Half-sandwich Complexes of Ruthenium;

Synthesis and Application to Catalysis

Sun Hwa Lee

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Brock University

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Abstract

This thesis describes syntheses and catalytic reactivity of several half-sandwich complexes of ruthenium. The neutral ruthenium trihydride complex, $Cp(PPr^{i}_{3})RuH_3$ (**1**), can efficiently catalyse the H/D exchange reaction between various organic substrates and deuterium sources, such as benzene-d_6. Moreover, the H/D exchange reactions of polar substrates were also observed in D_2O, which is the most attractive deuterium source due to its low cost and low toxicity. Importantly, the H/D exchange under catalytic conditions was achieved not only in aromatic compounds but also in substituted aliphatic compounds. Interestingly, in the case of alkanes and alkyl chains, highly selective deuterium incorporation in the terminal methyl positions was observed. It was discovered that the methylene units are engaged in exchange only if the molecule contains a donating functional group, such as O- and N-donors, C=C double bonds, arenes and CH_3.

The cationic half-sandwich ruthenium complex $[Cp(PPr^{i}_{3})Ru(CH_3CN)_2]^+$ (**2**) catalyses the chemoselective mono-addition of $HSiMe_2Ph$ to pyridine derivatives to selectively give the 1,4-regiospecific, *N*-silylated products. An ionic hydrosilylation mechanism is suggested based on the experiments. To support this mechanistic proposal, kinetic studies under catalytic conditions were performed. Also, the 1,4-regioselective mono-hydrosilylation of nitrogen containing compounds such as phenanthroline, quinoline and acridine can be achieved with the related Cp^* complex $[Cp^*(phen)Ru(CH_3CN)]^+$ (**3**) (phen = 1,10-phenanthroline) and $HSiMe_2Ph$ under mild conditions.

The cationic ruthenium complex **2** can also be used as an efficient catalyst for transfer hydrogenation of various organic substrates including carbonyls, imines, nitriles and esters. Secondary alcohols, amines, *N*-isopropylidene amines and ether compounds

can be obtained in moderate to high yields. In addition, other ruthenium complexes, **1**, **3** and $[Cp^{*}(PPr^{i}_{3})Ru(CH_3CN)_2]^{+}$ (**4**), can catalyse tre ansfer hydrogenation of carbonyls although the reactions were sluggish compared to the ones of **2**. The possible intermediate, $Cp(PPr^{i}_{3})Ru(CH_3CN)(H)$, was characterized by NMR at low temperature and the kinetic studies for the transfer hydrogenation of acetophenone were performed.

Recently, chemoselective reduction of acid chlorides to aldehydes catalysed by the complex **2** was reported. To extend the catalytic reactivity of **2**, reduction of iminoyl chlorides, which can be readily obtained from secondary amides, to the corresponding imines and aldehydes was investigated. Various substituted iminoyl chlorides were converted into the imines and aldehydes under mild conditions and several products were isolated with moderate yields.

Manuscripts based on this work

1. Lee, S. H.; Gutsulyak, D. V.; Nikonov, G. I., Chemo- and regioselective catalytic reduction of N-heterocycles by silane. *Organometallics*, **2013**, *32*, 4457-4464.
2. Lee, S. H.; Gorelsky, S. I.; Nikonov, G. I., Catalytic H/D exchange of unactivated aliphatic C-H bonds. *Organometallics*, **2013**, *32*, 6599-6604.
3. Lee, S. H.; Nikonov, G. I., Semi-catalytic reduction of secondary amides to imines and aldehydes. *Dalton Trans*., **2014**, *43*, 8888-8893.

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Abbreviations

Å	Angstrom
acac	Acetylacetonate
ACHN	1,1'-azobis(cyclohexanecarbonitrile)
Ar	Aryl
atm	Atmosphere (1atm = 101.3 kPa)
b	Broad (in NMR)
BAF	$B(C_6F_5)_4^-$
Bu	Butyl
t-Bu	Tert-butyl
Calc.	Calculated
cat	Catalyst
Conv.	Conversion
cod	Cyclooctadiene
coe	Cyclooctene
°C	Degrees Celcius
3c-2e	Three centre – two electron
Cp	η^5-C_5H_5
Cp*	η^5-C_5Me_5
Cp'	η^5-C_5H_5 or η^5-C_5Me_5, unless specified
d	Doublet (in NMR)
DFT	Density functional theory
DME	1,2-dimethoxyethane
DMF	Dimethylformamide
DMSO	Dimethyl sulphoxide
DPPE	1,2-Bis(diphenylphosphino)ethane
Et	Ethyl
Equiv.	Equivalents
Exc.	Excess
h	Hour
Hz	Hertz

J	Coupling constant (in NMR)
IR	Infrared
L_n	Ligands
M	metal
m	Meta
m	Multiplet (in NMR)
Me	Methyl
Mes	Mesityl
MO	Molecular orbital
NMR	Nuclear magnetic resonance
o	Ortho
OTf	triflate
p	Para
Ph	Phenyl
PMHS	Polymethylhydrosiloxane
Pr^i	isopropyl
Py	Pyridine
q	Quartet (in NMR)
RT	Room temperature
s	Singlet (in NMR)
sat	Satellite (in NMR)
Sept	Septet (in NMR)
t	Triplet (in NMR)
t	tertiary
TMDS	Tetramethyldisiloxane
TMP	2,2,6,6-tetramethylpiperidine
TBAF	Tetrabutylammonium fluoride
TOF	Turnover frequency
TON	Turnover number
Tp	Trispyrazolylborate
VT	Variable temperature
UV	Ultraviolet
δ	Chemical shift, ppm (in NMR)

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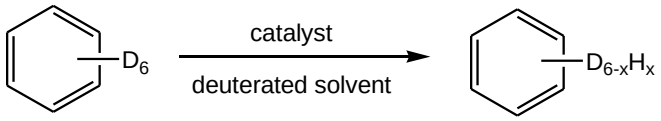
I. Introduction

Catalytic H/D exchange is an important method for investigating the mechanisms of activation of C-H bonds[1] and for preparing deuterium-labeled compounds.[2,3] Deuterium-labeled compounds are widely used for research and development of new drugs.[4] Moreover, deuterium-labeled polymers find applications in the manufacturing of organic light emitting diodes (OLEDs).[5] The H/D exchange between C-H bonds of aromatic compounds and C-D acidic substrates, such as deuterated acetone and chloroform, is well established.[1a,6,7] However, although a few examples of H/D exchange of aliphatic compounds have been reported,[8] the deuterium incorporation is limited only to the reactive allylic and benzylic positions.[6,9] Therefore, the catalytic deuteration of aliphatic compounds still needs to be developed.



Scheme 1. H/D exchange reaction of benzene

The neutral half-sandwich ruthenium complex $CpRu(PPr^i_3)H_3$ (**1**) efficiently catalyses the H/D exchange reactions between organic compounds and deuterated solvent, such as benzene-d_6 and D_2O (Scheme 1). A part of this study is devoted to the investigation of catalytic H/D exchange by using the efficient catalyst **1**.

Catalytic hydrosilylation is an important and a well-established method for the reduction of unsaturated organic compounds.[10] In addition, hydrosilylation reactions have been extensively studied for the preparation of valuable silicon containing compounds, which can be applied in silicon rubbers, adhesives and paper coatings.[11] The hydrosilylation of carbonyls, alcohols, esters, nitriles and pyridines catalysed by the cationic ruthenium complex $[CpRu(PPr^i_3)(CH_3CN)_2]^+$ (**2**) has been

previously studied by Nikonov and co-workers.[12] Based on a combined experimental and computational study, an ionic mechanism was proposed which includes the formation of a silane σ-complex, silylium ion transfer to the substrate (e.g. pyridine) to give an activated substrate (e.g. *N*-silyl pyridinium salt) and a neutral ruthenium hydride complex which then react to furnish the 1,4-addtion product (Figure 1). As a continuation of the research on the hydrosilylation of pyridines catalysed by **2**, the present thesis includes kinetic studies of the reactions.

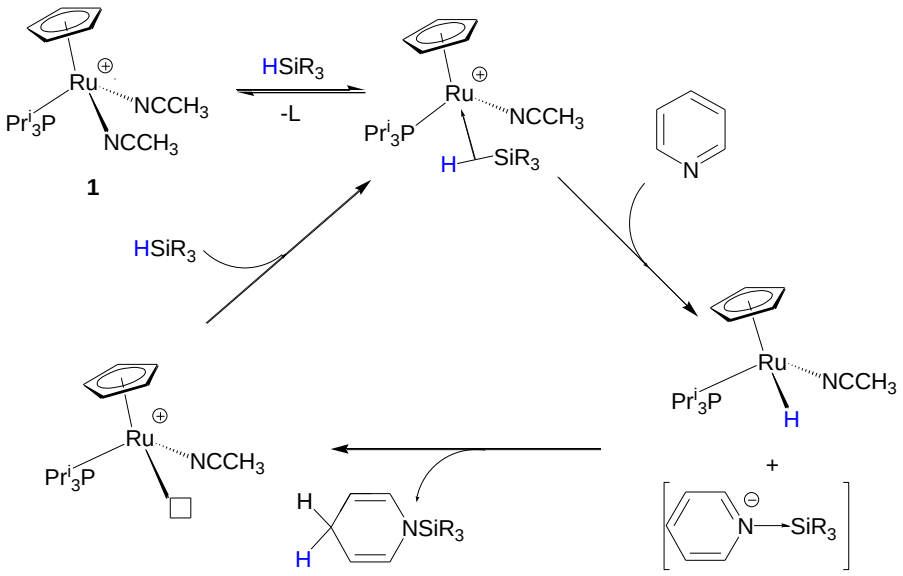
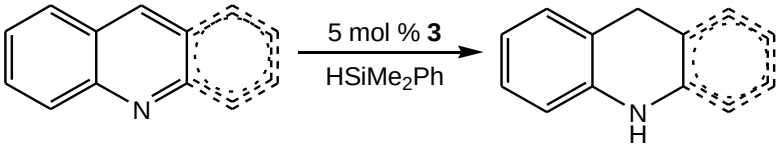


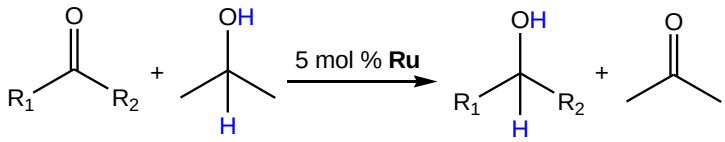
Figure 1. Proposed ionic mechanism for hydrosilylation of pyridines

The catalytic hydrosilylation of nitrogen containing compounds, such as quinoline and phenanthroline, has been considered as an important transformation due to its potential for the preparation of pharmaceutically active compounds.[13] However, such a reaction often requires harsh reaction conditions and makes the addition of silanes to nitrogen containing compounds very challenging. The cationic Cp^* ruthenium complex, $[Cp^*(phen)Ru(CH_3CN)]^+$ (**3**), is an efficient catalyst for the hydrosilylation of various heterocycles under mild condition (Scheme 2).



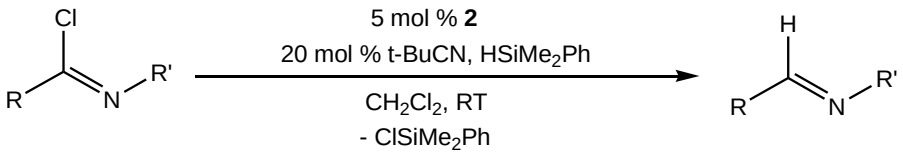
Scheme 2. Hydrosilylation of nitrogen containing compounds

Since the 1950s, transfer hydrogenation catalysed by transition-metal complexes has attracted much attention due to its mild reaction conditions and the importance of the formation of reduced organic compounds.[14] The use of hydrogen-donor solvents instead of hydrogen gas can not only simplify the reaction procedure but also reduce the reaction pressure.[14b] Transfer hydrogenation of a wide range of organic substrates including carbonyls, imines, nitriles and esters can be achieved with the ruthenium complexes (**1**, **2**, **3** and $[Cp^{*}(PPr^{i}_{3})Ru(CH_3CN)_2]^{+}$ (**4**)) in 2-propanol as a hydrogen source (Scheme 3). The cationic complex **2** shows the best results and most reactions can be achieved at room temperature.



Scheme 3. Transfer hydrogenation of carbonyls

Catalytic reduction of acid chlorides to aldehydes is a fundamental functional group transformation.[15] Recently the ruthenium complex **2** was reported as an efficient catalyst for the reduction of acid chlorides bearing various functional groups to aldehydes in the presence of $HSiMe_2Ph$.[16] This result encouraged us to study the reduction of iminoyl chlorides to imines under the similar reaction conditions (Scheme 4).



Scheme 4. Reduction of iminoyl chlorides to imines

The transition-metal catalysed reduction of amides to pharmaceutically important amines and aldehydes has been widely studied since 1990s.[17] Although imines are more difficult to generate from amides because they can be easily reduced to amines, imines with several functional groups were formed in the presence of **2** (Scheme 4). In addition to the formation of imines, aldehydes with different substituents were obtained under the same reaction conditions.

II. Historical

II.1. H/D exchange reactions catalysed by transition-metal complexes

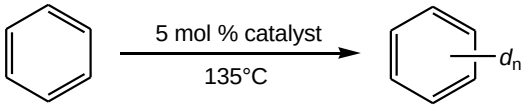
The H/D exchange reaction has attracted much attention because of its importance for the preparation of deuterium labeled compounds.[18,19] Deuterated compounds are widely used for different fields of science,[4,5,20] such as medicinal chemistry, polymer and material science, mechanistic studies, solvents for NMR *etc*. Labelled compounds are important for the development of a new drug as they help to study their metabolism.[4] The isotopic labeling of drugs usually involves the incorporation of ^{13}C and ^{2}H labels into a drug at the early stages of synthesis. However, due to the rapid development of new pharmaceutically active ingredients, more efficient isotopic labeling methods are required. In addition, deuterium labelled polymers have been evaluated for organic light emitting diodes (OLEDs).[5] Deuterated polymers are considered as useful materials for wave guides in optical communication due to their transparency in the red beam infrared area (500-800nm). Furthermore, deuterium labeled compounds can be used as internal standards in NMR spectroscopy.[3,18] As the development of spectrometers continues and their use in different areas increases, the importance of deuterated compounds becomes more and more significant. Also, H/D exchange reaction is a powerful tool for mechanistic investigations in catalysts and stoichiometric studies of organic and organometallic reaction pathways.[20] However, most of the known labelling procedures result in insufficient deuterium incorporation or are not chemo- and regioselective.[39,40a] Also, most transition-metal catalysed H/D exchange reactions require high temperatures. Therefore, the development of new mild, efficient and selective methodologies is an important and challenging task.

II.1.1. H/D exchange reactions catalysed by homogeneous metal catalysts

Since the early studies on H/D exchange reactions by soluble complexes in the late 1960s and early 1970s, many efficient methods for homogeneous metal catalysed H/D exchange reactions have been developed.[21] In general, H/D exchange reactions mediated by homogeneous metal catalysts can be achieved at elevated temperature with high tolerance towards a wide scope of functional groups.[3] Furthermore, in addition to the use of deuterium gas and D_2O, various deuterated organic solvents, such as acetone-d_6 and benzene-d_6, can be used as deuterium sources, which allows deuterium exchange reactions on less polar substrates.

In addition to their use in the activation of C-H bonds,[22] cationic iridium complexes have been widely employed as catalysts for H/D exchange reactions. Bergman and co-workers introduced several iridium catalysts for the deuteration of aliphatic and aromatic substrates.[23] Various deuterated solvents were screened as deuterium sources in H/D exchange reactions of benzene mediated by half-sandwich iridium complexes, $Cp^*(PMe_3)IrCl_2$ (**5**) and $Cp^*(PMe_3)Ir(H)_3$ (**6**) (Table 1).[23c] Complex **5** shows good catalytic activities for the H/D exchange in D_2O and in a mixture of D_2O and CD_3OD, but gives only modest deuterium incorporation in organic solvents, such as acetone-d_6, CD_3OD and DMSO-d_6. On the other hand, complex **6** performs well in organic solvents, e.g. acetone-d_6 and CD_3OD, whereas its performance in D_2O or mixed D_2O/CD_3OD is only modest.

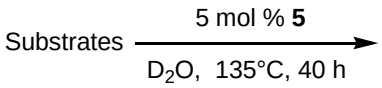
Table 1. The effect of deuterium source in the H/D exchange catalysed by Ir complexes

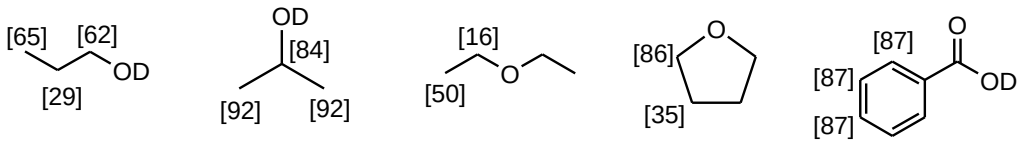


Entry	Solvent	$Cp^*(PMe_3)IrCl_2$ (**5**)		$Cp^*(PMe_3)Ir(H)_3$ (**6**)	
		% D_{inc} [a]	Time	% D_{inc} [a]	Time
1	D_2O	90	5 d	66	17 h
2	D_2O/CD_3OD	97	2 d	75	3 d
3	CD_3OD	58	2 d	95	3 d
4	DMSO-d_6	0	5 d	0	2 d
5	acetone-d_6	21	2 d	99	20 h

[a] Extents of deuterium incorporation.

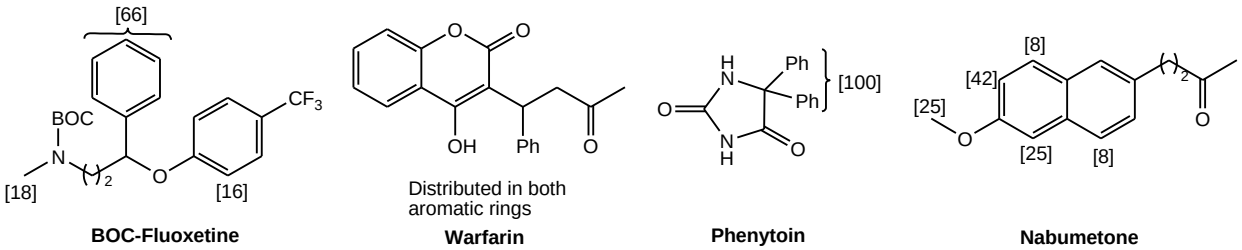
In the presence of the iridium phosphine complex **5**, good deuterium incorporation into various organic compounds, such as alcohols, carboxylic acids and ethers, was obtained (Scheme 5).[23b]





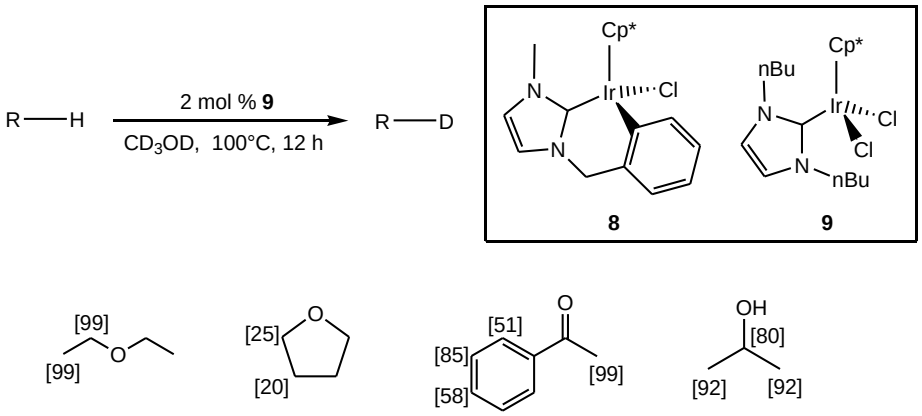
Scheme 5. H/D exchange reactions catalysed by **5** in D_2O

H/D exchange reactions of pharmaceutically important substrates in the presence of stoichiometric amount of the Ir(III) complex, $[Cp^*(PMe_3)Ir(Me)(CH_2Cl_2)]^+$ (**7**), were studied.[23d] As can be seen from Scheme 6, H/D exchange mostly takes place in the aromatic positions of substrates, resulting in good to excellent deuterium labeling of these groups with high efficiency.



Scheme 6. Deuterium labeling in pharmaceutical compounds by using **7**

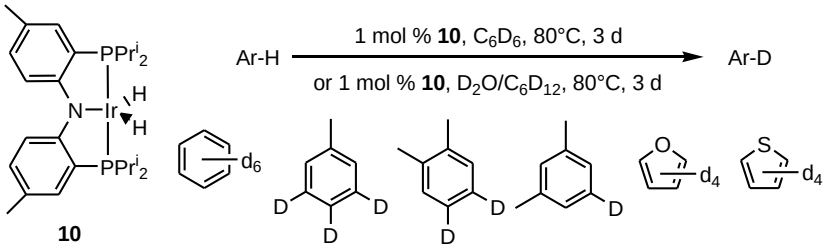
Catalytic H/D exchange reactions with *N*-heterocyclic iridium-carbene complexes **8** and **9** were studied by Peris *et al*.[24a] In the presence of 2 mol % of the catalysts, a good deuterium incorporation of a wide range of organic molecules, such as ethers, ketones and alcohols, was achieved in CD_3OD as a deuterium source (Scheme 7). Complex **9** results in higher deuterium incorporation compared to the complex **8**. In addition, the H/D exchange reactions with **8** or **9** show better results than its phosphine analogue **6** in terms of conversions, applicability and stability of the catalyst.



Scheme 7. The H/D exchange reactions catalysed by Ir-NHC complexes **8** and **9**

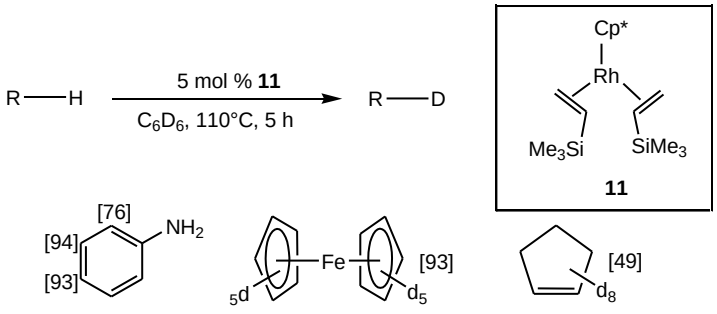
Grubbs and co-workers reported a selective and efficient H/D exchange between aromatic compounds and C_6D_6 or D_2O by using an iridium(III) pincer complex (**10**).[24b] The two hydrides of the complex **10** can be easily deuterated by heating at 80°C in C_6D_6 or D_2O/C_6D_{12} mixture for 1 hour. They also studied H/D exchange between arenes and C_6D_6 or D_2O in the presence of **10** (Scheme 8). High deuterium

incorporation (>95%) was observed in benzene derivatives and heterocycles in 3 days. It was found that steric factors played an important role because deuteration of toluene was observed only at the *meta* and *para* positions. Also, deuterium incorporation of *o*-xylene and *m*-xylene was observed only at the 4- and 5-positions and 5-position, respectively.



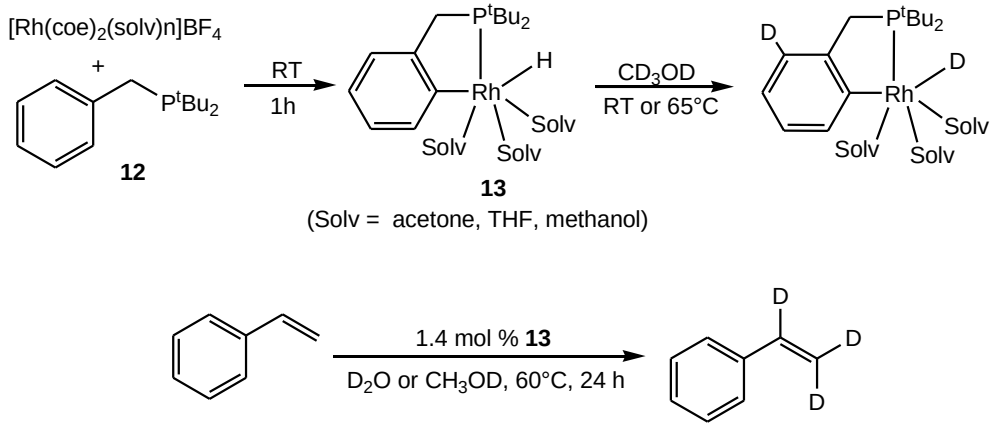
Scheme 8. The H/D exchange reactions catalysed by Ir pincer complexe **10**

Rhodium complexes are also suitable for H/D exchange reactions and many procedures with rhodium catalysts have been developed.[8b,25] Brookhart and co-workers reported H/D exchange reactions mediated by the rhodium-olefin complex **11**.[25a] A moderate to high degree of deuteration was achieved in the case of aniline, ferrocene and cyclopentene (Scheme 8). The 16-electron species [Cp*Rh(L)], which can be produced by the dissociation of bulky olefins from the Rh(I) centre of **11**, can catalyse C-H bond activation via oxidative addition. Also, these workers reported that deuterium can be transferred from C_6D_6 to the olefin ligands and, further, can be transferred to substrates.



