease of the MeO signal of *p*-methoxybenzonitrile in the ^1H NMR spectra as the reaction progressed. Under the pseudo-first-order conditions, the linearity of the plot of $-\ln([MePhCN]_t/[MePhCNe]_0)$ versus time reveals that the reaction rate is first-order with respect to substrate (Figures S1−S7). The slopes of the regression lines (k^{eff}) were then plotted versus the equivalents of IPA (Figure 1). The reaction showed saturation behavior at high concentrations of IPA.

Dependence of the Reaction Rate on Base. In a glovebox, five NMR samples were prepared, each containing 0.5 mol% of $Cp(IPr)RuH_3$ (**5**, 1.577 mmol, from a stock solution in IPA), an additional amount of IPA up to the total amount of IPA of 112.5 μL (mmol), *p*-methoxybenzonitrile (105.1 mmol), and a variable amount of $KOBu^t$ (from a stock solution in IPA) in the range 1.25−4 equiv with respect to catalyst **5**. For each sample, a timer was started when the sample was placed inside a Bruker DPX-600 NMR spectrometer preheated to 70 °C, and ^1H NMR spectra were obtained every 5 min for 1.5 h. The rate of the reaction under the pseudo-first-order conditions was determined from the decrease of the MeO signal of *p*-methoxybenzonitrile in the ^1H NMR spectra as the reaction progressed (Figures S8−S12). The slopes of the regression lines (k^{eff}) were then plotted versus the equivalents of $KOBu^t$ (Figure S13).

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.organomet.5b00967.

Further experimental details, characterization data, and kinetic plots (PDF)

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Notes

The authors declare no competing financial interest.

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