Scheme 9. The H/D exchange reactions catalysed by the rhodium-olefin complexes **11**

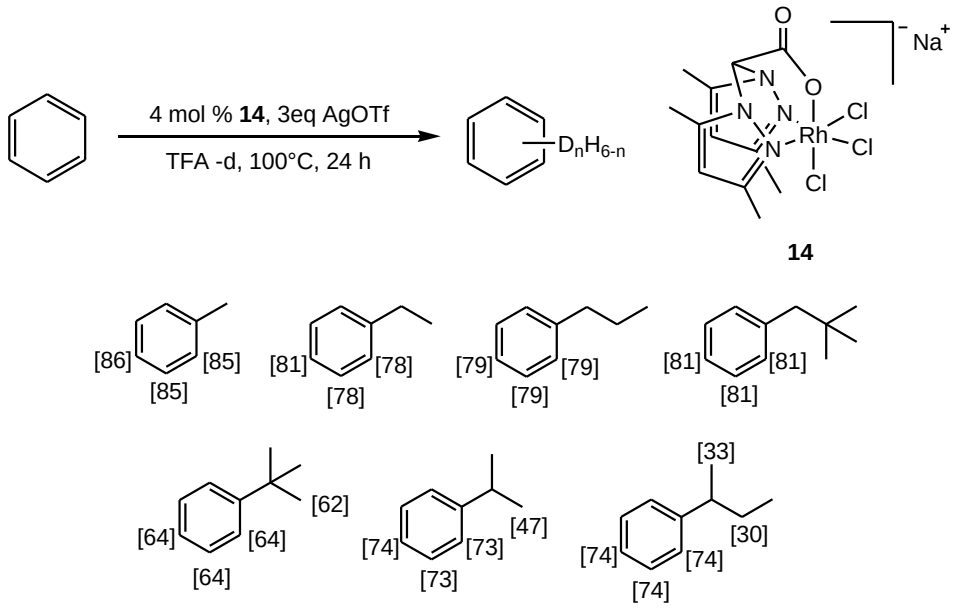
An aromatic PC-Rh complex **13** (PC = phosphine ligand) was synthesized from the reaction of an aryl-PC type ligand, benzyl(di-*tert*-butyl)phosphane (**12**), and $[Rh(coe)_2(solv)_n]BF_4$ (coe = cyclooctene, solv = acetone, THF and methanol) by Milstein and co-workers.[25b] Complete H/D exchange in the hydride and aromatic *ortho*-positions of complex **13** was achieved in 24 hours at room temperature or in 2 hours at 65°C in CD_3OD (Scheme 9, top). It was found that only the deuterium atoms of the O-D group are responsible for the H/D exchange because the CD_3 group of methanol-d_4 remained intact. H/D exchange of terminal olefins was also achieved in D_2O or CH_3OD at 60°C in the presence of catalyst **13**. Deuterium labeling was observed selectively in the vinylic positions of styrene but no other protons were substituted by deuterium (Scheme 9, bottom).



Scheme 10. H/D exchange of the complex **13** and catalytic H/D exchange in styrene

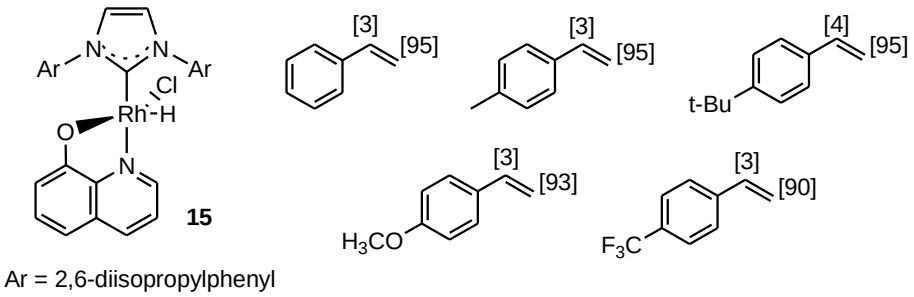
Recently, Jones *et al*. reported catalytic H/D exchange reactions of aromatic compounds mediated by a novel rhodium complex **14** with the chelate ligand, bis(3,5-dimethylpyrazol-1-yl)acetate (M^+=Li^+, Na^+).[8b] Trifluoroacetic acid-*d* was used as the deuterium source and the reaction was optimized by the addition of 3 equiv. of silver triflate which forms the active species *in situ* (Scheme 10). High deuterium incorporation in the aromatic positions was achieved. Furthermore, H/D exchange of

arenes bearing branched alkyl substituents was observed into the sp^3 β-C-H bonds but not into the usually more acidic α-C-H bonds.



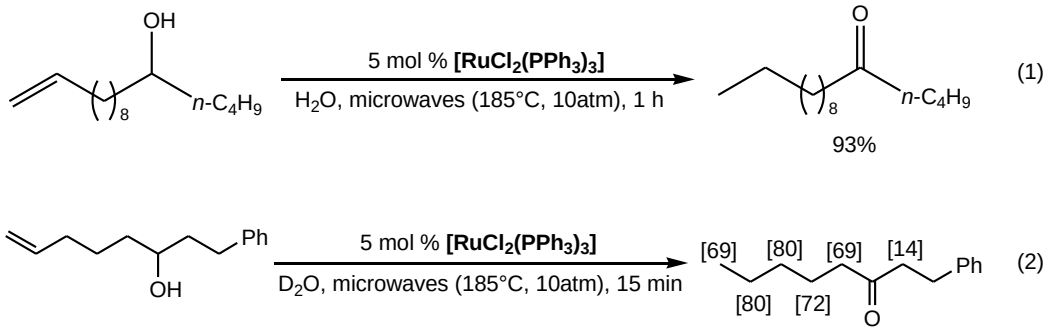
Scheme 11. H/D exchange of aromatic compounds catalysed by the rhodium complex **14**

A highly active and selective H/D exchange at the β-positions of aromatic α-olefins catalysed by a rhodium(III) complex (**15**) that contains a bulky *N*-heterocyclic carbene and a chelating quinolinate ligand was reported by Oro *et al*.[25c] Selective deuteration at the β-positions of aromatic alkenes was observed in the presence of 2 mol % of **15** in CD_3OD at 25°C in 2 to 6 hours (Scheme 12). The Oro group also introduced a rhodium NHC complex having a saturated imidazole skeleton and studied H/D exchange of styrene under the same reaction condition.[25d] Similar to the results with the complex **15**, a selective deuteration at the β-positions (92 %) of styrene was observed in 1 hour, while only a trace amount of deuterium incorporation was observed in the α-position.



Scheme 12. H/D exchange of aromatic alkenes catalysed by rhodium complex **15**

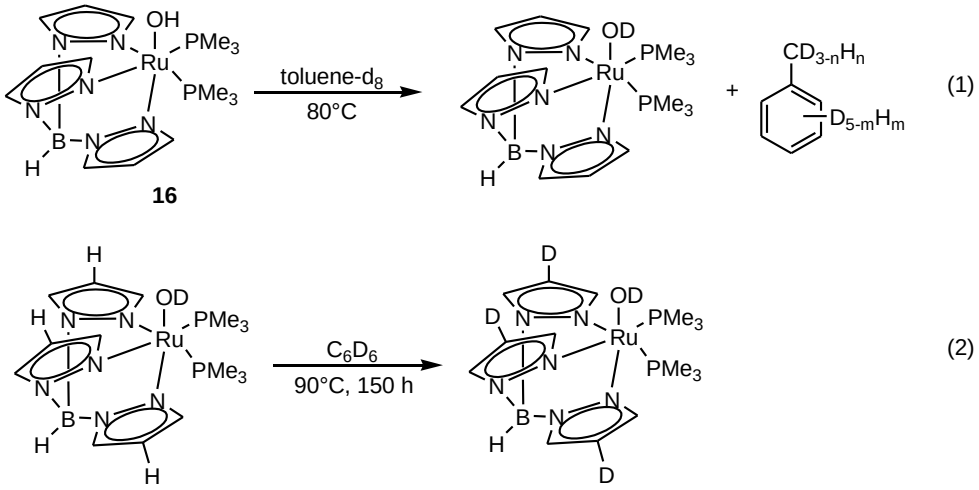
The use of homogeneous ruthenium complexes in H/D exchange reactions has been widely investigated in recent years.[26] Matsubara and co-workers introduced the isomerization of alkenols into alkanones through migration of the C-C double bond by using $[RuCl_2(PPh_3)_3]$ in water under microwave irradiation (Scheme 13, eq. 1).[26a] In addition, under similar reaction conditions, efficient H/D exchange reactions took place with substrates bearing electron donors, such as double bonds, hydroxyl groups and amino groups in D_2O (Scheme 13, eq. 2).



Scheme 13. Isomerization and H/D exchange reaction catalysed by $[RuCl_2(PPh_3)_3]$

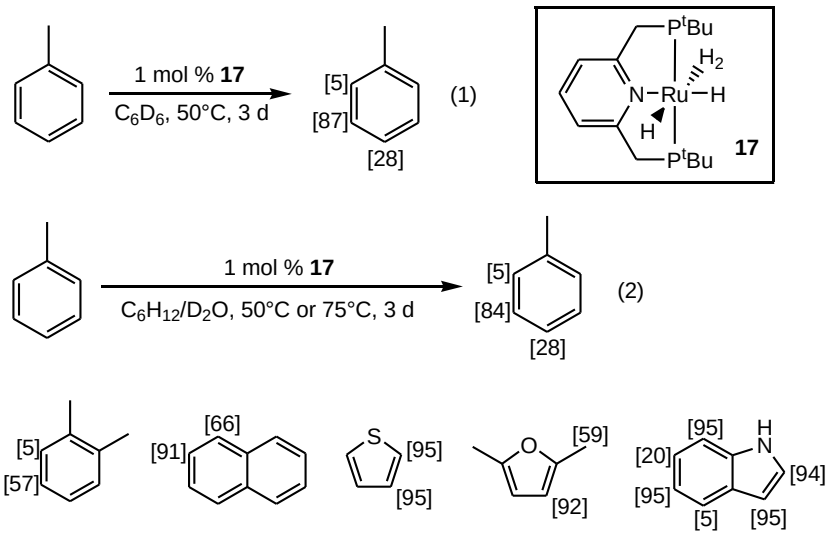
A regioselective H/D exchange between $TpRu(PMe_3)_2OH$ (**16**) and deuterated arene solvents, such as C_6D_6 and toluene-d_8, at elevated temperature was reported by Gunnoe *et al.*[26b] H/D exchange of the hydroxide ligand of **16** was achieved when the complex reacted in toluene-d_8 at 80°C (Scheme 14, eq. 1). Higher hydrogen incorporation was observed in the aromatic ring of toluene-d_8 compared to the methyl

group. In addition, regioselective H/D exchange at the 4-position of the Tp ligand was observed upon prolonged heating of **16** in C_6D_6 without the exchange at the 3- or 5-positions of Tp or the PMe_3 ligands (Scheme 14, eq. 2).



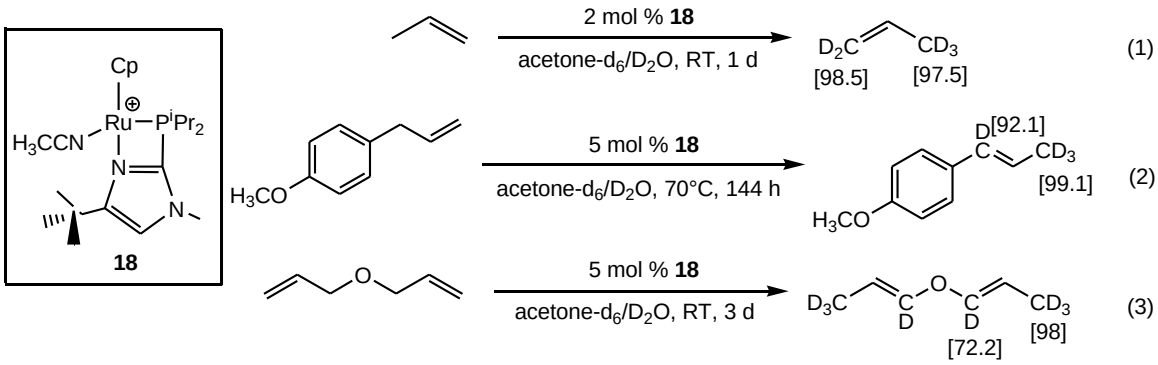
Scheme 14. Regioselective H/D exchange of the complex **16** in deuterated arenes

Leitner and co-workers introduced a selective and efficient H/D exchange of arenes at relatively low temperature (50°C) by using pincer-type ruthenium hydride complex **17**.[26c] In the case of toluene, high selectivity of H/D exchange at the *meta*-position was observed (Scheme 15, eq. 1). In addition to the use of C_6D_6, a two-phase solvent system comprised of cyclohexane and D_2O can be used as a deuterium source (Scheme 15, eq. 2). A significant chemo- and regioselectivity was observed in the reaction of aromatic and heteroaromatic compounds, such as thiophene and indole, in this biphasic solvent system.



Scheme 15. Selective H/D exchange of aromatic compounds in C_6D_6 and biphasic solvent system

H/D exchange reactions at allylic positions with excellent control of isomerization were achieved by using a bifunctional ruthenium catalyst **18**.[26d] A mixture of acetone-d_6 and a sufficient amount of D_2O, which can provide 20 deuterium atoms per an exchangeable proton, was used as the solvent for the exchange reaction. At room temperature, deuterium incorporation was observed only at the C1 and C3 positions of propene, whereas the single proton at the C2 position remained intact (Scheme 16, eq. 1). In the case of 4-allylanisole, similar deuteration at the C1 and C3 positions was observed upon heating at 70°C (Scheme 16, eq. 2). When a diallyl ether was used as the substrate, only (*E*,*E*)-dipropenyl ether was obtained as a result of isomerization, without any (*E*,*Z*)- or (*Z*,*Z*)-isomer being present. In the presence of D_2O, the H/D exchange at the C1 and C3 positions was achieved at room temperature (Scheme 16, eq. 3).

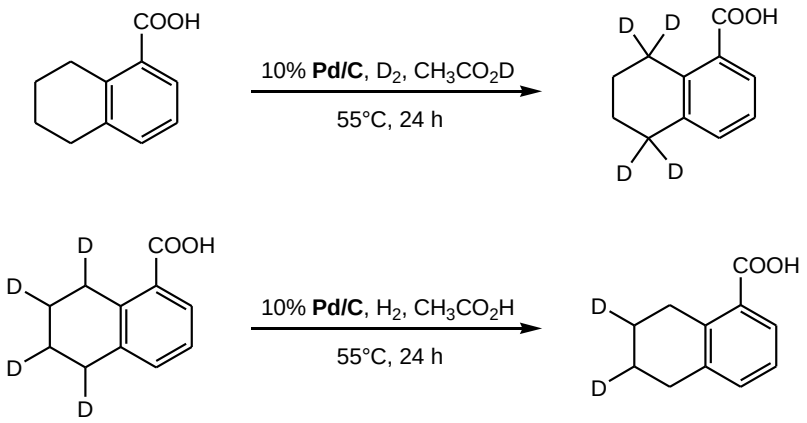


Scheme 16. H/D exchange of allylic compounds in a mixture of acetone-d_6 and D_2O

II.1.2. H/D exchange reactions catalysed by heterogeneous metal catalysts

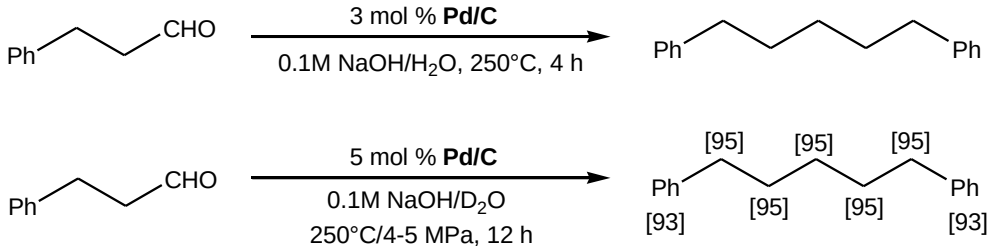
In general, heterogeneous metal catalysts have an important advantage over their homogeneous counterparts in that the catalyst can be easily removed by simple filtration from the mixture at the end of the reaction.[3] In the early work on heterogeneous H/D exchange reactions, palladium, platinum and rhodium catalysts were introduced.[27] In these studies, gaseous deuterium, D_2O and deuterated solvents were used as deuterium sources.

In early studies on heterogeneous catalytic deuteration palladium-based catalysts were usually used.[28] Selective deuteration in the benzylic positions of tetrahydronaphthalene carboxylic acid was reported by Stock and co-workers.[28a] The reaction of 5,6,7,8-tetrahydronaphthalene-1-carboxylic acid and deuterated acetic acid in the presence of Pd/C in the D_2 atmosphere showed a selective benzylic deuteration and generated the product, 5,6,7,8-tetrahydronaphthalene-carboxylic-5,5,8,8-d_4-acid (Scheme 17, top). In addition, protonation exclusively in the benzylic positions of 5,6,7,8-tetrahydronaphthalene-carboxylic-5,6,7,8-d_4-acid was achieved with acetic acid and H_2 (Scheme 17, bottom).



Scheme 17. A selective benzylic deuteration catalysed by Pd/C in acetic acid-d_1

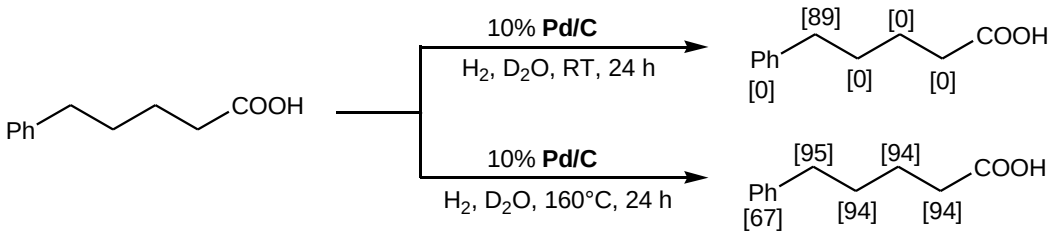
Matsubara *et al*. introduced palladium-catalysed decarboxylation of carboxylic acids and decarbonylation of aldehydes.[28b] Also, these degradation reactions can be used for the preparation of deuterated compounds. Complete deuteration of aromatic or aliphatic hydrocarbons was achieved under harsh reaction conditions. For example, the hydrocinnamaldehyde was transformed into 1,5-diphenylpentane through a decarbonylation reaction in the presence of Pd/C under hydrothermal conditions in aqueous NaOH (Scheme 18, top). The same reaction performed in D_2O instead of water formed the product with high deuterium incorporation (Scheme 18, bottom).



Scheme 18. Decarbonylative deuteration reaction catalysed by Pd/C

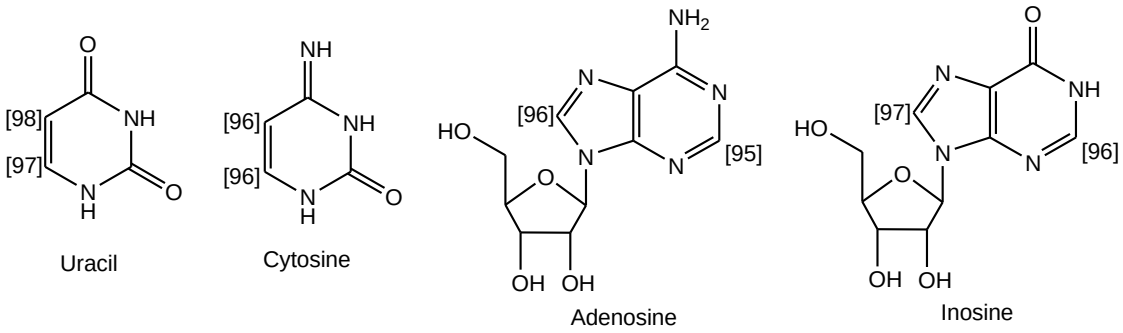
An efficient deuterium incorporation into different types of inactivated C-H bonds by using the Pd/C-D_2O-H_2 system was developed by Sajiki and co-workers.[28c] It was found that the H/D exchange between D_2O and organic compounds is dependent on

the temperature of the reaction. In the case of 5-phenylvaleric acid, considerable influence of the reaction temperature on the deuterium incorporation was observed (Scheme 19). Thus, the selective deuteration of the benzylic position was achieved at room temperature. On the other hand, at 160°C the less active aliphatic positions as well as arene C-H bonds were also involved in the H/D exchange reaction.



Scheme 19. Temperature dependent H/D exchange reaction

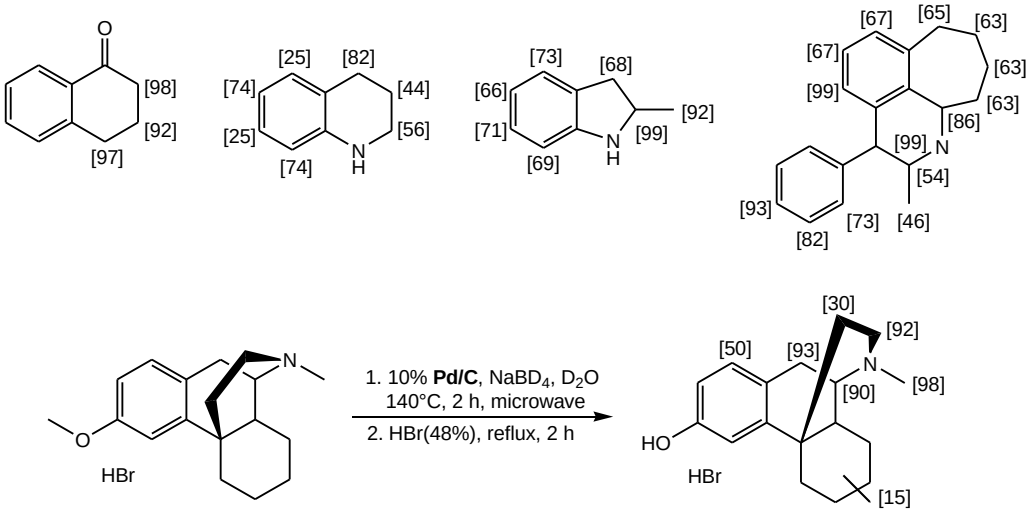
A selective H/D exchange reactions of biologically important pyrimidine bases and nucleosides was reported.[28d] In the reaction of uracil and cytosine, selective deuteration in the 5- and 6-positions was achieved in the presence of 10% Pd/C in D_2O at 160°C (Scheme 20). Moreover, the reaction of adenosine and inosine resulted in selective deuteration in the 2- and 8-positions under the same reaction conditions.



Scheme 20. H/D exchange of pyrimidine bases and nucleosides

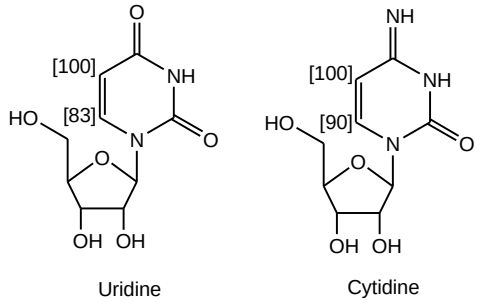
Derdau and Atzrodt reported an efficient method for H/D exchange of various aromatic compounds.[28e] Moderate to high deuterium incorporation was observed in the reaction of carbocyclic compound 1-tetralone, tetrahydroquinoline, indole derivatives and the highly substituted piperidine derivative in D_2O in the presence of

10% Pd/C and 5 mol % $NaBD_4$ used as an activator (Scheme 21, top). This catalytic condition was also applied for the preparation of deuterated dextrorphan, which is frequently used for the investigation of the selective enzyme inhibition of cytochrome P450 2D6 in drug development (Scheme 21, bottom).



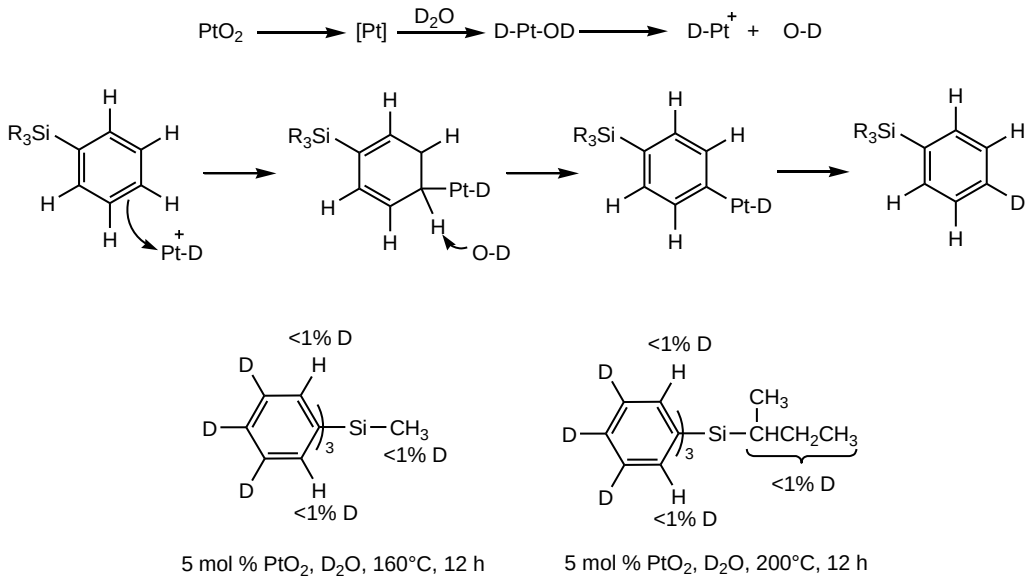
Scheme 21. H/D exchange of heterocycles and the preparation of deuterated dextrorphan

Platinum-catalysed H/D exchange reactions have shown essentially similar results as the palladium-catalysed reactions.[29] By irradiation with ultraviolet light or γ-radiation, PtO_2 can be activated and used as a catalyst for the selective deuteration of nucleosides.[29a] The 5-positions of uridine and cytidine were completely deuterated at ambient temperature, although the reaction required an almost stoichiometric amount of PtO_2 (catalyst : substrate = 1 : 1.1) (Scheme 22). The reactions with PtO_2 were found to be more dependent on the amount of catalyst than the reaction temperature, whereas high reaction temperatures were required in the case of Pd/C.[29d]



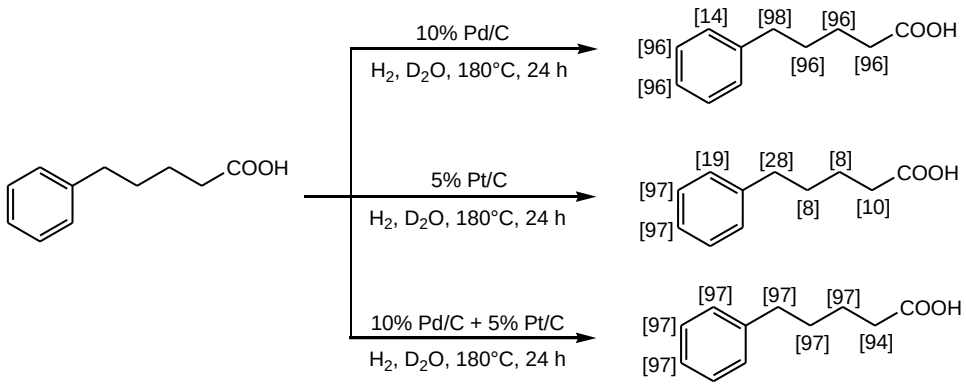
Scheme 22. H/D exchange of nucleosides catalysed by PtO_2

The formation of metallic platinum from PtO_2 under hydrothermal conditions was studied by Matsubara *et al*.[29b] The insertion of the metallic platinum into D_2O generates the complex D-Pt-OD, which can then dissociate with the formation of the cationic D-Pt^+ species (Scheme 23). The aromatic ring of aryl silanes interacts with D-Pt^+ and a selective H/D exchange in the aryl ring of the silanes can be achieved. Due to the steric hindrance, the deuterium incorporation at the *ortho* positions was not obtained.



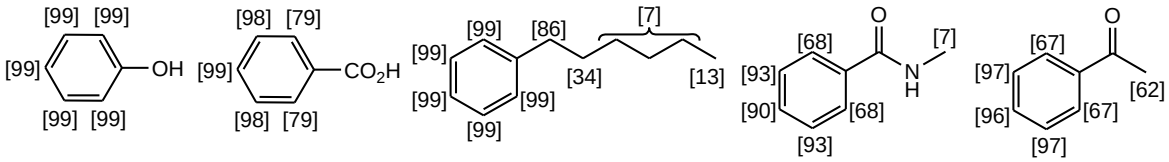
Scheme 23. The formation of D-Pt^+ and H/D exchange of aryl silanes

Mixed catalyst systems of palladium and platinum can be used for the deuteration of aromatic compounds.[29c] The reaction of 5-phenylvaleric acid catalysed by a mixture of Pd/C and Pt/C showed high deuterium incorporation in all C-H bond positions including the sterically hindered *ortho* position, whereas only 14% and 19% of H/D exchange at the *ortho* position was achieved with Pd/C and Pt/C catalysts, respectively, when they were used alone (Scheme 24). A synergistic effect of the mixed catalyst was postulated, although the possible reaction mechanism is still unknown.



Scheme 24. H/D exchange of 5-phenylvaleric acid catalysed by Pd/C-Pt/C mixed catalyst

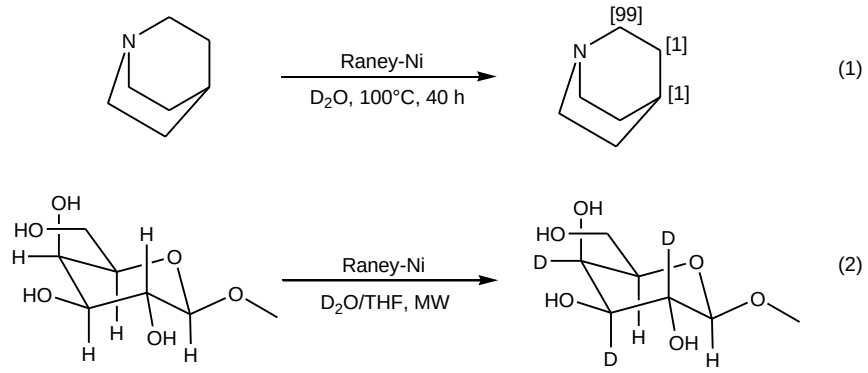
Recently, an efficient H/D exchange reaction of arenes bearing different functional groups in the mixture of Pr^iOH-cyclohexane-D_2O and Pt/C was reported.[29d] The possible up-front deuterium sources are both D_2O and Pr^iOD, which can be generated by mixing Pr^iOH and D_2O. Various aromatic compounds bearing alcohol, carboxyl, alkyl, amide and carbonyl functional groups were readily deuterated under argon atmosphere (Scheme 25).



Scheme 25. H/D exchange of various aromatic compounds

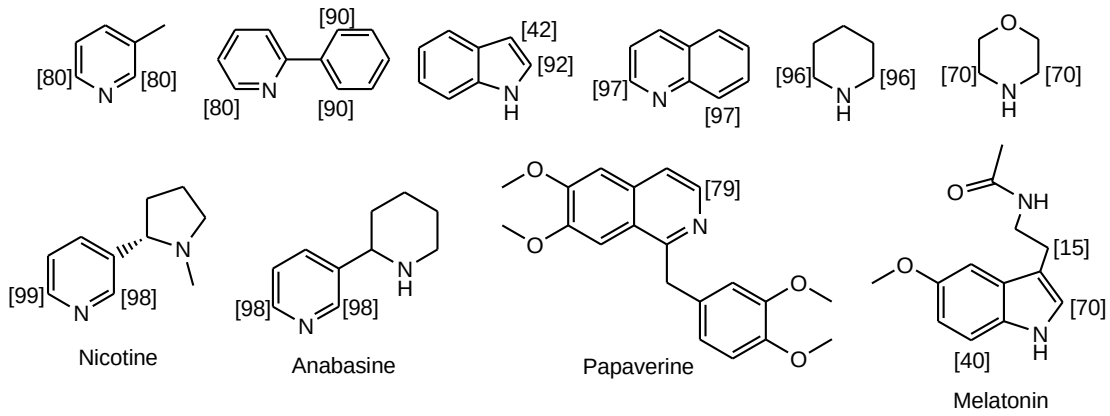
Since the first study of H/D exchange reactions catalysed by Raney nickel was reported by Lauer *et al.*[30a] and Bonner,[30b] Raney nickel has been used for the H/D exchange reactions of aromatic substrates.[30] A selective deuteration at the α-position of quinuclidine was achieved by Dinnocenzo and co-workers.[30c] High deuterium incorporation was observed at the α-carbon atoms in the presence of Raney nickel at elevated temperature, whereas less than 1% of deuteration was observed at the β- and γ-positions (Scheme 26, eq. 1). A microwave-assisted deuteration by using Raney

nickel was investigated by Cioffi and co-workers.[30d,e] This catalytic reaction allowed deuteration of non-reducing carbohydrates with the retention of configuration. Heating the substrate, 1-*O*-methyl-β-$_D$-galactopyranoside, for 15 seconds up to 36 times in a simple multi-mode domestic microwave oven showed positive results for the exchange of C-H and C-D bonds in the model carbohydrate without epimerization or decomposition of the compound (Scheme 26, eq. 2).



Scheme 26. Raney nickel catalysed H/D exchange reactions

Very recently, selective deuteration of nitrogen containing compounds was achieved in the presence of ruthenium nanoparticles under mild reaction condition.[30f] Efficient H/D exchange of a large diversity of heterocycles, such as pyridines, quinolines and indoles, was observed when 3 % RuNp@PVP (Np : nanoparticles, PVP : polyvinylpyrrolidone) and 1 - 2 bar of D_2 were used as a catalyst and a deuterium source, respectively (Scheme 27, top). Reactions were achieved at room temperature or 55°C and the labeled products were recovered by simple filtration. In addition, deuterium labeling of biologically active compounds, such as nicotine, anabasine, papaverine and melatonin, was achieved under the same condition (Scheme 27, bottom). It is important to mention that the level of isotopic enrichment is suitable for metabolomic studies in most cases.



Scheme 27. Ru nanoparticle catalysed H/D exchange

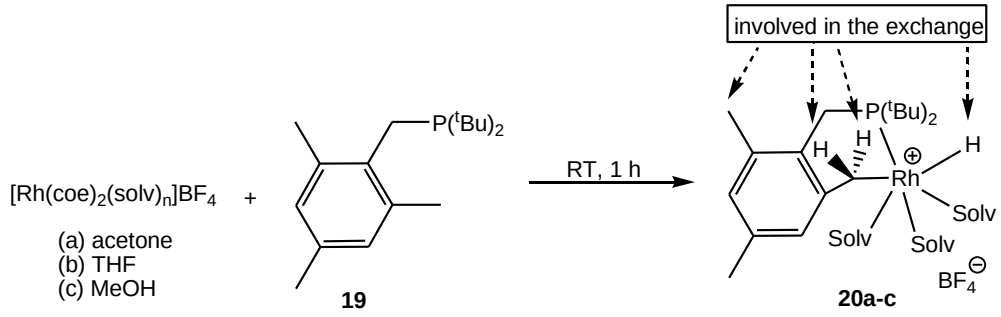
II.1.3. C-H bond activation catalysed by transition metal complexes

Hydrocarbons are inexpensive and the most abundant feedstock for organic chemicals.[31,32] In addition, they are readily available from petrochemicals and natural gas. Preparation of value-added chemicals by an efficient and selective activation of C-H bonds of hydrocarbons presents an appealing alternative to the conventional methods which will have a large economic advantage.[31a] Furthermore, the functionalization of unreactive C-H bonds can bring the development of new synthetic routes to pharmaceuticals and natural products and new methods for the production of molecular materials and polymers.[32b] However, functionalization of hydrocarbons that involves the cleavage of C-H bonds is a highly difficult task because the C-H bonds in hydrocarbons are thermodynamically strong and kinetically inert.[31a]

Since the early studies on C-H bond activation with transition metal complexes,[33-35] the research of stoichiometric[36] and catalytic[37] C-H bond activation has been widely investigated. Homogeneous catalysis mediated by transition metal complexes, heterogeneous C-H bond activation by metal surfaces and reactions of alkanes with ions in the gas phase are the most efficient ways to achieve highly active and selective C-H bond activation.[31b] With the increasing number of reports for the C-

H activation catalysed by transition metal complexes,[38] deuterium incorporation into the C-H bonds of organic compounds has been also intensively studied. Deuterium labeling of organic molecules is important not only for the use of deuterated solvents for NMR spectroscopy but also for the investigation of mechanistic pathways of organic or organometallic reactions.[39-43]

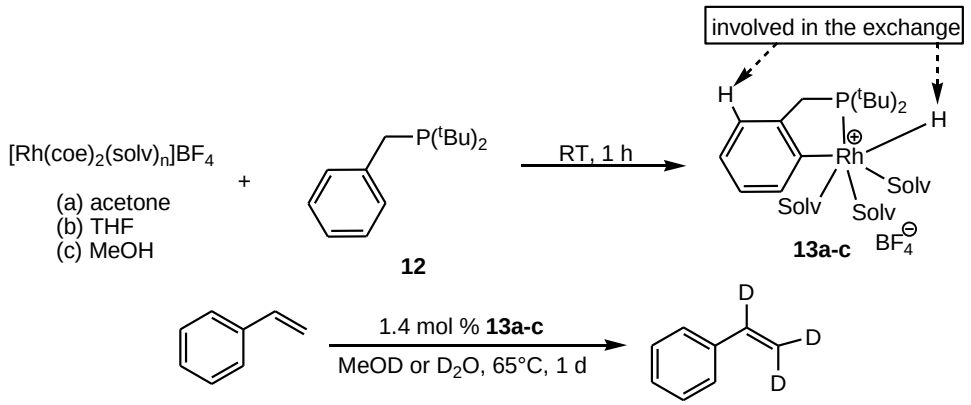
Milstein and co-workers reported alkylrhodium(III) hydride complexes that are stabilized by solvent coordination.[39a,44] The rhodium complexes **20a-c** showed an interesting mode of reversible C-H bond activation, which is presumably controlled by strong agostic interactions (Scheme 28). The selective irradiation of the hydride signal of **20** in spin saturation transfer experiments revealed that the two methylene protons of the Rh-CH_2-aryl unit, the *ortho* methyl protons and the hydride are involved in the exchange upon increasing temperature. No H/D exchange was observed between **20** and deuterated solvents, such as acetone-d_6, methanol-d_4 and D_2O.



Scheme 28. Exchange observed in the rhodium complexes

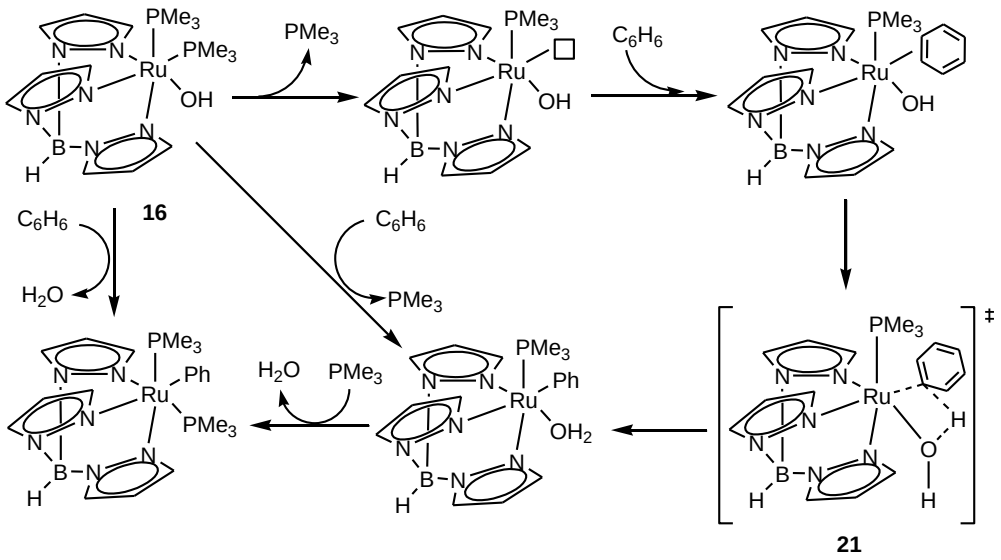
Later, these workers also reported similar PC-Rh (PC = phosphine ligand) complexes based on the ligand **12** (Scheme 29, top).[39b] In this case, chemical exchange between the hydride of **13a-c** and the *ortho* proton of the aryl ligand was observed at 23°C in spin saturation transfer experiments involving selective irradiation of the hydride ligand. The complex **13** promoted selective catalytic H/D exchange between the vinylic hydrogens of terminal olefins and deuterium sources, such as D_2O and

CH_3OD, whereas the complex **20** did not show H/D exchange with deuterated solvents (Scheme 29, bottom). Based on their computational DFT study, Milstein *et al*. explained the different reactivity of two complexes in terms of the differences in agostic C-H bonding of the aliphatic (ligand **19**) and aromatic (ligand **12**) PC-Rh systems.



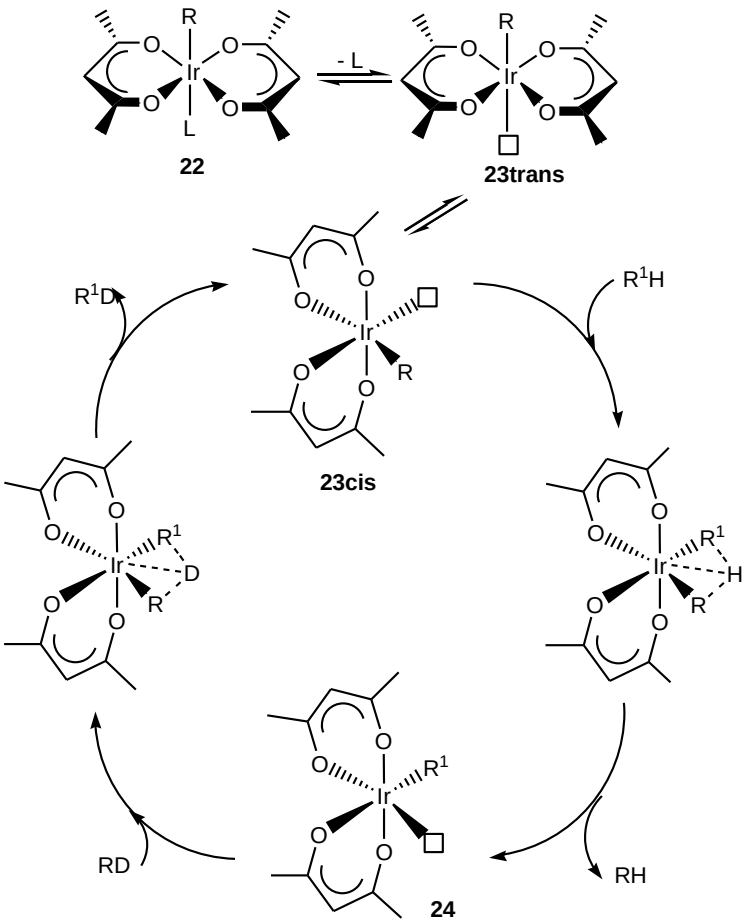
Scheme 29. Exchange observed in **13** and H/D exchange of the hydrogens of styrene

Gunnoe and co-workers introduced the ruthenium hydroxide complex $TpRu(PMe_3)_2OH$ (**16**).[41a] H/D exchange at the hydroxide ligand of **16** and the formation of $C_6D_{6-x}H_x$ were observed when a mixture of **16**, H_2O and C_6D_6 was heated at 80°C. The proposed mechanism for the H/D exchange involves dissociation of PMe_3 and reversible addition of the C-H bond of benzene across the Ru-OH bond. This would produce the intermediate $TpRu(PMe_3)(Ph)(HOD)$ (**21**) and provide a pathway for H/D scrambling between the hydroxide and C_6D_6 (Scheme 30).



Scheme 30. A possible mechanism of the H/D exchange of **16** and C_6D_6

Periana *et al*. introduced a novel iridium complex, $(acac\text{-}O,O)_2Ir(R)(L)$ (**22**) (R = acac (acetylacetonate), alkyl and aryl , L = pyridine) and studied C-H activation of arenes in the presence of **22**.[38b,40b] It was found that the ligand exchange occurs via coordination of substrate and formation of *trans*-five-coordinate intermediate (**23trans**), while their experimental and theoretical studies showed that the C-H activation requires further reaction of **23trans** to generate the *cis*-intermediate, **23cis**, before reaction. Overall the C-H activation with **22** occurs via a loss of pyridine ligand to generate a *trans*-five-coordinate intermediate **23trans**, which can be isomerized to the *cis*-intermediate **23cis**. Coordination of benzene generates a phenyl complex (**24**), which can enters the C-H activation step (Scheme 31).



Scheme 31. A proposed mechanism of the H/D exchange via arene C-H activation by **22**

II.2. Reduction of pyridine derivatives with silanes

The catalytic hydrosilylation of nitrogen containing compounds is an important transformation allowing for the formation of useful *N*-containing heterocycles, imines and amines, which find applications in the synthesis of pharmaceutically active ingredients and in agrochemistry.[12c] In particular, the dearomatization of pyridine and pyridine derivatives gives rise to a range of functionalized compounds that can be used for further synthesis.[51] Although these transformations can be achieved by various reducing reagents, they usually proceed in several steps. Direct addition of silanes to nitrogen containing heterocycles is challenging and usually requires harsh reaction conditions. There are only a handful examples of catalytic hydrosilylation of amides, nitriles and nitroarenes,[47c-f] and the hydrosilylation of pyridine derivatives is especially rare. Therefore, the development of efficient catalysts for this reductive transformation is a remaining synthetic challenge.

II.2.1. Hydrosilylation and hydroboration of pyridine derivatives

Reduction of pyridine derivatives has attracted much attention because the possible products, dihydropyridines, are important building blocks of natural compounds.[13,47] Dihydropyridines are often found in pharmaceutical and biological compounds, such as the coenzyme reduced nicotinamide adenine dinucleotide (NADH) (Figure 2, left), and in Hantzsch esters (Figure 2, right), which are used in some countries (e.g. China) in agrochemistry.

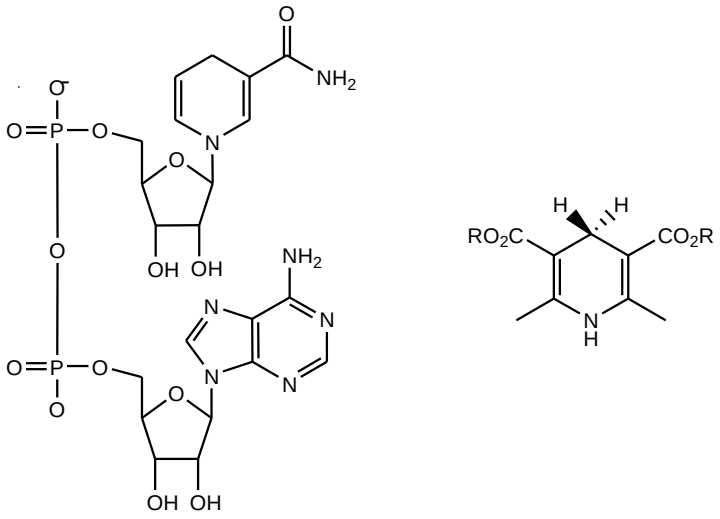
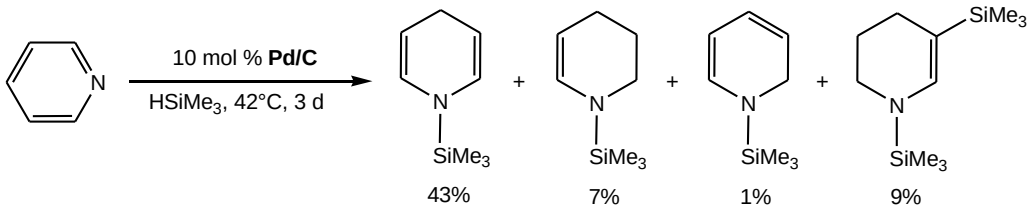


Figure 2. NADH (left) and Hantzsch ester (right)

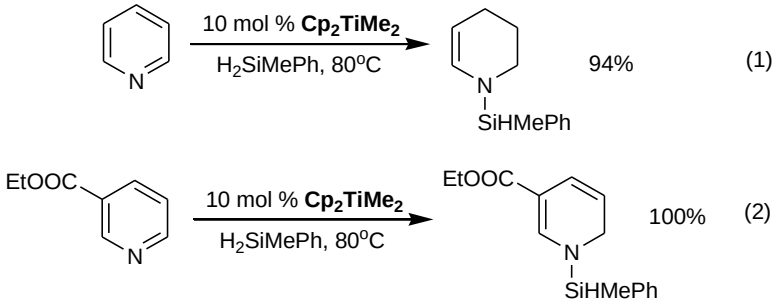
Catalytic additions of silanes to pyridine derivatives has been scarcely studied. Especially, the selective reduction of stable aromatic compounds is a challenging task. The first example of hydrosilylation of pyridines was introduced by Cook and Lyons in 1965.[48] They found that the reaction between pyridine and $HSiMe_3$ at 42°C in the presence of a heterogeneous palladium catalyst generates the 1,4-addition product, *N*-silyl dihydropyridine, as well as 1,2-regioisomers and silylated tetrahydropyridines (Scheme 32).



Scheme 32. Hydrosilylation of pyridine in the presence of Pd catalyst

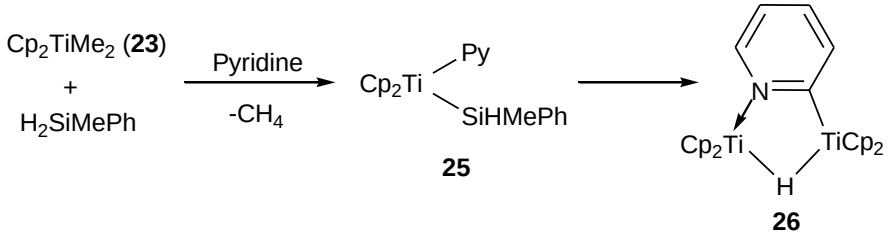
The first hydrosilylation of pyridine derivatives with a homogeneous catalyst, Cp_2TiMe_2, was reported by Harrod and co-workers.[49] The reactions were performed with 2 equiv. $H_2SiMePh$ in the presence of 10 mol % of the titanium catalyst at 80°C.

Partially hydrosilylated pyridine was obtained with 94% yield in 8 hours (Scheme 33, eq. 1). This group found that the reactions tolerate certain functional groups, such as ester groups. High chemoselectivity was observed in the reaction of nicotinic ester (Scheme 33, eq. 2). The 1,2-addition product was selectively produced with a quantitative yield.

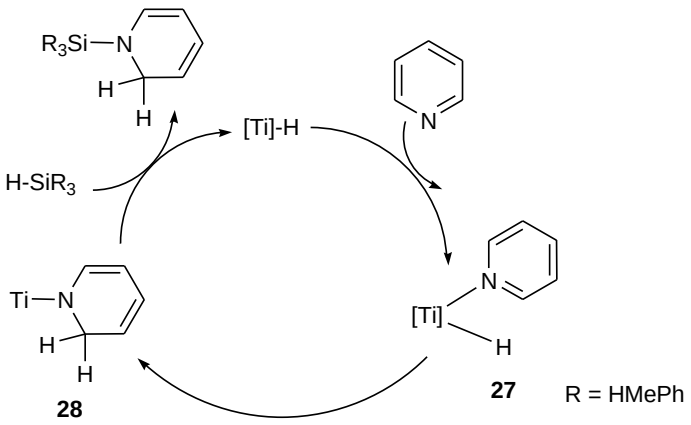


Scheme 33. Hydrosilylation of pyridine in the presence of Cp_2TiMe_2

It was found that a stoichiometric reaction of Cp_2TiMe_2 and $H_2SiMePh$ in the presence of excess pyridine proceeded via the titanium silyl complex **25**, which then slowly converts into the hydride bridged bimetallic titanium complex **26** (Scheme 34). Based on their experimental results, Harrod *et al*. suggested a Ti-H based catalytic cycle (Scheme 35). According to this mechanism, the catalytic cycle starts with the formation of a key intermediate Ti-H species. Coordination of pyridine affords the hydride pyridine adduct **27** which undergoes insertion of the N=C bond into the Ti-H bond to give a 1,2-dihydropyridyl derivative **28**. The latter species then undergoes σ-bond metathesis between the Ti-N and Si-H bonds to produce the final product and regenerates the catalytic Ti-H species.

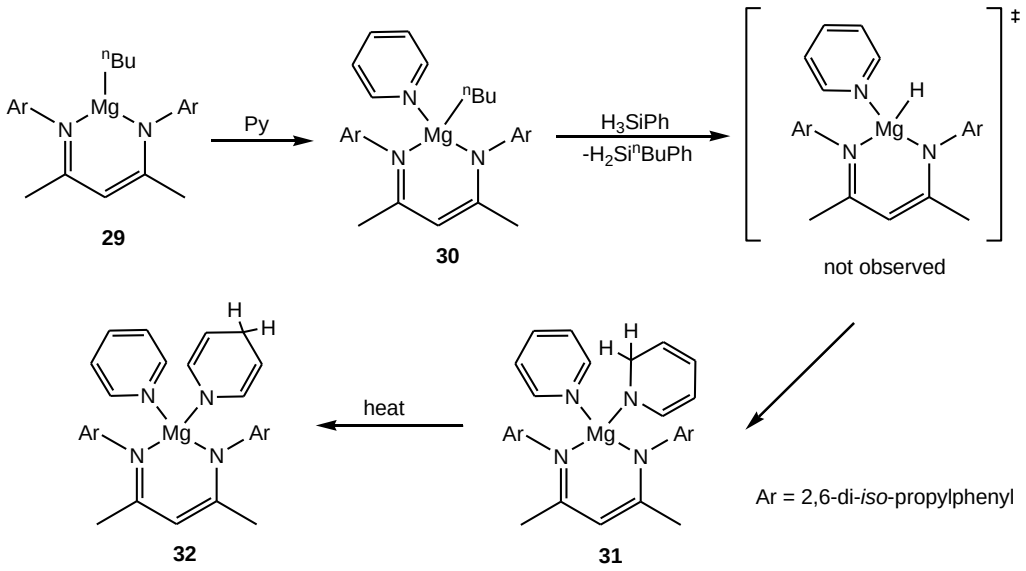


Scheme 34. The stoichiometric reaction of Cp_2TiMe_2 and $H_2SiMePh$



Scheme 35. The proposed mechanism of hydrosilylation of pyridine catalysed by Cp_2TiMe_2

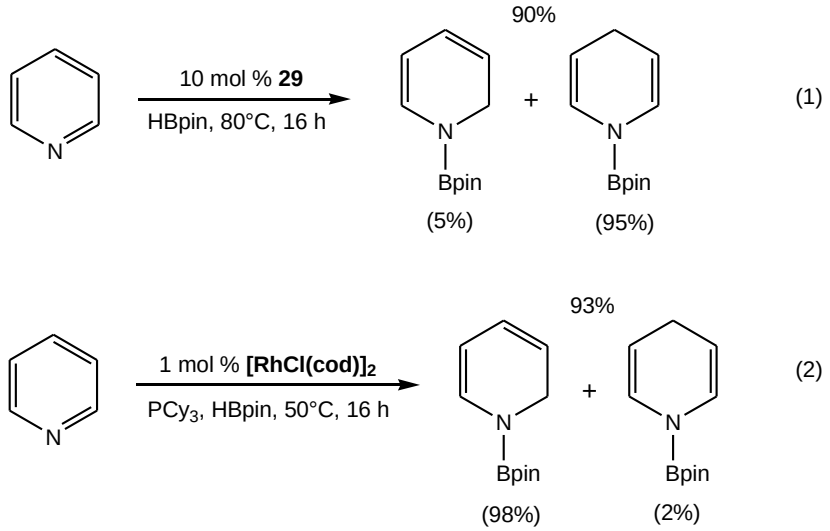
Hill *et al*. reported a reaction of the *β*-diketiminato-supported *n*-butyl magnesium complex $[HC\{(CH_3)CN(2,6\text{-}Pr^i_2C_6H_3)\}]_2Mg\text{-}^nBu$, **29**, with pyridine (Scheme 36).[50] This reaction produced a pyridine adduct of the *n*-butylmagnesium starting material, **30**, which appears to be the first example of a magnesium alkyl species containing a *N*-donor co-ligand. Two isomeric 1,2- (**31**) and 1,4-dihydropyridide (**32**) fragments along with *n*-butylphenylsilane were obtained upon the addition of H_3SiPh to **30**. Heating the mixture solution at 60°C for 12 hours resulted in complete conversion to the 1,4-dihydropyridide isomer.



Scheme 36. The reaction of **30** with H_3SiPh

These workers also studied catalytic hydroboration of pyridine derivatives in the presence of complex **29** (Scheme 37, eq. 1).[51a] A high regioselectivity towards the 1,4-addition product was observed in the reaction of pyridine with HBpin in 16 hours at 80°C. However, almost a 1:1 ratio of the 1,2- and the 1,4-addition products was obtained in 2 days at a lower temperature. Pyridine derivatives bearing methyl and phenyl groups reacted with HBpin and generated the corresponding *N*-Bpin-1,2- and/or *N*-Bpin-1,4-dihydropyridine derivatives. On the other hand, the results did not show tolerance toward aldehyde, ester and cyano groups.

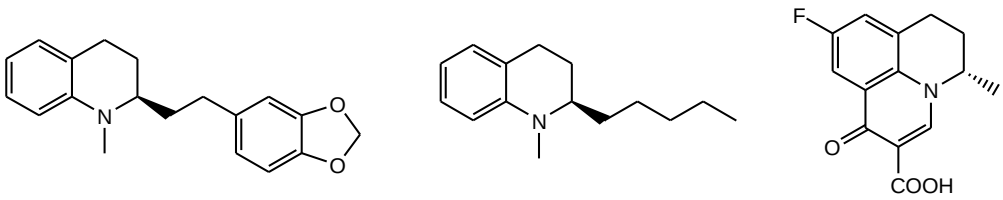
More recently, another example of hydroboration of pyridines has been reported by Ohmura and Suginome *et al.*[51b] They used $[RhCl(cod)]_2$ (cod = cyclooctadiene) as a catalyst and different phosphine ligands, such as PCy_3 and PPh_3 were screened. Under their catalytic conditions, a high selectivity towards the 1,2-addition product was observed (Scheme 37, eq. 2).



Scheme 37. Hydroboration of pyridine catalysed by **29** and $[RhCl(cod)]_2$

II.2.2. Reduction of quinoline derivatives

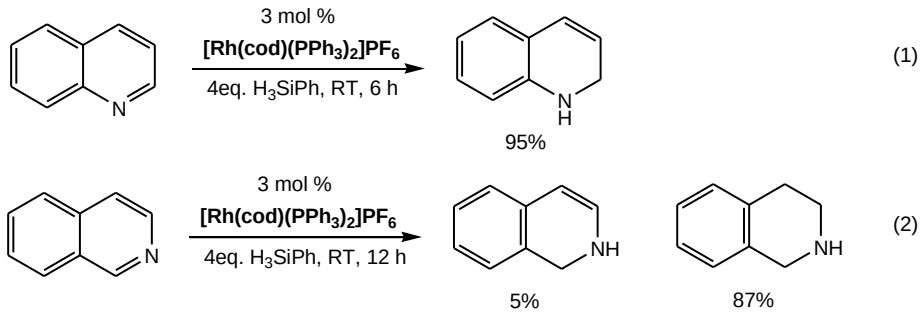
Reduction of quinolines has been considered as an important reaction due to the pharmaceutical and biological importance of the possible products.[52] Especially, 1,2,3,4-tetrahydroquinoline derivatives have attracted considerable attention not only due to their important roles in the synthesis of drugs, agrochemicals and dyes but also as structural moieties in natural occurring alkaloids (Figure 3).[52d,54b]



(+)-galipinine (-)-angustureine (*S*)-flumequine

Figure 3. Bioactive alkaloids containing 1,2,3,4-tetrahydroquinoline

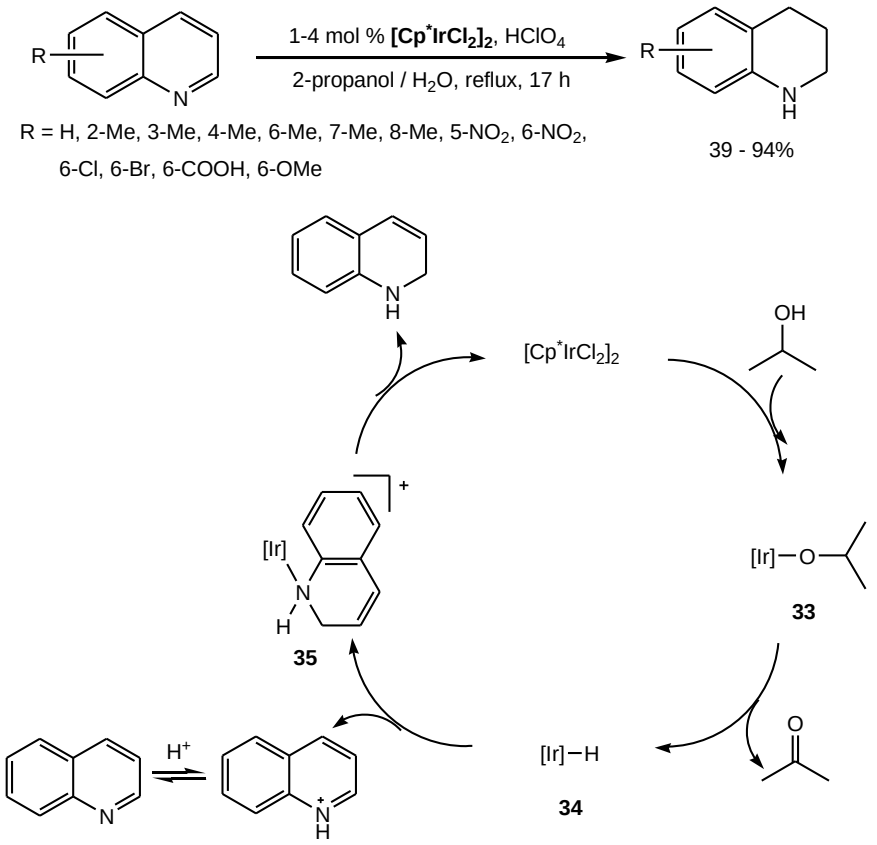
Hydrosilylation of quinoline derivatives was for the first time observed by Crabtree *et al*.[53a] The reactions were mediated by $[Rh(cod)(PPh_3)_2]PF_6$ in the presence of excess H_3SiPh. Two possible products, the dihydro- and tetrahydroquinoline derivatives, can be obtained depending on the nature of the substrate and the catalytic conditions. Based on their mechanistic experiments, Crabtree *et al*. concluded that the active reducing species in the mixture was the silane SiH_4, which presumably was formed as a result of silane rearrangement.[53b] In the case of hydrosilylation of quinoline, the 1,2-dihydroquinoline was obtained as a sole product (Scheme 38, eq. 1). The reaction of isoquinoline, however, produced a mixture of the dihydro- and tetrahydro- derivatives, although a high regioselectivity towards the tetrahydro- derivative was observed (Scheme 38, eq. 2).



Scheme 38. Hydrosilylation of quinoline derivatives catalysed by $[Rh(cod)(PPh_3)_2]PF_6$

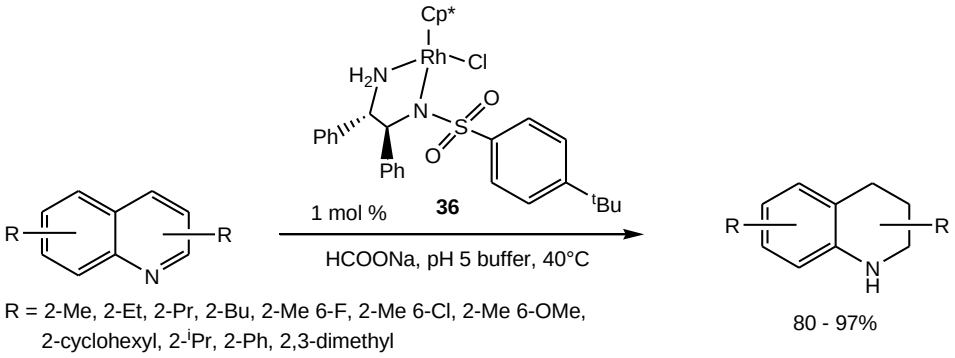
It is also relevant to mention that Fujita and Yamaguchi *et al*. reported Cp^*Ir-catalysed transfer hydrogenation of quinoline derivatives in the mixture of 2-propanol and H_2O (95 : 5).[54a] In the presence of catalytic amount of the catalyst, $[Cp^*IrCl_2]_2$, 1,2,3,4-tetrahydroquinoline was obtained in 76% yield. The addition of acid, $HClO_4$, significantly accelerated the reaction so that the same product was generated in 93% yield (Scheme 39, top). These workers also achieved transfer hydrogenation of quinoline derivatives which contained different functional groups, such as alkyl, halogen, carboxyl and methoxy groups, under the same reaction conditions. A possible mechanism would involve the formation of the iridium isopropoxide **33** by the reaction of the catalyst with 2-propanol (Scheme 39, bottom). Then *β*-H elimination from alkoxide affords acetone and iridium hydride **34**. The insertion of the carbon-nitrogen double bond of quinolinium ion generated by the protonation of quinoline into the iridium-hydride bond of **34** would generate the 1,2-dihydroquinoline intermediate **35**. Dissociation of the heterocycle closes the catalytic cycle. Then the reaction is completed essentially by repetition of these steps: the carbon-carbon double bond of 1,2-dihydroquinoline inserts into the iridium-hydride bond of **34** followed by protonolysis to give 1,2,3,4-tetrahydroquinoline as a final product. Although the 1,2-dihydroquinoline intermediate could not be detected, this

mechanism is supported by the fact that the reaction of 1,2-dihydroquinoline under the similar condition produced 1,2,3,4-tetrahydroquinoline in high yield.



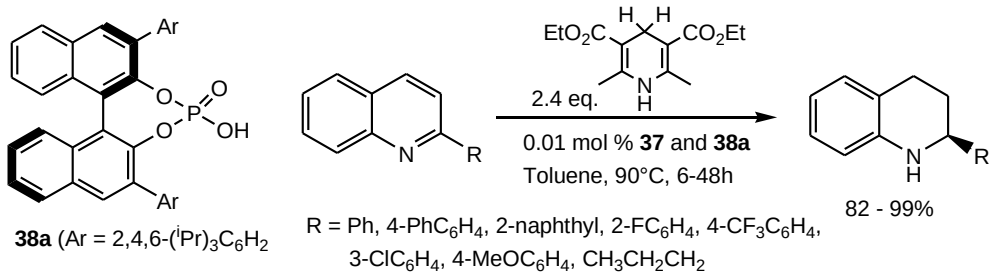
Scheme 39. Transfer hydrogenation of quinoline derivatives catalysed by $[Cp^*IrCl_2]_2$ (top) and the proposed mechanism (bottom)

Asymmetric transfer hydrogenation of quinoline[54b] and pyridine derivatives[54c] was introduced by Xiao and co-workers. The rhodium complex **36** containing a Ts-dpen (diphenylethylenediamine) ligand was prepared from the 4-*tert*-butylphenyl-substituted ligand and $[(Cp^*RhCl_2)_2]$. The reactions were performed in an aqueous formate solution buffered to pH 5 with HCOONa (Scheme 40). High yields and excellent enantioselectivities (86 - 98%) were observed for a broad range of substituted quinolines.



Scheme 40. Transfer hydrogenation of quinoline derivatives catalysed by **36**

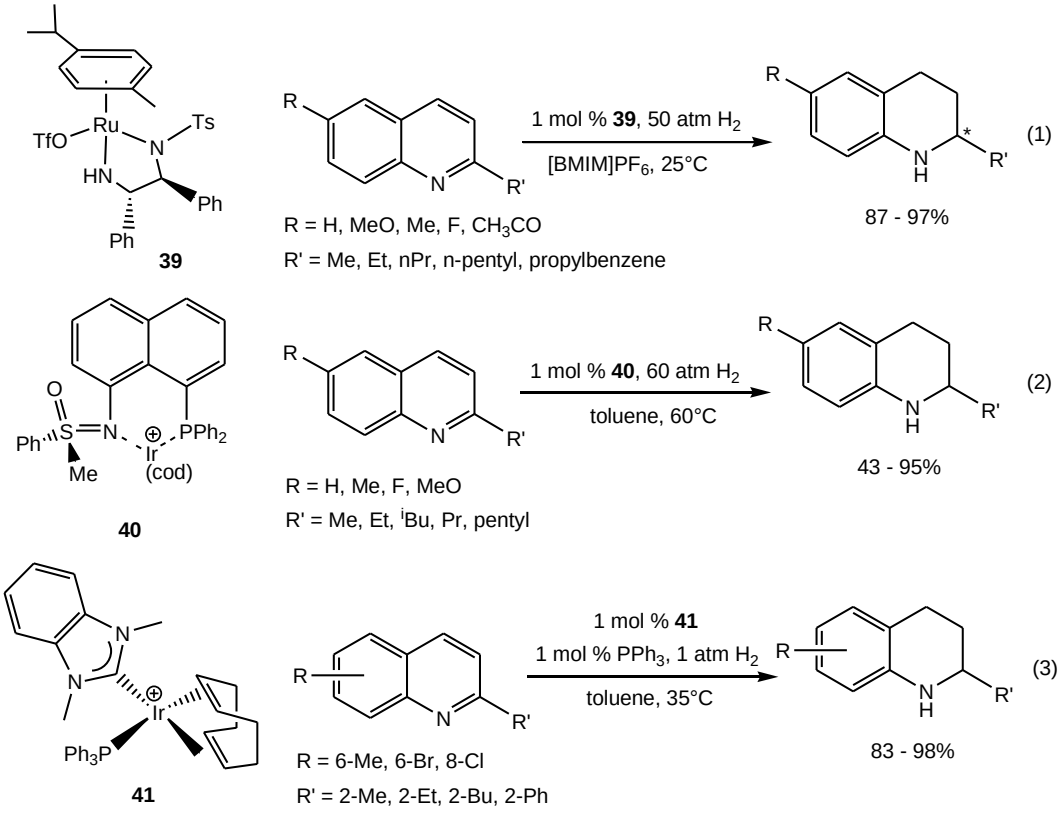
Recently, Gong and co-workers reported a highly efficient asymmetric transfer hydrogenation of quinolines catalysed by *in situ* generated chiral gold phosphate complex, [(IMes)AuMe] (**37**) (IMes = 1,3-bis-(2,4,6-trimethylphenyl)imidazol-2-ylidene).[54d] Hantzsch ester was used as the hydrogen source and the addition of a chiral phosphoric acid **38a** improved the stereochemical outcome to 93 - 98% *ee*. In the presence of a very small amount of **37**, different quinoline derivatives were reduced to tetrahydroquinolines (Scheme 41).



Scheme 41. Asymmetric transfer hydrogenation of quinolines catalysed by **37**

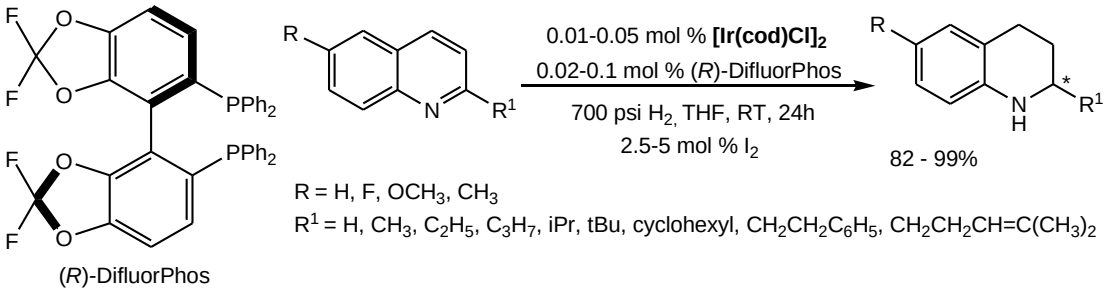
Enantioselective hydrogenation of quinoline was reported by Chan and co-workers.[55a] They introduced the first phosphine free cationic Ru/Ts-dpen catalyst **39**, which efficiently catalysed hydrogenation of quinoline derivatives in neat ionic liquid, 1-*n*-butyl-3-methylimidazolium ([BMIM]PF_6), to generate tetrahydroquinolines in high yields and enantioselectivity (Scheme 42, eq. 1). The use of an ionic liquid enhances the stability and facilitates the recyclability of the catalyst. Chan *et al*.

suggested a mechanism, which involved proton transfer from the ruthenium dihydrogen complex to quinoline followed by hydride transfer to the protonated substrate. Bolm *et al*. also introduced asymmetric hydrogenation of quinolines with the iridium complex (**40**) and naphthalene-bridged P,N-type sulfoximine ligands.[55b] The complex **40** was readily synthesized from the reaction of $[Ir(cod)Cl]_2$ and the ligand. In the presence of the catalyst, tetrahydroquinolines were obtained with moderate to good yields and good enantioselectivity (Scheme 42, eq. 2). Recently, hydrogenation of quinoline derivatives under low hydrogen pressures mediated by an air- and moisture-stable catalyst was reported by Crabtree and co-workers.[55c] They found that the ancillary NHC ligand is crucial and the addition of PPh_3 significantly improves the activity of the catalyst. In the presence of the catalyst **41**, a wide variety of quinolines having functionalities at the 2-, 6-, and 8-positions were reduced under 1 atm H_2 pressure and at ambient temperature (Scheme 42, eq. 3).



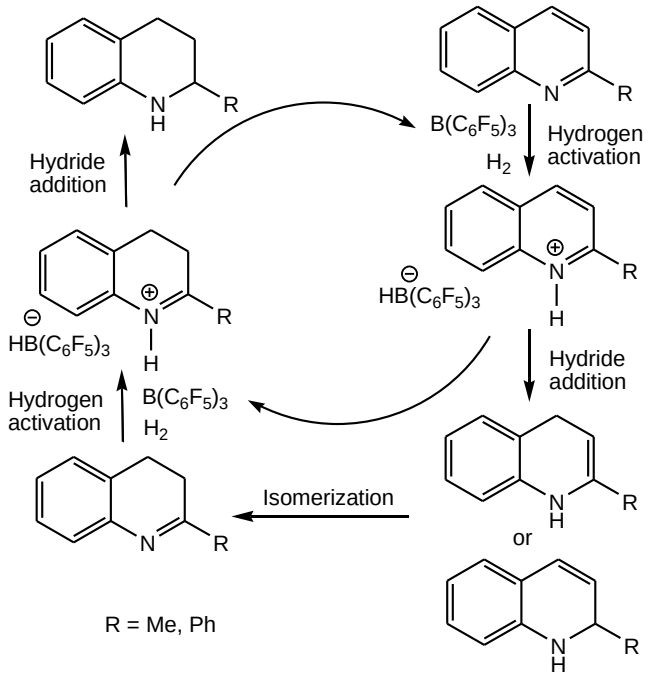
Scheme 42. Hydrogenation of quinoline derivatives catalysed by metal complexes

Highly efficient asymmetric hydrogenation of quinoline derivatives with $[Ir(cod)Cl]_2$ and commercially available diphosphine ligand ((*R*)-DifluorPhos) was reported by Xu and co-workers.[55d] It is found that the catalytic performance is related to the amount of additive I_2 since no reaction took place in the absence of iodine. Asymmetric hydrogenation of various quinolines was carried out with their system at high substrate/catalyst ratios (2000-50000) at room temperature. High isolated yields and excellent enentioselectivities were observed (Scheme 43).



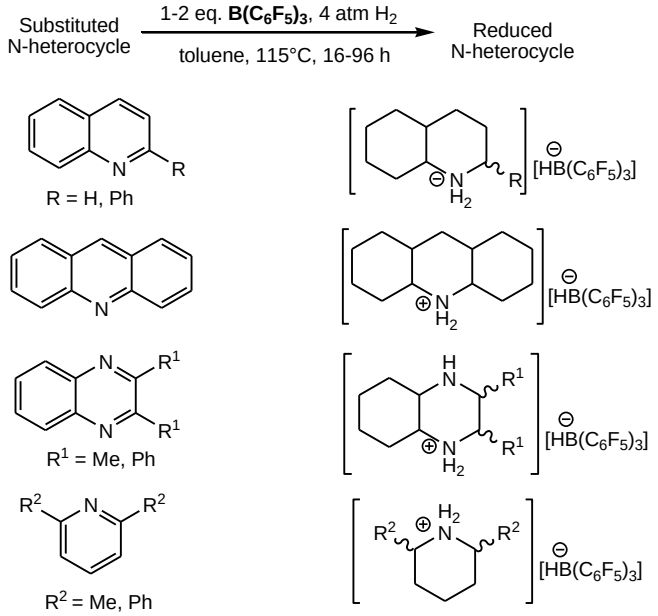
Scheme 43. Asymmetric hydrogenation of quinolines catalysed by Ir-DifluorPhos catalyst

Stephan *et al*. reported metal-free hydrogenation of bulky quinolines with Frustrated Lewis Pairs (FLPs).[55e] In the presence of 5 mol % $B(C_6F_5)_3$ and under 4 atm H_2 at room temperature, quinolines with substituents in the 2- or 8-positions were converted into the corresponding tetrahydroquinolines, which were obtained with good isolated yields (74-88%). In the proposed mechanism, it is suggested that quinolines form weak adducts with $B(C_6F_5)_3$ as a result of FLPs activation of H_2 (Scheme 44). Hydride addition to either the 2- or 4-position occurs because in protonated quinolines both sites are electrophilic. Both the 1,2-addition product (1,2-dihydroquinoline) and the 1,4-addition product (enamine) can undergo isomerization to regenerate imines, which can be subsequently hydrogenated to generate tetrahydroquinolines.



Scheme 44. Proposed mechanism of the hydrogenation of quinolines with FLPs

The Stephan group has recently introduced metal-free reduction of pyridyl- and aniline-type rings in nitrogen containing compounds into the corresponding ammonium hydridoborates.[55f] Heating substrates with stoichiometric amount of $B(C_6F_5)_3$ under 4 atm H_2 at 115°C readily generates the corresponding reduced products (Scheme 45).

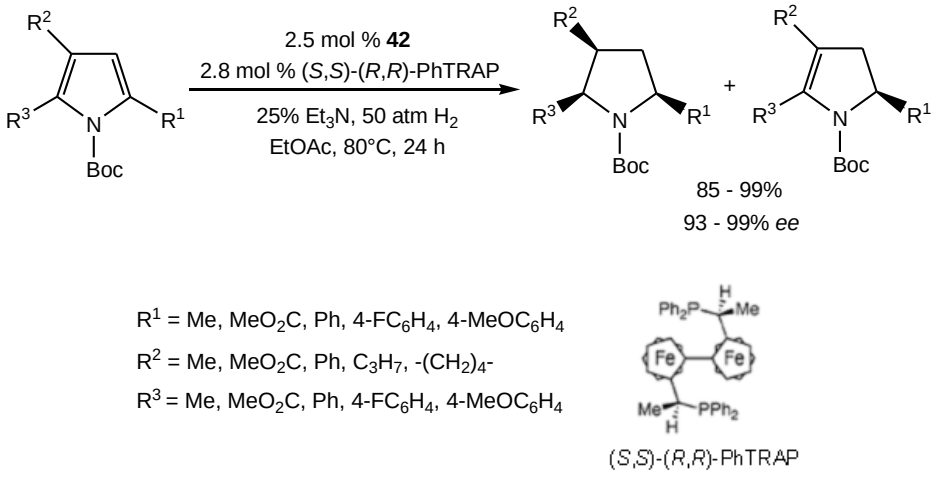


Scheme 45. Hydrogenation of substitutied heterocycles and pyridines with $B(C_6F_5)_3$

II.2.3. Reduction of other nitrogen containing compounds

The catalytic asymmetric hydrogenation of heteroaromatics, such as pyrroles, indoles and quinoxalines, is a versatile method for the preparation of ubiquitous structural motifs in naturally occurring alkaloids and many biological active molecules.[56] In this regard, hydrosilylation of heterocycles can also be as an important transformation.

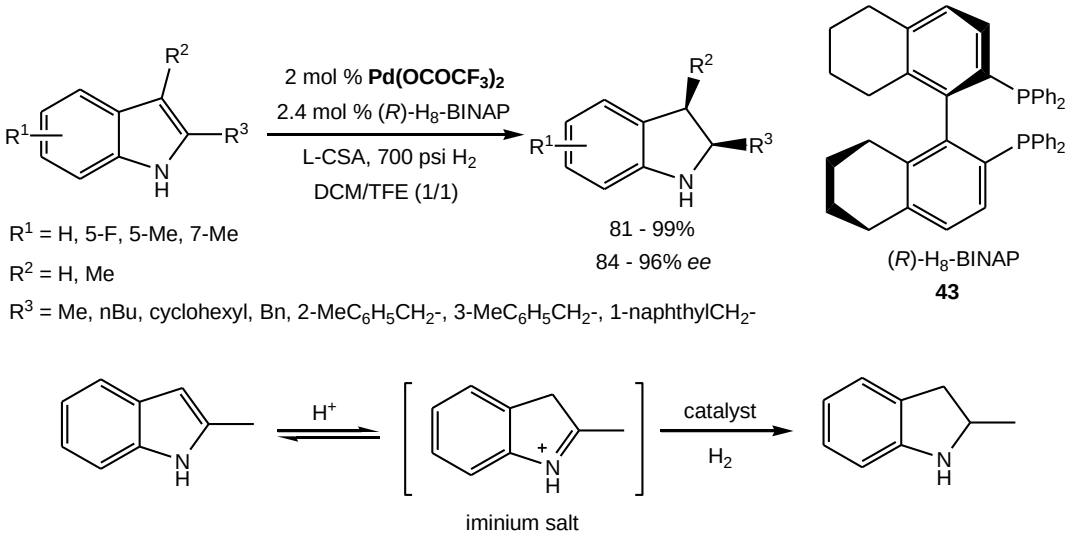
The first highly enantioselective hydrogenation of *N*-Boc-pyrroles (Boc = *tert*-butyloxycarbonyl) with a chiral ruthenium catalyst was reported by Kuwano *et al*.[56a] The active catalyst was generated *in situ* from the *trans*-chelating bisphosphine ligand (*S*,*S*)-(*R*,*R*)-PhTRAP and Ru(η^3-methallyl)$_2$(cod) (**42**) (Scheme 46). Partly hydrogenated products, pyrrolidines and/or dihydropyrroles, were obtained in high yields and enantioselectivities from the reactions of 2,3,5-trisubstituted pyrroles under 50 atm H_2 pressure in the presence of the catalyst.



Scheme 46. The chelating bisphosphine ligand (left) and hydrogenation of 2,3,5-trisubstituted pyrroles (right)

Zhou and Zhang *et al*. reported a highly enantioselective palladium-catalysed hydrogenation of unprotected indoles in the presence of a Brønsted acid and a chiral

bisphosphine ligand.[56b] The best results were obtained when they used $Pd(OCOCF_3)_2$, the chiral ligand (*R*)-H8-BINAP (**43**), and $_L$-camphorsulfonic acid ($_L$-CSA) as the activator (Scheme 47, top). Chiral indolines bearing a broad scope of substituents were generated in good yields and high enantioselectivities. In their proposed reaction mechanism, it is believed that simple unprotected indoles can react with the Brønsted acid to form the iminium salts by protonation of the carbon-carbon double bond. Since the aromaticity of indoles is destroyed, these *in situ* generated iminium salts can be hydrogenated (Scheme 47, bottom).

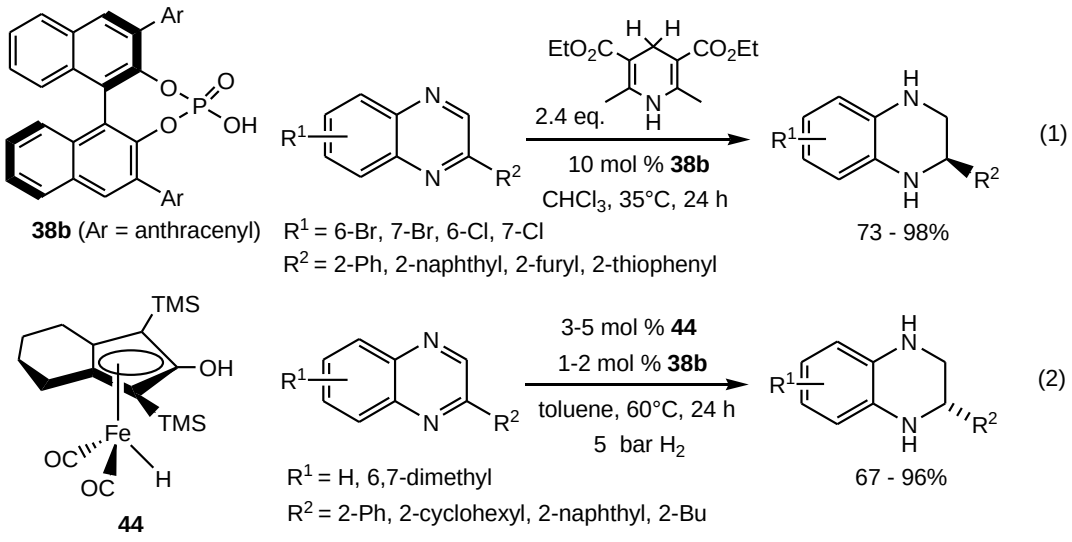


Scheme 47. Hydrogenation of unprotected indoles (top, left), the chiral ligand (top, right) and the proposed reaction pathway (bottom)

Rueping *et al*. developed the first highly enantioselective reduction of quinoxalines to form tetrahydroquinoxalines, which possess important biological and pharmacological properties.[56c] Transfer hydrogenation of quinoxalines to generate the corresponding products was achieved in the presence of a Brønsted acid and Hantzsch esters (dihydropyridines), which were used as hydride sources. The best results with regard to conversion and enantioselectivities were observed when a

diphenylphosphate bearing the anthracenyl group (**38b**) and Hantzsch diethyl ester were used (Scheme 48, eq. 1). Under these catalytic conditions, the reduction of diverse aryl-substituted quinoxalines with excellent enantioselectivities (up to 98% *ee*) was achieved.

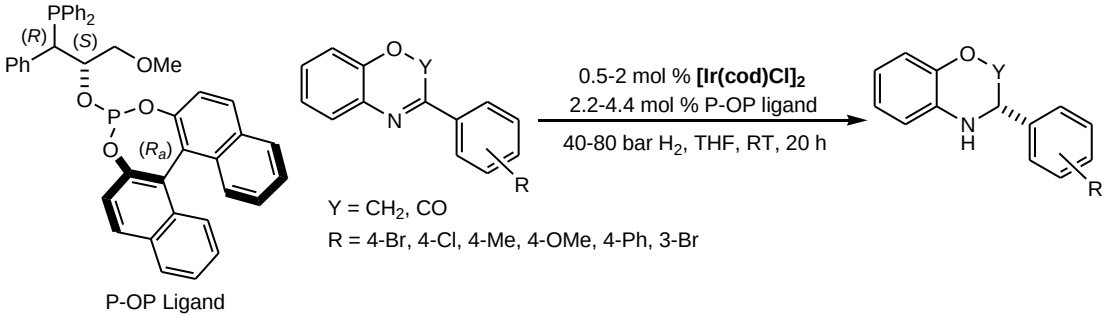
Recently, enantioselective hydrogenation of quinoxalines with an iron/Brønsted acid catalyst pair was reported by Beller and co-workers.[56d] The combination of an achiral iron catalyst **44** with a chiral Brønsted acid allows for the highly enantioselective hydrogenation of various 2-substituted quinoxalines to the corresponding chiral tetrahydroquinoxalines in high yields with excellent enantiomeric ratios (up to 97:3). In the presence of a catalytic amount of **44** and diphenylphosphate **38b**, an efficient hydrogenation of quinoxalines was observed (Scheme 48, eq. 2). Moreover, employing H_2 as the reducing agent makes their catalytic transformation as an ideal atom-economical process.



Scheme 48. Hydrogenation of quinoxalines with Brønsted acid **38b**

Vidal-Ferran *et al*. reported enantioselective hydrogenation of benzoxazine and benzoxazinone derivatives with $[Ir(cod)Cl]_2$ and a P-OP ligand (Scheme 49).[56e]

Benzoxazines bearing different substituents, such as halides, alkyl and aryl, were efficiently hydrogenated in the presence of the catalyst [Ir(Cl)(cod)(P-OP)] and 40 bar H_2. Although higher H_2 pressure (80 bar) and catalyst loading (2 mol %) were required, benzoxazinones were efficiently reduced with a high enantioselectivity.



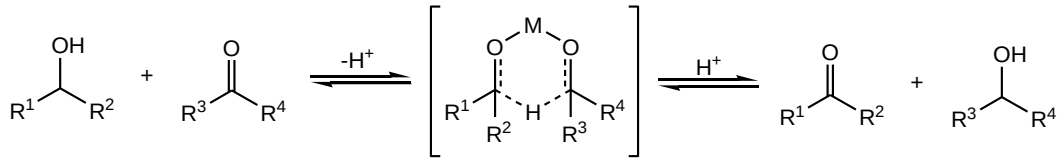
Scheme 49. Hydrogenation of benzoxazine and benzoxazinone derivatives

II.3. Transfer hydrogenation catalysed by transition-metal complexes

Transfer hydrogenation has been considered as a mild methodology for reduction of different organic compounds, such as ketones, aldehydes, imines and nitriles.[57,58] Most importantly, the use of H_2-donor solvents, such as 2-propanol and 2-butanol, is not only environmentally friendly, but also easy to handle. Also, products bearing various substituents can be obtained by using chemoselective catalysis. However, most catalytic conditions for transfer hydrogenation require high temperature to achieve the completion of reactions.[60-65] Therefore, it is important to develop new catalysts, which can efficiently catalyse transfer hydrogenation at ambient temperature.

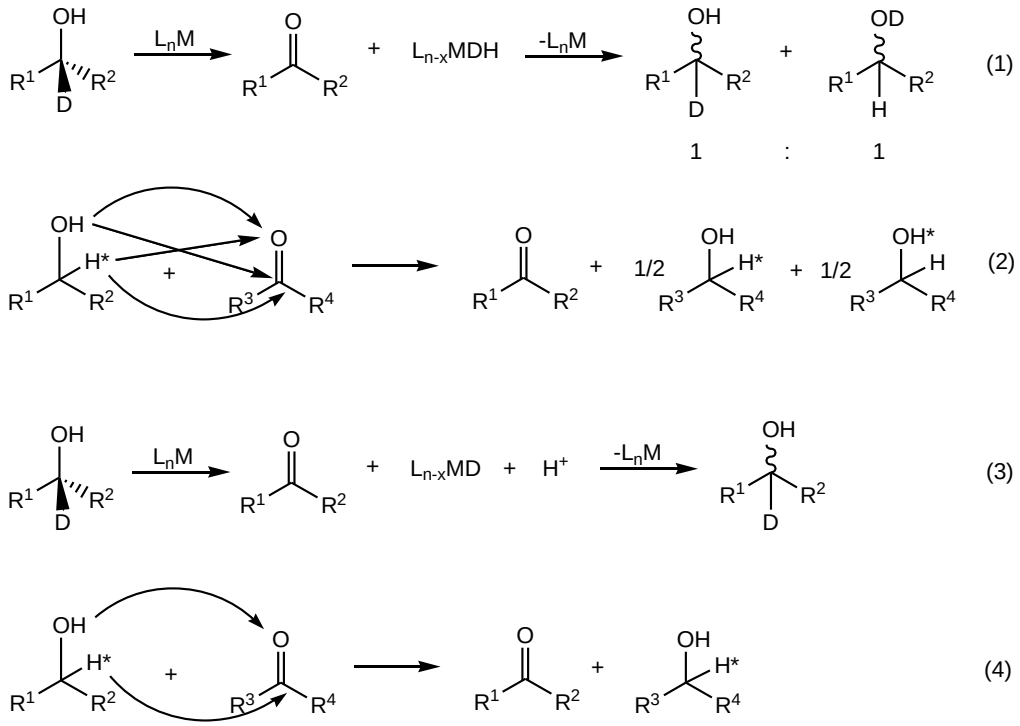
II.3.1. Transfer hydrogenation of carbonyls

Transition metal-catalysed transfer hydrogenation reaction of ketones is an environmentally friendly methodology for the synthesis of secondary alcohols.[57] Generally, two main reaction pathways have been proposed for hydrogen transfer from alcohols, usual H_2-donor solvents, to ketones: direct hydrogen transfer and a hydride route.[58] The direct hydrogen transfer is considered to be the main pathway for main group metal catalysts, which involve the transition state in which both the hydrogen donor and the hydrogen acceptor are coordinated to the metal centre (Scheme 50). This is the classical Meerwein-Ponndorf-Verley-Oppenauer (MPVO) mechanism of transfer hydrogenation.



Scheme 50. A direct hydrogen transfer pathway

On the other hand, the hydride route is thought to be a more typical pathway for transition metal catalysts.[58a] In the reaction with transition metals, a metal hydride species is considered as a key intermediate. The hydride route can be further divided into two routes: dihydridic and monohydridic. In the dihydride mechanism, the hydrogens of the C-H and O-H bonds of the hydrogen source lose their identity and become equivalent when they are transferred first to the metal and then to the ketone (Scheme 51, eq. 1 and 2). Therefore, if a partially deuterated alcohol, such as RCD(OH)R', is used as a hydrogen source, the deuterium will be scrambled between the carbon and oxygen positions of the ketone. When the reaction is achieved through the monohydride mechanism, the hydrogen atoms of the hydrogen donor keep their identity (Scheme 51, eq. 3 and 4). Therefore, for example, the C-H of the donor will become the C-H of the product. This is because the C-H hydrogen of the donor becomes the hydride on the metal while the hydrogen of the O-H of the donor stays as a proton during the process.

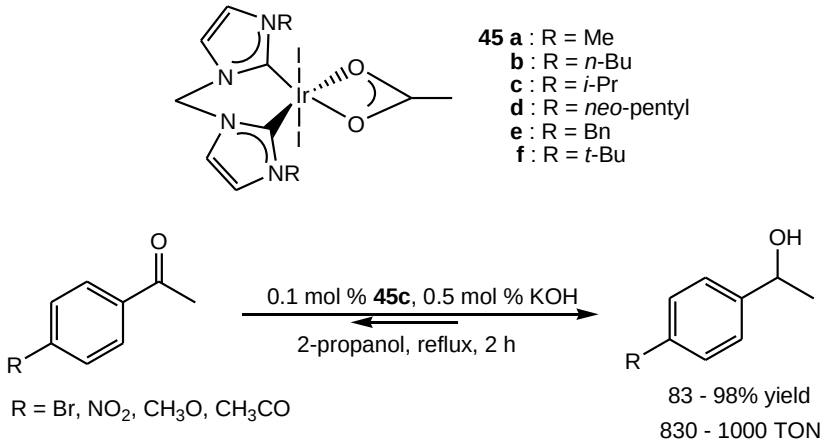


Scheme 51. Dihydride (eq. 1 and 2) and monohydride (eq. 3 and 4) mechanism

One of the early studies of transfer hydrogenation of ketones was reported by Sasson and Blum in 1971.[59a] At a high temperature, hydrogen transfer from benzyl alcohol to the 1-phenyl-1-buten-3-one was achieved in the presence of $RuCl_2(PPh_3)_3$. Bäckvall *et al*. studied the effect of the addition of a base on the catalytic activity in transfer hydrogenation.[59b] In the presence of NaOH, $RuCl_2(PPh_3)_3$ efficiently catalysed the transfer hydrogenation of various ketones in 2-propanol at 82°C. Their proposed mechanism involves the formation of a highly active species $RuH_2(PPh_3)_3$.

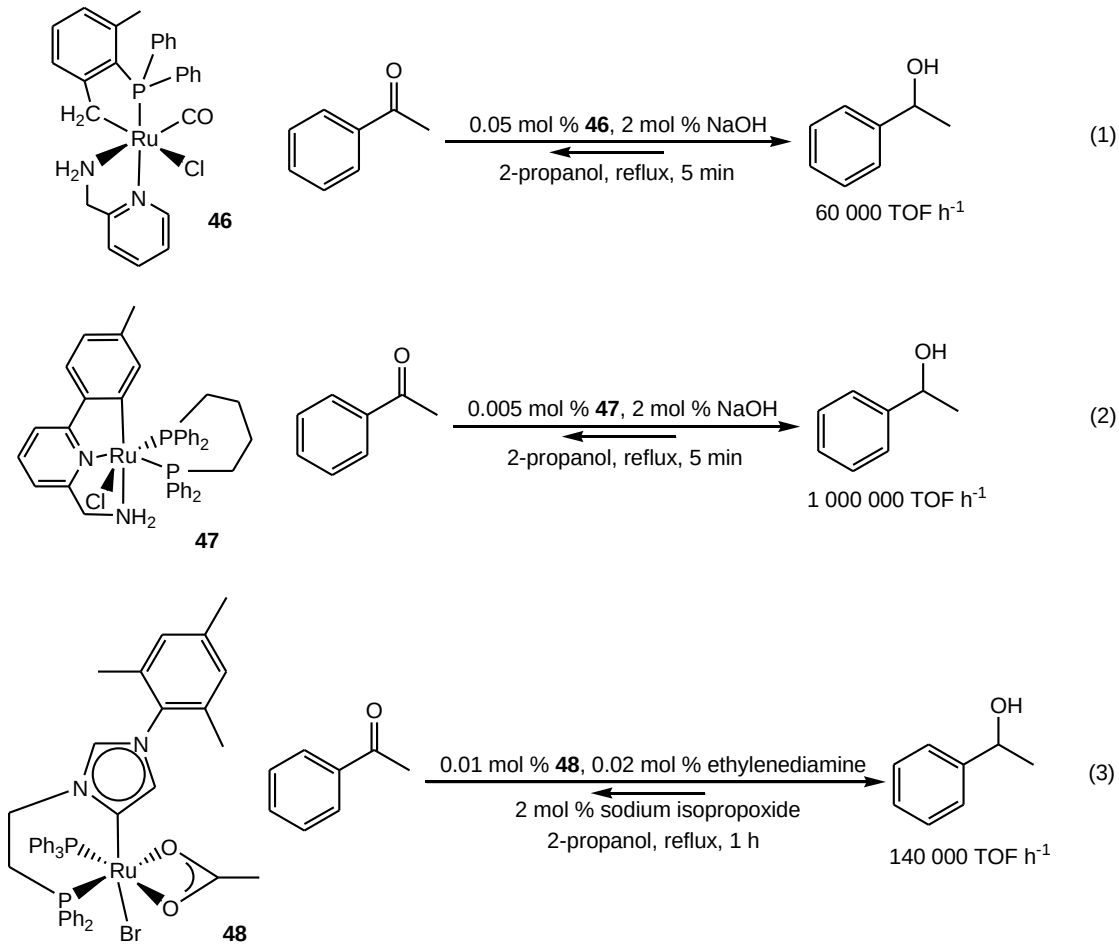
Air-stable iridium(III) complexes were introduced as catalysts for transfer hydrogenation of ketones by Crabtree and co-workers.[60a] Iridium bis-carbene complexes **45a-f** were synthesized from the reaction of $[IrCl(cod)]_2$ and bis-imidazolium salts. The complex **45c** bearing isopropyl groups at the R positions showed the best results. In the presence of a catalytic amount of **45c** and KOH in 2-

propanol at reflux, transfer hydrogenation reactions of acetophenone derivatives were achieved and the products were obtained in good yields (Scheme 52).



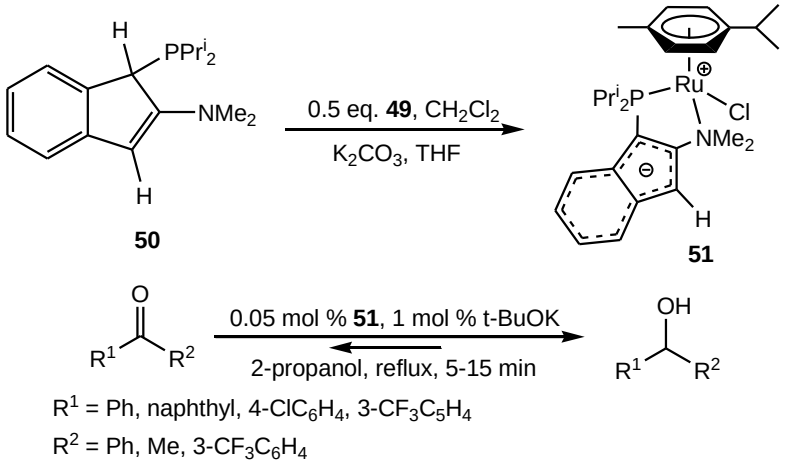
Scheme 52. Transfer hydrogenation of ketones catalysed by Ir-carbene complexes

Baratta *et al*. reported transfer hydrogenation of ketones catalysed by a cyclometalated ruthenium complex **46** with high TOFs.[61a] Very low catalyst loading (0.05 mol %) was required for the reactions when NaOH was used as a base. The reaction of acetophenone at 82°C under the catalytic conditions resulted in the formation of 1-phenylethanol with high TOF (60 000 TOF h^{-1}) rapidly (Scheme 53, eq. 1). Higher TOFs were obtained with the ruthenium tridentate complex **47**.[61b] The complex **47** was obtained from the reaction of [$RuCl_2(PPh_3)$(dppb)] (dppb = 1,4-bis(diphenylphosphino)butane) with 6-(4'-methylphenyl)-2-pyridylmethylamine in 2-propanol. In the case of the reaction of acetophenone, 1-phenylethanol was generated with a high TOF (1 000 000 TOF h^{-1}), approaching the rate of enzymatic reactions, in the presence of even lower catalyst loading (0.005 mol %) (Scheme 53, eq. 2). Recently, this group also introduced an abnormal *N*-heterocyclic carbene-phosphine ruthenium complex **48** as a catalyst for transfer hydrogenation of ketones.[61c] In the reaction of acetophenone, the product was obtained with a good TOF (Scheme 53, eq. 3). Interestingly, the reaction rate and productivity increased upon addition of a co-ligand, ethylenediamine or benzylamine, and up to 140 000 h^{-1} TOF was achieved.



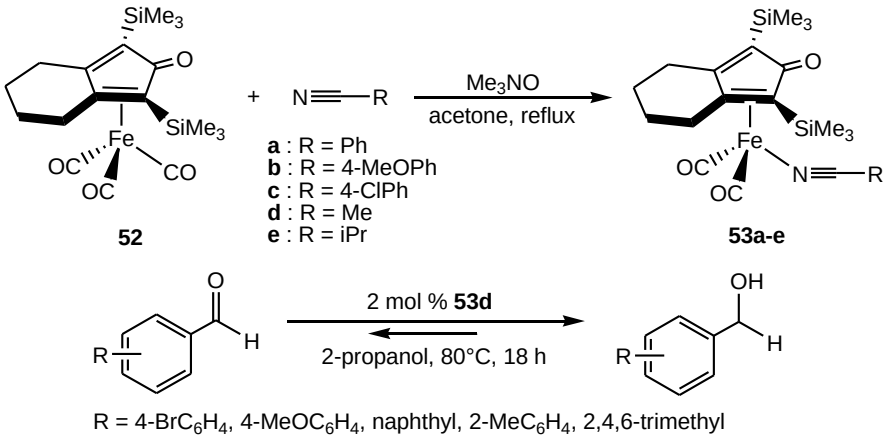
Scheme 53. Efficient transfer hydrogenation catalysed by Ru complexes

A highly active catalyst for transfer hydrogenation, which did not feature the NH group, was introduced by Stradiotto and co-workers.[61d] The zwitterion ruthenium complex **51** was obtained by reacting [{(η^6-*p*-cymene)$RuCl_2$}] (**49**) and the P- and N-donor ligand **50** (Scheme 54, top). The zwitterion complex efficiently catalyses transfer hydrogenation of ketones in 2-propanol. A number of substrates, such as acetophenone, benzophenone, cyclohexanone and 2-heptanone, were converted to the corresponding alcohols and high TOFs (54 000 - 220 000 TOF h^{-1}) were obtained (Scheme 54, bottom). This result is of interest because it shows that high activity can be achieved in the absence of the NH group which is responsible for the bifunctional catalytic effect suggested by Noyori and Ikariya.[59c-f]



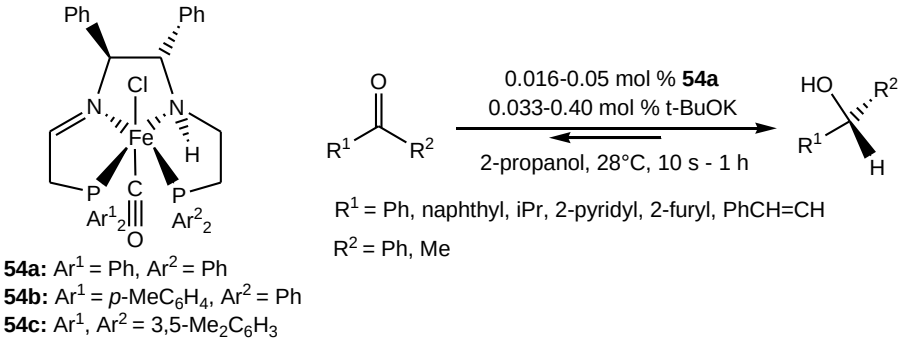
Scheme 54. Synthesis of the zwitterion complex **51** and transfer hydrogenation of ketones

Recently, transfer hydrogenation of carbonyls mediated by a nitrile-ligated Shvo-type iron complexes was reported by Funk and co-workers.[62a] The reaction of a commercially available iron carbonyl complex **52** and nitriles produced the air-stable nitrile-ligated iron complexes **53a-e** with good yields (Scheme 55, top). The complex bearing acetonitrile, **53d**, showed the best results in transfer hydrogenation of ketones. The corresponding alcohols were obtained with moderate to high isolated yields (63 – 98%) in the presence of 5 mol % of **53d** in 2-propanol at 80°C. It is important to mention that the transfer hydrogenation reactions were achieved without the addition of a base. The complex **53d** also efficiently catalyses transfer hydrogenation of a wide scope of aldehydes to primary alcohols under the same reaction conditions (Scheme 55, bottom). Benzaldehyde derivatives bearing electron donating and/or withdrawing groups were tolerated and the products were obtained with high isolated yields.



Scheme 55. Synthesis of the iron complexes **53a-e** and transfer hydrogenation of aldehydes

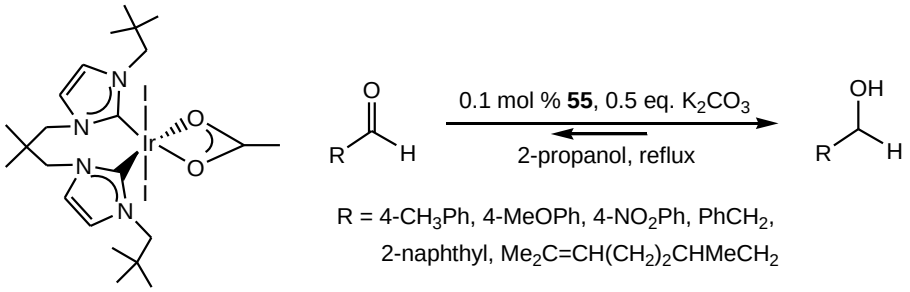
Recently, new iron complexes (**54a-c**) with a partially saturated P-NH-N-P framework were introduced by Morris and co-workers.[62b] The complex **54a** was found to be an effective precatalyst for the efficient reduction of ketones and imines. In the presence of a very small amount of **54a**, various secondary alcohols were obtained in good yields and high selectivities at ambient temperature (Scheme 56). In addition, high catalytic activity was observed in the reduction of imines, although the reactions required a slightly higher catalyst loading (1 mol %).



Scheme 56. Asymmetric transfer hydrogenation of ketones catalysed by **54a**

Crabtree *et al*. reported transfer hydrogenation of aldehydes by using *N*-heterocyclic carbene iridium complex **55**, which is analogous to complexes **45a-e**.[60b]

High yields and good TONs were obtained from the reactions of various aldehydes bearing different functional groups (Scheme 57).



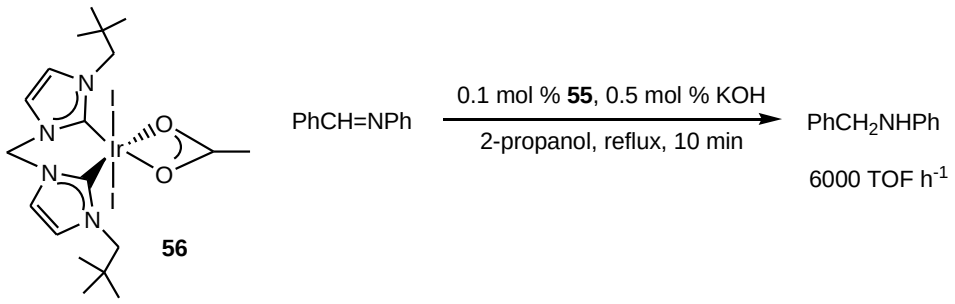
55

Scheme 57. Transfer hydrogenation of aldehydes catalysed by Ir NHC complex **55**

II.3.2. Transfer hydrogenation of imines

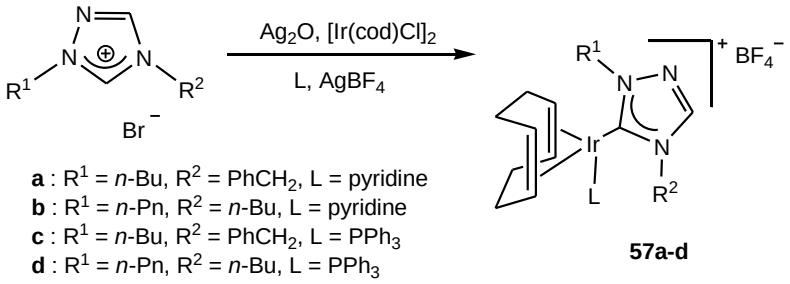
In addition to the extensively explored transfer hydrogenation reactions to C=O double bonds, reductions of C=N bonds have been also studied.[63] Due to the biological and pharmaceutical importance of amines, transfer hydrogenation of imines is a reaction of a great interest.[57]

Crabtree *et al*. have introduced a series of iridium(III) *N*-heterocyclic carbene complexes for transfer hydrogenation of carbonyls.[60] The complex **56** bearing the bis-imidazole ligand efficiently catalyses transfer hydrogenation of imines as well as ketones and aldehydes.[63a] Like the case of carbonyls, the reactions of imines proceeded well with low catalyst loading (0.1-1.0 mol %). A wide range of imines, including naphthyl and mesityl groups, were screened and the use of KOH or K_2CO_3 showed the best results, with up to quantitative yields and high TOFs. In the case of the reaction of *N*-benzylideneaniline, *N*-benzylbenzeneamine was produced with a high TOF at the reflux temperature (Scheme 58).



Scheme 58. Transfer hydrogenation of imines catalysed by Ir bis-carbene complex **56**

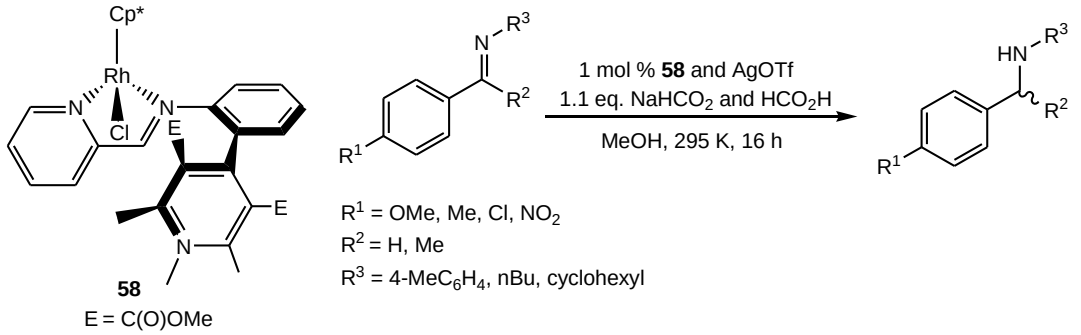
Triazole-based iridium(I) carbene complexes **57a-d** were also synthesized and used as catalysts for transfer hydrogenation of imines.[63b] The reactions of 1,2,4-triazolium salts, $[Ir(cod)Cl]_2$ and the ligands produced the complexes **57a-d** with good yields (Scheme 59). The complex **57d** having neopentyl and *n*-butyl groups on the triazole and triphenyl phosphine as a ligand showed the best catalytic activity. A quantitative yield of *N*-benzylbenzeneamine was obtained from the reaction of *N*-benzylideneaniline in the presence of 1 mol % of **57d** in 2-propanol.



Scheme 59. Synthesis of triazole-derived iridium(I) carbene complexes

Colbran and co-workers reported a bio-inspired design of a homogeneous catalyst in which an organo-transition-metal centre is tethered to an organohydride donor (OHD).[63c] Hantzsch ester, such as 2,6-dimethyl-1,4-dihydropyridine-3,5-dicarboxylate (HEH), was employed as a OHD centre due to its wide use in transfer hydrogenations of unsaturated substrates. Complex **58**, which has *ortho*-phenyl-

bridged pyridinium (HE^+) and $[Cp^*Rh(NN)Cl]^+$ centres (NN = diimine) was synthesized. In the presence of **58**, efficient transfer hydrogenation of imines was achieved with stoichiometric amount of formate ion ($NaHCO_2$) and formic acid at ambient temperature (Scheme 60).



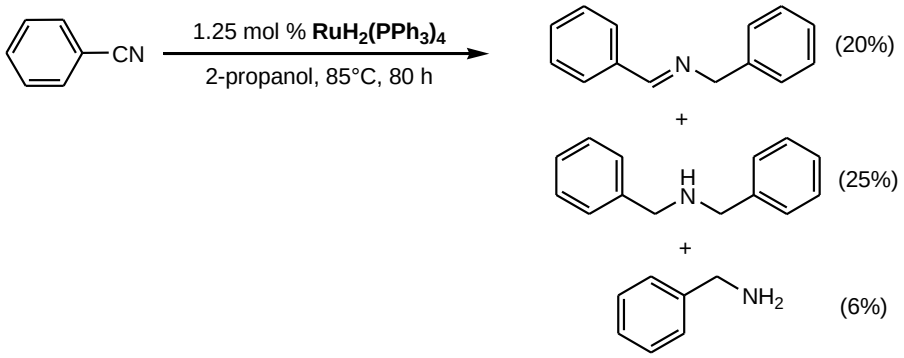
Scheme 60. Transfer hydrogenation of imines catalysed by Rh complex **58**

II.3.3. Transfer hydrogenation of nitriles

Reduction of nitriles to amines is considered to be an essential transformation because amines are important in pharmaceuticals, agrochemicals, and biological processes.[64,65] Catalytic reduction of imines and reductive amination reaction of carbonyls would be the most general processes for the formation of amines. However, catalytic hydrogenation of nitriles to produce amines is less investigated.[65d-e] Specifically, there are only a few reports related to transfer hydrogenation of nitriles in recent decades.[64,65a-c]

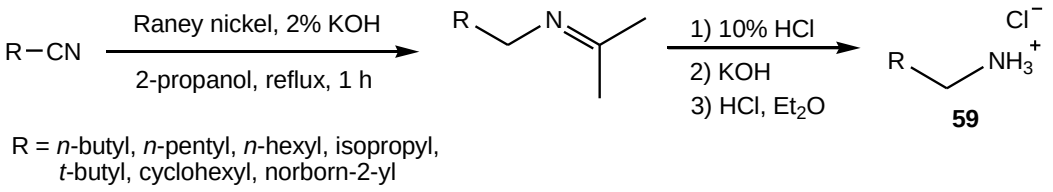
Ruthenium(II) hydride complex, $RuH_2(PPh_3)_4$, was used as a catalyst for transfer hydrogenation of benzonitrile by Yamagishi and co-workers.[64a] The reaction was performed in 2-propanol at 85°C without the addition of a base (Scheme 61). Although a longer reaction time (80 hours) was required compared to reactions of ketones and imines (3-18 hours), a mixture of benzylamine (6 %), benzylidenebenzylamine (20 %), and dibenzylamine (25 %) after 51 % conversion of

the substrate was obtained. It is believed that benzylamine and benzylidenebenzylamine were formed via the reduction to an imine and transamination of the imine, respectively.



Scheme 61. Transfer hydrogenation of benzonitrile catalysed by $RuH_2(PPh_3)_4$

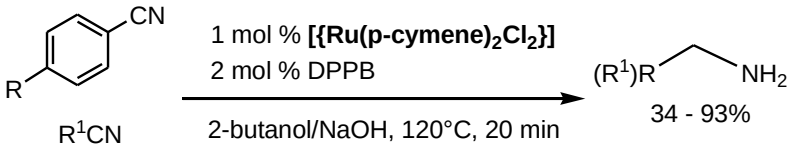
Mebane *et al*. reported transfer hydrogenation of various nitriles mediated by Raney nickel, which is a commonly used heterogeneous catalyst for reductive transformation of organic compounds.[65] Various nitriles bearing alkyl and norbornene groups were used as substrates for the reactions. Initially, the corresponding *N*-isopropylidene amines were produced and the free amines of **59** were obtained with high isolated yields (88-98 %) after acid hydrolysis followed by a base workup (Scheme 62).



Scheme 62. Transfer hydrogenation of nitriles catalysed by Raney nickel

Recently, Beller and co-workers reported transfer hydrogenation of nitriles catalysed by different ruthenium complexes ($[RuCl_2(PPh_3)_3]$, $[\{Ru(cod)Cl_2\}_n]$, $[\{Ru(benzene)_2Cl_2\}_2]$ and $[\{Ru(p\text{-cymene})_2Cl_2\}_2]$) and phosphine ligands (1,2-

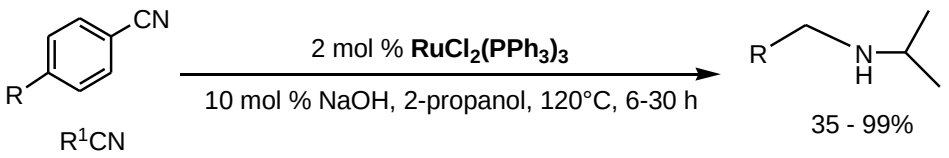
bis(diphenylphosphino)ethane (DPPE), 1,3-bis(diphenylphosphino)propane (DPPP), 1,4-bis(diphenylphosphino)butane (DPPB), 1,5-bis(diphenylphosphino)pentane (DPPPE), and 1,1'-bis(diphenylphosphino)ferrocene (DPPF)).[64b] The catalytic condition, which involved [{Ru(*p*-cymene)$_2$Cl$_2$}$_2$] and DPPB, showed the best result in the reaction of benzonitrile. Interestingly, using 2-butanol showed better results than using 2-propanol. Under their optimized reaction conditions, transfer hydrogenation of a variety of nitriles bearing electron withdrawing, electron donating, halogen groups and heterocycles, was achieved and the corresponding amines were obtained in good to high yields (Scheme 63).



R = Me, MeO, F, Cl, Br, CF_3, Ph
R^1 = naphthyl, 3-thiophenyl, cyclohexyl, adamantyl

Scheme 63. Transfer hydrogenation of nitriles catalysed by [{Ru(*p*-cymene)$_2$Cl$_2$}$_2$]

Transfer hydrogenation of nitriles was also achieved by using $RuCl_2(PPh_3)_3$ as a catalyst.[64c] A wide range of nitriles with aromatic, aliphatic, and heteroaromatic substituents were reduced in the presence of a base. With this catalytic condition, nitriles were converted into *N*-monoalkylated amines through *N*-monoalkylation reaction with 2-propanol (Scheme 64). Although high temperature was required, the secondary amines were obtained with good yields.



R = Me, MeO, F, Ph
R^1 = naphthyl, Et, pentyl, cyclohexyl, adamantyl

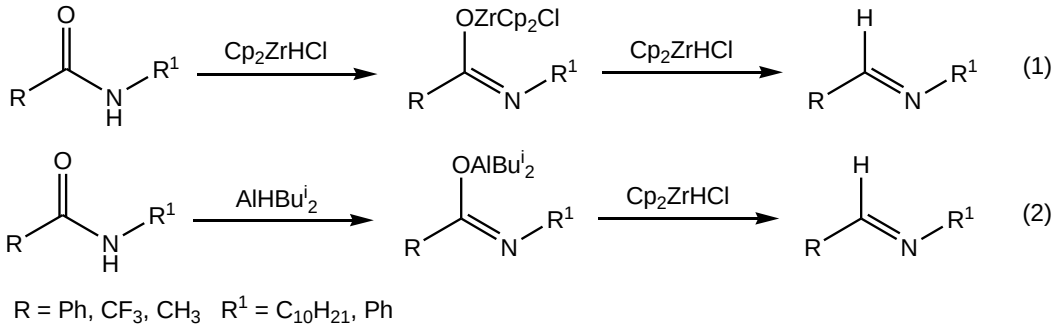
Scheme 64. Transfer hydrogenation of nitriles to amines catalysed by $RuCl_2(PPh_3)_3$

II.4. Reduction of secondary amides to imines and aldehydes

Reduction of amides to amines, aldehydes and imines has been widely studied due to the pharmaceutical and biological importance of the products.[66-71] Therefore, it is important to develop mild and chemoselective catalysts for the reduction of amides to generate nitrogen containing compounds as products. Reduction of carboxamides with reducing agents such as silanes is a convenient route to amines and especially reduction of tertiary amides has been actively investigated.[69-71] It is usually difficult to stop this reductive transformation at the imine stage because imines are reduced to amines more easily than amides. Therefore, only a few studies on stoichiometric and catalytic reduction of amides to the corresponding imines have been reported.[66,67]

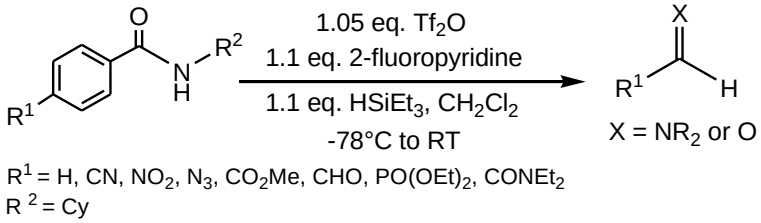
II.4.1. Reduction of secondary amides to imines

The first controlled reduction of secondary amides to the corresponding imines was reported by Ganem *et al*.[66a,b] The reduction was achieved in the presence of two equiv. of Schwartz reagent Cp_2ZrHCl through the formation of zirconium enolates (Scheme 65, eq. 1). The products, *N*-substituted imines, were produced with moderate to good yields. However, using two equiv. Cp_2ZrHCl gives a major disadvantage to this reduction method because of the high cost of this reagent. To solve this problem, $AlHBu^i_2$ was added prior to the addition of Cp_2ZrHCl to generate the intermediate diisobutylaluminum enolate (Scheme 65, eq. 2). In this case, only one equivalent of Schwartz reagent is used to give comparable results with what was observed in the former reduction method.



Scheme 65. Reduction of secondary amides mediated by Cp_2ZrHCl

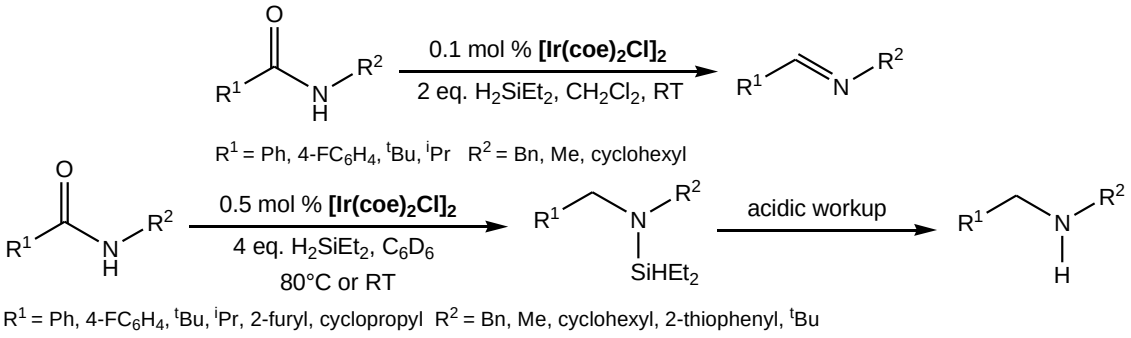
Charette and co-workers reported metal-free reduction of secondary amides by using electrophilic activation with triflic anhydride (Tf_2O).[66c] The corresponding imines were obtained as products without the formation of amines when $HSiEt_3$ and 2-fluoropyridine were used as a reducing agent and a base additive, respectively (Scheme 66). Various secondary amides bearing a wide range of substituents, such as aldehyde, ester, nitrile, alkyne and heterocycle, were efficiently reduced at -78°C to room temperature and high isolated yields were obtained. It was also found that the reaction can produce imines, when the medium is quenched under basic conditions, and aldehydes when the crude product is hydrolyzed in the presence of an aqueous buffer of citric acid and THF.



Scheme 66. Reduction of secondary amides by using Tf_2O and $HSiEt_3$

Recently, Brookhart *et al*. reported catalytic reduction of secondary amides to imines by using the commercially available iridium complex $[Ir(coe)_2Cl]_2$ and H_2SiEt_2.[67] A very small amount of catalyst and exactly 2 equiv. of silane were

required for this reaction and the full conversion was achieved at room temperature with high efficiency. The imines with different functional groups were obtained within 1 hour in high yields (Scheme 67). In addition, the reactions with 4 equiv. of silane at 80°C or at room temperature produced *N*-silyl amines and the corresponding secondary amines were obtained after an aqueous HCl workup.



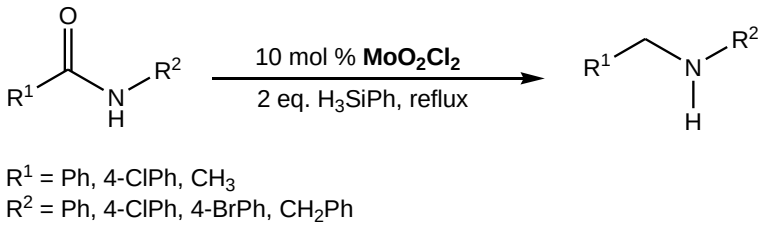
Scheme 67. Reduction of secondary amides to imines and amines catalysed by $[Ir(coe)_2Cl]_2$

II.4.2. Reduction of primary and secondary amides to amines

Transformation of amides to amines under mild conditions is of significant interest not only for the pharmaceutical industry but also for the production of agrochemicals.[68-71] Reduction of tertiary amides to amines by hydrosilanes has recently received significant attention. In contrast, hydrosilylation of secondary amides remains virtually untouched.[68]

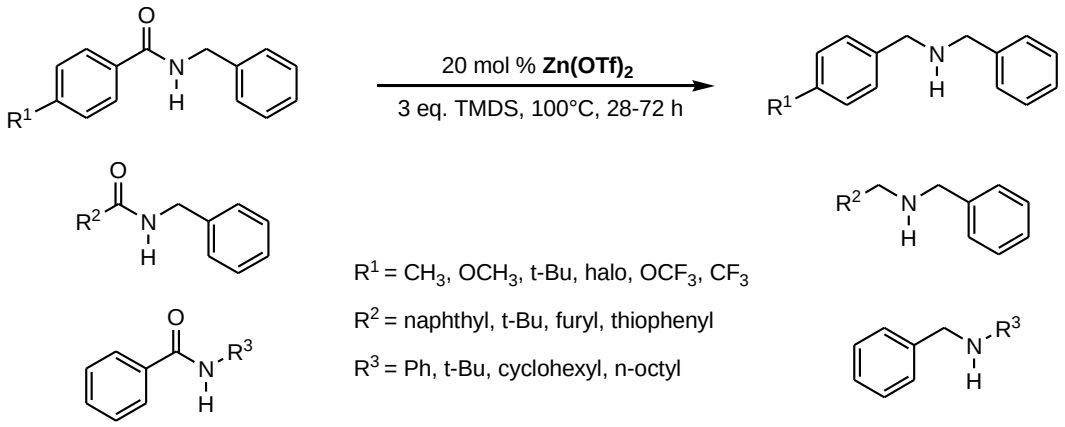
For examples, Fernandes *et al*. reported reduction of secondary and tertiary amides to amines catalysed by the high valent dioxomolybdenum complex, MoO_2Cl_2.[68a] In their optimized conditions, H_3SiPh was used as a reducing agent and all reactions were performed in toluene. Simple secondary amides, such as *N*-benzylbenzamide and *N*-phenylbenzamide, were successfully reduced to the corresponding secondary amines in the presence of 10 mol % catalyst (Scheme 68). Also, moderate to good isolated yields were obtained, and some sensitive

functionalities, such as halo groups, were tolerated. Reduction of tertiary amides with bulky *N*-substituents, such as acetylindoline, was also achieved with good yields.



Scheme 68. Reduction of secondary amides to amines catalysed by MoO_2Cl_2

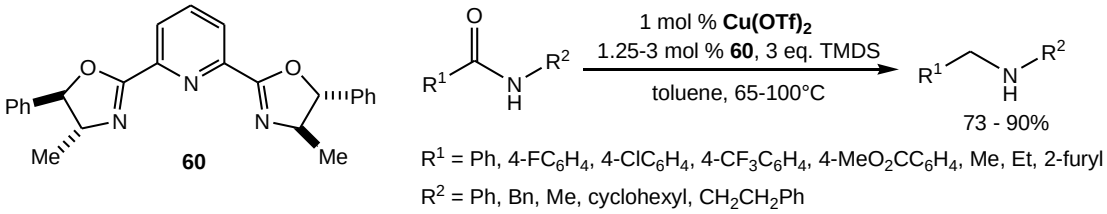
Zinc-catalysed reduction of a wide range of secondary and tertiary amides was reported by Beller and co-workers.[68b] Interestingly, the use of a commercially available zinc complex, $Zn(OTf)_2$, and TMDS showed the best results for the reduction of secondary amides, whereas the reduction of tertiary amides was optimized with the use of $Zn(OAc)_2$ and $HSiMe(EtO)_2$. Although a high catalyst loading and a long reaction time were required, the desired secondary amines were obtained with good yields (50 – 86%) (Scheme 69). In addition, this reduction procedure was tolerant of various functional groups in the R^1, R^2 and R^3 positions.



Scheme 69. Reduction of secondary amides to amines catalysed by $Zn(OTf)_2$

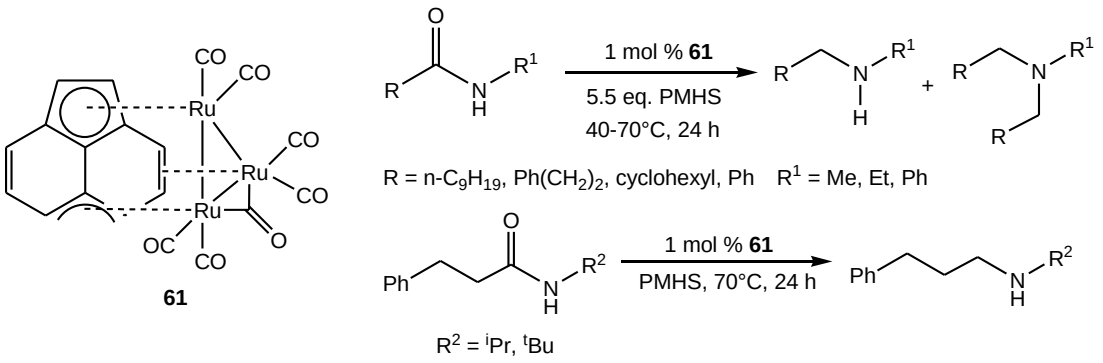
The same group also reported the first general copper-catalysed hydrosilylation of secondary amides to the corresponding amines.[68c] It was found that

$Cu(OTf)_2$ and TMDS showed the best catalytic activities in toluene at 65-100°C (Scheme 70). Applying nitrogen ligand having a pyridine (bis)oxazoline substituent (**60**) gave excellent yields up to 97% within 24 hours. Various secondary amides were efficiently reduced to amines with a high functional group tolerance.



Scheme 70. Reduction of secondary amides to amines catalysed by $Cu(OTf)_2$

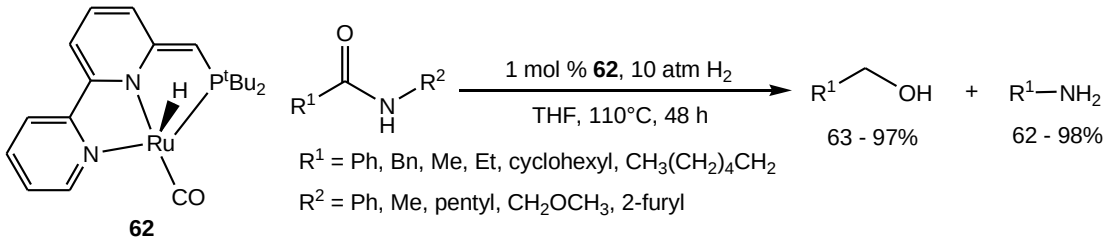
Recently, Nagashima and co-workers extended their research on the ruthenium-catalysed reduction of amides to the secondary amides.[68d] This group introduced the ruthenium cluster complex **61** and used it as a catalyst for the reduction of secondary amides to a mixture of two types of amines, which depended on the nature of the silane and solvent. When PMHS was used as the reducing agent in tetrahydropyran, the reduction of secondary amides that had small substituents such as methyl, ethyl and benzyl groups on the nitrogen atom showed the formation of both secondary and tertiary amines (Scheme 71, top). However, the formation of only secondary amines was observed in the case of amides bearing bulky substituents (e.g. isopropyl and *tert*-butyl) on the nitrogen centre (Scheme 71, bottom). On the other hand, reduction of secondary amides with TMDS in DME upon moderate heating (40-60 °C) in the presence of **61** resulted in selective production of secondary amines. In addition, the catalyst **61** can be also used for the reduction of tertiary amides with $HSiMe_2Ph$.[71a] The latter reactions were achieved at room temperature and the corresponding tertiary amines were obtained in high yields.



Scheme 71. Ruthenium cluster complex **61** and reduction of secondary amides to amines

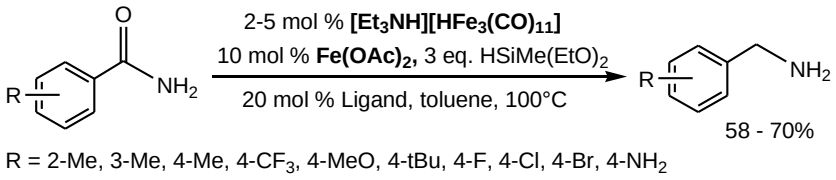
Reeves *et al*. reported hydrosilylation of primary, secondary and tertiary amides by using $Ru_3(CO)_{12}$ and excess TMDS in toluene.[68e] Secondary and tertiary amides with various substituents were efficiently reduced at relatively low temperature (50°C) and the corresponding amines were obtained with good yields. Reduction of more challenging primary amides was also achieved with the same catalytic condition, although a higher reaction temperature (70°C) was required to complete the reaction.

Selective hydrogenation of secondary amides was introduced by Milstein and co-workers.[68f] The dearomatized bipyridine-based pincer complex **62** efficiently catalysed hydrogenation of secondary amides to form amines and alcohols as products (Scheme 72). This catalytic protocol showed a broad substrate scope, providing a variety of amines and alcohols in good to excellent yields.



Scheme 72. Hydrogenation of secondary amides to amines catalysed by **62**

The first iron-catalysed reduction of primary amides to amines was introduced by Beller and co-workers.[68g] Interestingly, the desired transformation does not proceed in the presence of a single metal catalyst. However, applying two iron complexes, $[Et_3NH][HFe(CO)_{11}]$ and $Fe(OAc)_2$, in a consecutive manner allowed for the reduction of primary amides to amines (Scheme 73). Various primary amides were reduced to amines with the ligand, 3,4,7,8-tetramethyl-1,10-phenanthroline, and inexpensive silane $HSiMe(EtO)_2$ at 100°C.



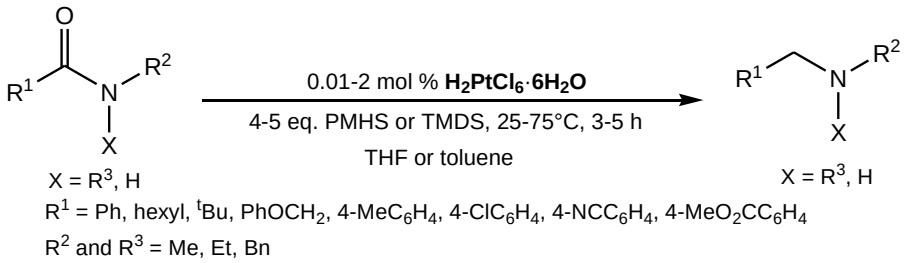
Scheme 73. Reduction of primary amides to amines catalysed by two iron complexes

II.4.3. Reduction of tertiary amides to amines

In addition to the reduction of secondary amides to amines, transformation of tertiary amides to amines in the presence of catalysts and different silanes has been widely explored.[69-71]

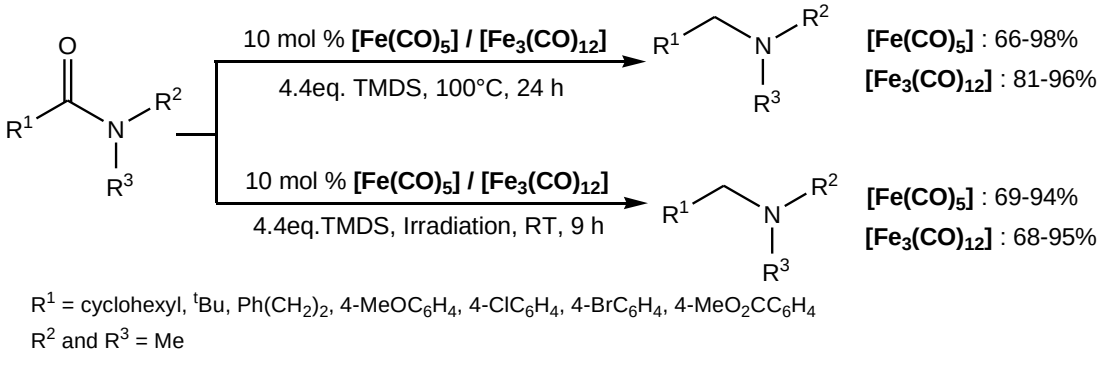
Nagashima *et al*. reported reduction of tertiary amides by using platinum complex H_2PtCl_6 as the active catalyst.[69a,b] Interestingly, the complex is inert with the hydrosilanes having only one Si-H group in the molecule, whereas it efficiently catalyses the reduction under mild conditions of tertiary amides with siloxanes, such as PMHS and TMDS, containing two separated Si-H centres. Amides having various substituents were reduced in the presence of a small amount of the catalyst at 25°C – 75°C (Scheme 74). At the end of the reaction, the metallic residue can be easily removed from the reaction mixtures due to the self-encapsulation of the platinum residue to the insoluble siloxane resin. The amine products were obtained with less

than 1 ppm of platinum content after purification by a short Al_2O_3 column. In addition, when TMDS was used as the reducing agent, secondary amides were reduced under the same reaction conditions.



Scheme 74. Reduction of tertiary amides to amines catalysed by H_2PtCl_6

Iron carbonyl complexes, $[Fe(CO)_5]$ and $[Fe_3(CO)_{12}]$, were also used by Nagashima and co-workers as efficient catalysts for the reduction of tertiary amides.[70a] The reactions were achieved in the presence of excess PMHS or TMDS. Both complexes are useful catalysts for the thermal and photoassisted reductions of tertiary amides to amines and show comparable yields (Scheme 75). Interestingly, the photoassisted reaction under irradiation with a 400 W high-pressure mercury lamp allows the reduction at room temperature. Beller *et al*. also reported reduction of tertiary amides to amines by using $[Fe_3(CO)_{12}]$.[70b] The best results were observed when PMHS was used, allowing for various tertiary amides with different substituents to be selectively reduced to the corresponding tertiary amines.



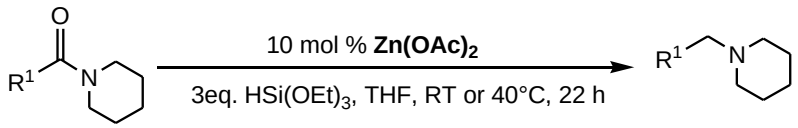
Scheme 75. Thermal and photoassisted reduction of tertiary amides to amines

An iron catalyst generated *in situ* from $Fe(OAc)_2$ and the imidazolium salt, 1-(2-hydroxy-2-phenylethyl)-3-methylimidazolium triflate ([Ph-HEMIM][OTF]) (**63**), was reported by Buitrage, Adolfsson and co-worker.[70c] The catalytic reaction exhibited a broad substrate scope and functional group tolerance and showed improved selectivity upon the addition of LiCl (Scheme 76). A variety of tertiary benzamides were reduced with good yields in relatively short reaction times.

R^1 = Ph, 4-FC_6H_4, 4-BrC_6H_4, 4-$MeOC_6H_4$, naphthyl, 2-furyl, 2-thiophenyl

Scheme 76. Reduction of tertiary amides with $Fe(OAc)_2$ and the imidazolium salt **63**

Beller and co-workers introduced the first zinc-catalysed reduction of tertiary amides to amines with $Zn(OAc)_2$ and excess $HSi(OEt)_3$.[71b] The reduction was achieved at ambient temperature (room temperature to 40°C) and the catalyst showed excellent chemoselectivity and various functional group tolerance (Scheme 77).

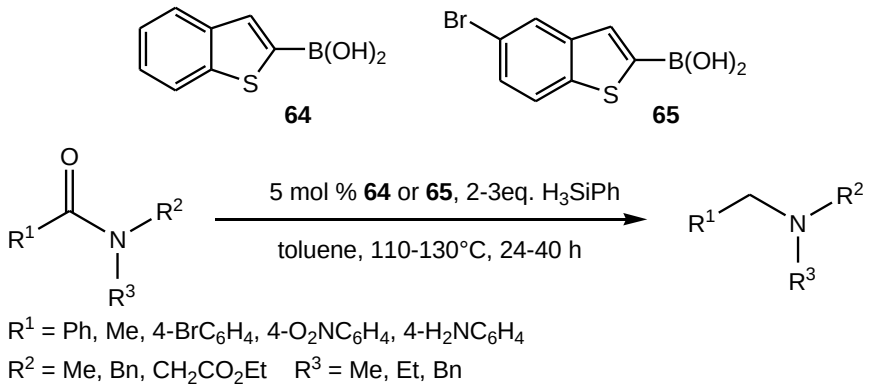


R^1 = Ph, 4-FC_6H_4, 4-BrC_6H_4, 4-$MeOC_6H_4$, naphthyl, 2-furyl, 2-thiophenyl, $Ph(CH_2)_2$, cyclohexyl

Scheme 77. Zinc-catalysed reduction of tertiary amides to amines

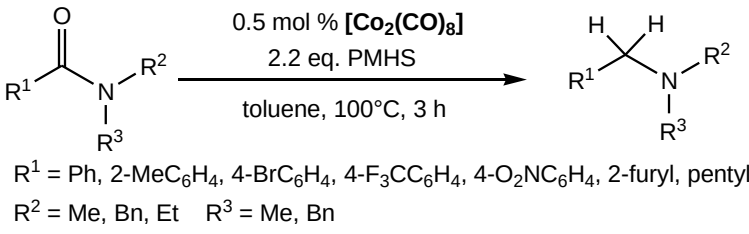
More recently, Beller's group also reported the first metal-free hydrosilylation for the reduction of amides to amines in the presence of boronic acids.[72] The reactions were chemoselective and tertiary, secondary and primary amides were reduced equally well. The benzothiophene-derived boronic acids **64** and **65** show the best results when

excess amount of H_3SiPh (2-3 equiv.) was used as the reducing agent. Although this process required relatively high temperatures (110 - 130°C), a wide range of substituted amides were efficiently reduced to the corresponding amines (Scheme 78).



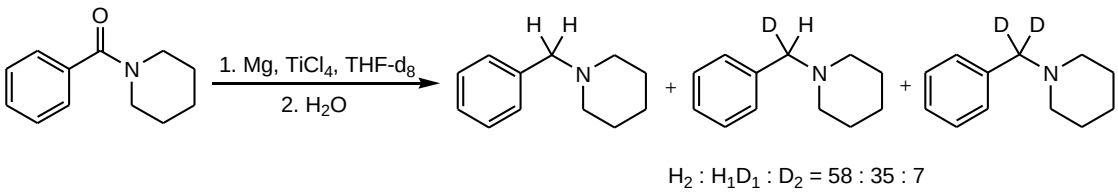
Scheme 78. Boronic acid-catalysed reduction of amides to amines

Similar to the catalytic reactions of $Fe(CO)_5$ or $Fe_3(CO)_8$,[70b] Darcel and Sortais *et al*. reported reduction of various carboxamides to the corresponding amines catalysed by $[Co_2(CO)_8]$ (Scheme 79).[73] Similar high conversions were observed upon monitoring the reaction either at 100°C for 3 hours or under UV activation (350 nm) at room temperature for 15 hours. Due to their low price, PMHS and TMDS were selected as reducing agents, although more expensive silane H_3SiPh can increase both conversion and yield for sterically hindered substrates. Excellent chemoselectivities (>99%) for the reduction of benzamides were observed in catalytic competition experiments with esters and alkenes.



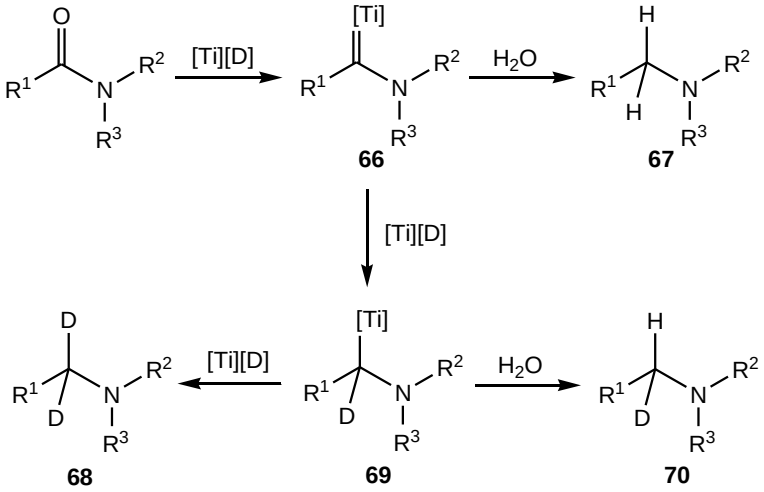
Scheme 79. Reduction of tertiary amides to amines catalysed by $Co_2(CO)_8$

Very recently, Luo and co-workers have reported reduction of amides to amines by using low-valent titanium as a mild and cost-effective agent.[74] Although a number of reagents, such as $LiAlH_4$, alkali metals and zinc, can reduce $TiCl_4$ to a low-valent titanium, magnesium powder was chosen for simplicity and convenience. The optimized results were observed when the molar ratio of amides:$TiCl_4$:Mg was 1:5:10 and when THF was used as solvent. The reduction of tertiary and secondary amides was achieved at room temperature and a wide range of amides were reduced to the corresponding tertiary and secondary amines with good yields. Primary amides were also reduced under this reaction condition except that the reduction was carried out at 0°C. Moderate to good yields were also observed from the reduction of primary amides (68-80%). To address the question of where the hydrogen atoms come from, Luo *et al*. prepared a [Ti][D] species from the magnesium reduction of $TiCl_4$ in THF-d_8 (Scheme 80). The reduction of phenyl(piperin-1-yl)methan-one with this reagent showed the formation of *N*-benzylpiperidine together with its deuterated derivatives in the 58:35:7 ratio.



Scheme 80. Reduction of amides to amines mediated by $TiCl_4$/Mg in THF-d_8

Based on these results, the authors suggested that a titanium carbene intermediate **66** can be involved in the reaction mechanism (Scheme 81). Non-deuterated amine **67** would be obtained from the hydrolysis of **66**. With two deuterium atoms, the amine **68** can be produced through the intermediate **69**. Also, hydrolysis of **69** would generate the product **70** with one deuterium atom.



R^1 = Ph, 4-MeC_6H_4, 4-$MeOC_6H_4$, 4-$H_2NC_6H_4$, 4-ClC_6H_4, Me

R^2 = H, Me, Et

R^3 = Ph, 4-FC_6H_4, 4-$MeO_2CC_6H_4$, 3-HOC_6H_4, cyclohexyl, Bn

Scheme 81. Proposed mechanism of reduction of amides with $TiCl_4$/Mg

III. Results and Discussion

III.1. H/D exchange reactions catalysed by Ru complexes

Since the mid-1990s, H/D exchange reactions have attracted much attention due to their importance for the preparation of deuterium labeled compounds.[18] The H/D exchange can be achieved in the presence of homogeneous and heterogeneous transition-metal complexes. Recently, ruthenium, iridium and rhodium complexes have recognized as potential catalysts for the H/D exchange. However, due to the harsh reaction conditions usually required for these reactions, the development of new efficient catalysts is a remaining challenge. Another important aspect to highlight is the lack of catalytic methods utilising D_2O as the source of deuterium. In this section, H/D exchange reactions in C_6D_6 and D_2O catalysed by the half-sandwich ruthenium complex $CpRu(PPr^i_3)H_3$ (**1**) and the possible reaction pathways will be discussed.

III.1.1. H/D exchange reactions catalysed by $Cp(PPr^i_3)RuH_3$ in C_6D_6

The impetus for our research came from the unexpected discovery that the complex $Cp(PPr^i_3)RuH_3$ (**1**) shows catalytic activity at elevated temperature. Namely, we observed that the Cp signal in the ^1H NMR spectrum of **1** in C_6D_6 disappears after heating the solution at 100°C overnight. After that, gradual disappearance of the methine and methyl signals of the phosphine was also noted. Concomitantly, we observed that the signal of protonated solvent, C_6D_5H, increased in the ^1H NMR spectrum. In addition, we confirmed deuteration of all of C-H positions of the complex by ^2H NMR. The activations of C-H bonds in the Cp ligand and the alkyl groups of phosphine ligands have many precedents.[75] The discovery of H/D exchange between the complex itself and the deuterated solvent encouraged us to study the

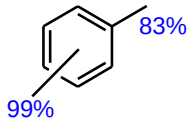
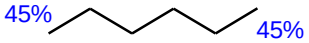
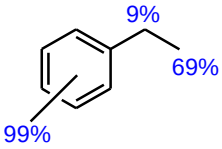
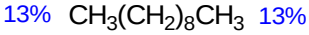
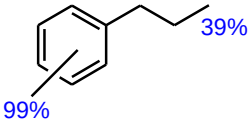
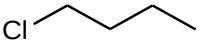
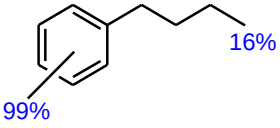
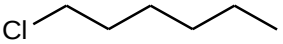
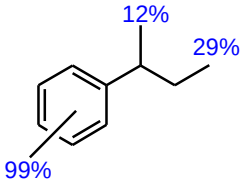
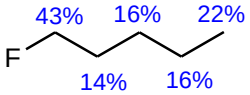
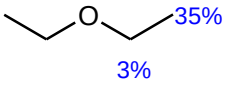
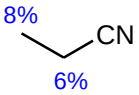
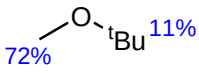
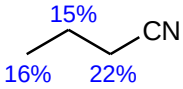
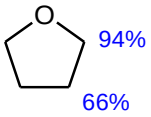
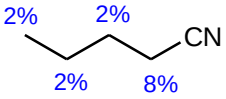
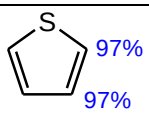
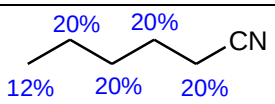
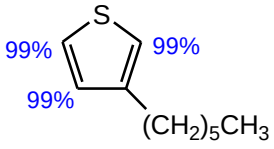
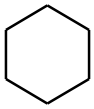
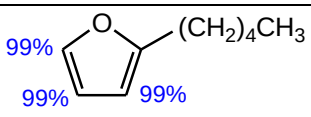
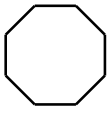
possibility of H/D exchange reactions of a variety of organic substrates in the presence of $Cp(PPr^{i}_{3})RuH_3$ (**1**) as a catalyst.[76]

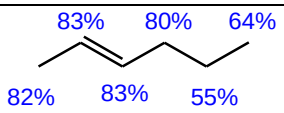
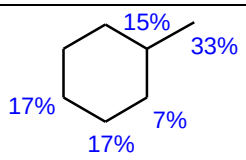
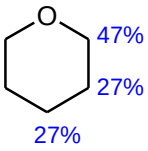
In the reactions of alkylbenzenes (Table 2, entry 1-5), deuteration of the C-H positions of the benzene rings occurs much faster compared to the reactions in the alkyl groups. Interestingly, terminal positions of alkyl groups are deuterated faster than internal positions and benzylic positions, which are normally more reactive. In the case of 1-phenylpropane (Table 2, entry 3) and 1-phenylbutane (Table 2, entry 4), only terminal positions are involved in exchange. This result is opposite to the usual expectation that the benzylic positions, which are more acidic, would react faster.[78]

Deuteration of ether is achieved easily and shows selective deuteration of the less acidic *β*-position (Table 2, entry 6). In the case of methyl *tert*-butyl ether, deuteration in the methyl group occurs more rapidly, although the unactivated and remote *t*-Bu group is also engaged in exchange (Table 2, entry 7). Deuteration of *α*- and *β*-positions of THF shows comparable results in both positions (Table 2, entry 8). Reactions of C-H positions of heteroaromatic substrates show high deuterium incorporation in a relatively short time (Table 2, entry 9-11). Unlike the reactions of alkylbenzenes, the alkyl chains of heteroarenes do not show deuteration even upon monitoring the reactions for long time (Table 2, entry 10-11). We believe that this happens because of a better donating ability of heteroaromatics and their stronger coordination to the metal. In the reaction of 1-hexene, we observed initial isomerization into an internal olefin, 2-hexene, followed by deuteration (Table 2, entry 12). Previously, competitive C-H activation of propane and pentane by a Rh complex was reported.[79] This study suggested that secondary C-H bonds coordinate to metal centres 1.5 times faster than methyl groups, however, C-H oxidative cleavage occurs much faster on the primary C-H bonds. In our experiment, a similar preference

was observed in the H/D exchange of linear alkanes. Deuterium incorporation was achieved only in the terminal methyl groups of hexane and decane (Table 2, entry 13-14). However, chloroalkanes do not show deuteration, presumably due to catalyst deactivation by the chlorine (Table 2, entry 15-16). The possible pathway for such deactivation could be H/Cl exchange with a ruthenium hydride intermediate. On the other hand, fluoropentane, which has a more robust C-F bond, shows deuteration in all positions without significant catalyst deactivation (Table 2, entry 17). It shows a slight selectivity for the most acidic α-protons. Strong kinetic preference of methyl group activation and the thermodynamic preference of α–CH_2 group activation were reported in the case of activation of nitriles.[80] In the reactions of aliphatic nitriles, comparable deuterium incorporation in the primary and secondary C-H positions is observed (Table 2, entry 18-21). Importantly, the results of H/D exchange reactions of nitriles do not depend on the C-H acidity and the lengths of the alkyl chains. Most interestingly, no deuterium incorporation is observed in the case of both cyclohexane and cyclooctane, which have only methylene groups (Table 2, entry 22-23). But, surprisingly, deuteration of the methyl, methylene as well as the methine positions of methylcyclohexane is observed (Table 2, entry 24). In addition, tetrahydropyran also shows deuterium scrambling in its methylene positions (Table 2, entry 25). These results show that the H/D exchange can occur only in the alkyl chains which have donating functional groups, such as arene, C=C double bond, O- and N- donors, or the methyl group.

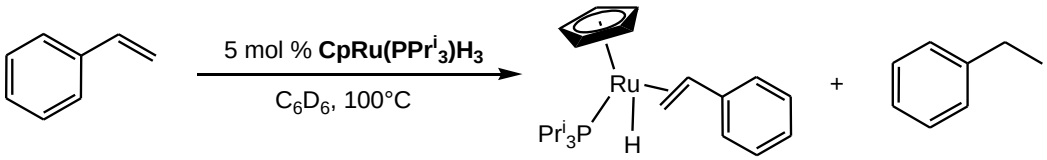
Table 2. H/D exchange reactions catalysed by $Cp(PPr^{i}_{3})RuH_3$ (**1**) in C_6D_6 [a]

Entry	Substrate/Deuteration	Time	Entry	Substrate/Deuteration	Time
1		6 d	13		3 d
2		33 d	14		10 d
3		15 d	15		7 d
4		10 d	16		4 d
5		6 d	17		4 d
6		5 d	18		4 d
7		3 d	19		4 d
8		1d	20		4 d
9		1 d	21		4 d
10		3 d	22		18 d
11		1 d	23		10 d

12		3 d	24		9 d
			25		4 d

[a] Reaction condition: 5 mol % $Cp(PPr^i_3)RuH_3$, substrate (0.3 mmol), C_6D_6 (0.6 mL), 100ºC, an internal standard (Cp_2Fe).

The attempted H/D exchange reaction of styrene under the same conditions results in catalyst deactivation (Scheme 82). We observed that this reaction generates an equivalent of ethylbenzene and the complex $Cp(PPr^i_3)RuH$(styrene), which was characterized by NMR.



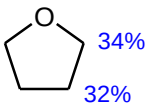
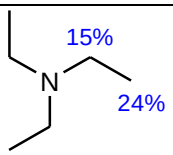
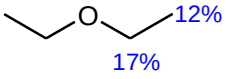
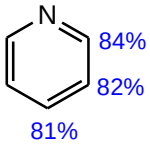
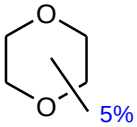
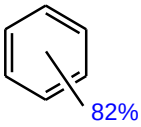
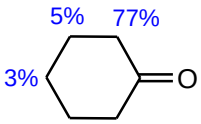
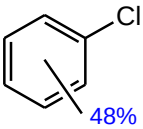
Scheme 82. Reaction of $CpRu(PPh_3)H_3$ and styrene

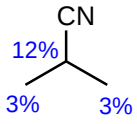
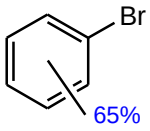
III.1.2. H/D exchange reactions catalysed by $Cp(PPr^i_3)RuH_3$ (1) in D_2O

D_2O is a cheapest source deuterium and an environmentally friendly solvent, therefore its use in H/D exchange reactions is a long term goal. For this reason, we studied H/D exchange of different organic compounds in D_2O instead of C_6D_6.[76] However, due to the poor solubility of the catalyst in D_2O, the substrate scope was limited to polar substrates, such as 1,4-dioxane, THF and cyclohexanone. In the presence of a polar substrate, the miscibility with water increased and, therefore, the exchange reaction could be achieved.

Comparable deuterium incorporation in the α- and β-CH positions of THF and ether was observed (Table 3. entry 1-2). In the case of 1,4-dioxane, very little deuteration was achieved even after heating the sample for 6 days (Table 3. entry 3). H/D exchange in cyclohexanone and Pr^iCN occurs preferably at the α-position, which could indicate acid-catalysed exchange reactions (Table 3. entry 4-5). Triethylamine showed deuterium scrambling in both α- and β-positions (Table 3. entry 6). Pyridine and other aromatic compounds, including those bearing halogen groups, react easily in relatively short reaction time (Table 3. entry 7-10). In general, there is little correlation between the C-H acidity and the deuterium incorporation in the H/D exchange in D_2O. This observation is in contrast with the C-H activation on Tp(L)RuX, which correlates with the acidity of substrates (R-H) and the basicity of the ligand X (X = CH_3, OH, NHR').[41b]

Table 3. H/D exchange reactions catalysed by $Cp(PPr^i_3)RuH_3$ (**1**) in D_2O [a]

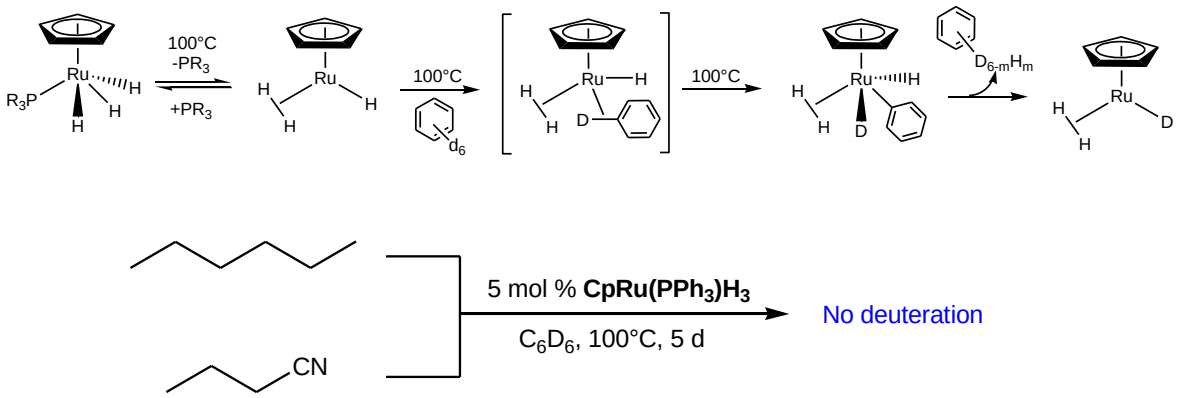
Entry	Substrate/Deuteration	Time	Entry	Substrate/Deuteration	Time
1		8 d	6		2 d
2		2 d	7		1 d
3		6 d	8		1 d
4		3 d	9		1 d

5		4 d	10		1 d

[a] Reaction condition: 5 mol % $Cp(PPr^{i}_{3})RuH_3$, substrate (0.3 mmol), D_2O (0.6 mL), 100 ºC, an internal standard (Cp_2Fe).

III.1.3. H/D exchange reactions catalysed by $Cp(PPh_3)RuH_3$ in C_6D_6

To evaluate further possible reaction pathways, we performed H/D exchange reactions mediated by $CpRu(PPh_3)H_3$ (**71**) in C_6D_6. Our reasoning was that the catalytically active species could be generated by the phosphine dissociation (Scheme 83, top). At elevated temperature, phosphine dissociation would form a dihydrogen monohydride (or a trihydride) ruthenium intermediate, which could then react with C_6D_6 to generate a ruthenium(IV) species. Then, the H/D exchange and reductive elimination of the partially protonated solvent would generate a ruthenium monodeuteride complex, which can continue the oxidative addition, H/D exchange and reductive elimination sequence. If the H/D exchange were achieved through this pathway, the reactions catalysed by **71** would be faster than those catalysed by $CpRu(PPr^{i}_{3})H_3$ (**1**) because PPh_3 is less electron donating and thus should dissociate easier. We then found that 1-hexane and butylnitrile are not engaged in H/D exchange in the presence of $CpRu(PPh_3)H_3$ under the same conditions as applied in the catalysis by **1** (Scheme 83, bottom). Therefore, this result allows us to rule out phosphine dissociation from the metal centre as an initial step of a possible reaction mechanism.

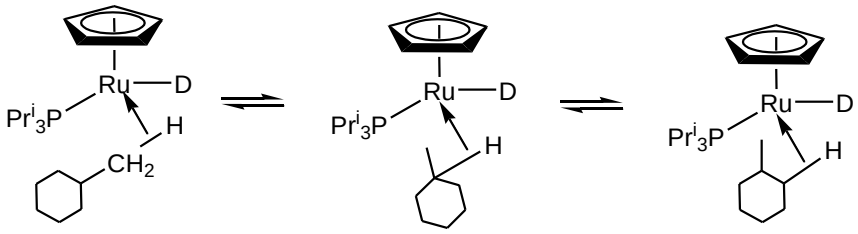


Scheme 83. A possible reaction pathway and H/D exchange reaction catalysed by $Cp(PPh_3)RuH_3$

III.1.4. Possible reaction pathways

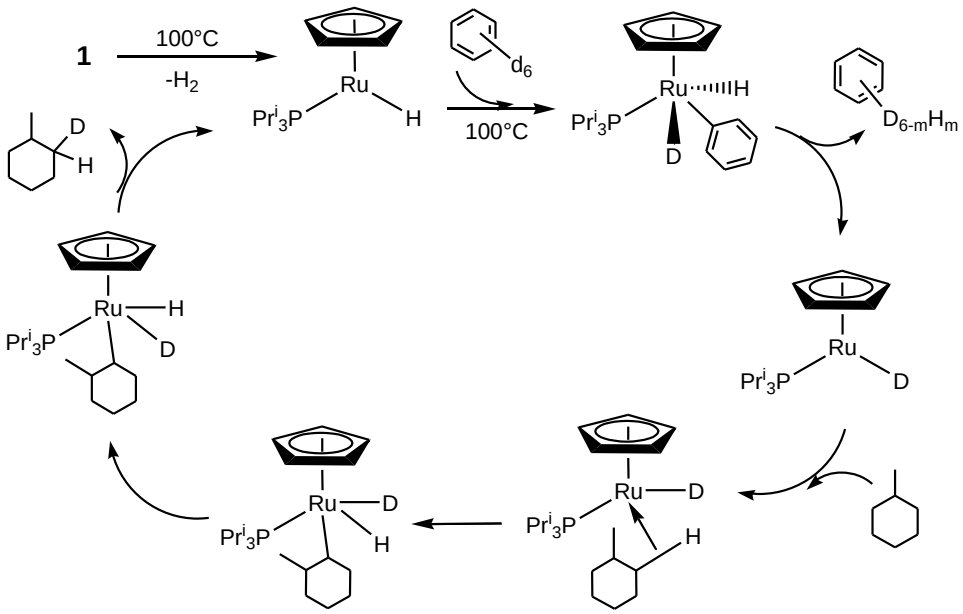
Based on the results of our experiments, we suggest that the H/D exchange reactions are initiated by anchoring of substrates to the complex as a prerequisite for the C-H bond activation. Such an anchoring can be provided by donation of a lone pair of a heteroatom to the metal or by formation of a σ-complex between the C-H bond in arenes or methyl and metal.[41b,77a-c] As shown above, the H/D exchange in alkyl chains of substrates occurs only if the substrates are featuring electron donating functionalities, such as arene, O- and N- donors, or the CH_3 group (Table 2). Once the functional group of substrate coordinates to the metal centre, it would initiate the C-H bond activation, and the activation goes to the next C-H bond along the chain. The anchoring effect in the H/D exchange reaction of methylcyclohexane is shown in Scheme 84. The reaction would start with the coordination of the methyl group to the complex. Then oxidative addition of the methyl group and H/D exchange will result in deuterium scrambling into the methyl group. The activation would then proceed to the methine C-H bond and further to the methylene groups of the cyclohexane ring. We believe that this activation of different positions occurs under equilibrium.

Therefore, when a substrate has a functional group that can act like an anchor, the H/D exchange reaction would be initiated.



Scheme 84. The anchoring effect in the H/D exchange reaction

As described above, the experiment with $CpRu(PPh_3)H_3$ allowed us to rule out the mechanism based on phosphine dissociation. We suggest another possible reaction pathway of the H/D exchange reaction catalysed by $Cp(PPr^i_3)RuH_3$ (**1**) using methylcyclohexane as a substrate (Scheme 85). Dehydrogenation of the catalyst upon heating a C_6D_6 solution of **1** would generate an intermediate monohydride complex of ruthenium. Then, the oxidative addition of the C-D bond of C_6D_6 to the metal centre gives a ruthenium phenyl derivative. This ruthenium(IV) species, $Cp(PPr^i_3)Ru(H)(D)(R)$, is stabilized by the presence of the electron rich Cp ligand. This situation is in contrast to what happens for the isoelectronic but less electron donating Tp ligand. Thus, for the related $Tp(PMe_3)Ru$ fragment, the H/D exchange proceeds via a ruthenium(II) σ–complex, $Tp(PMe_3)Ru(\eta^2\text{-R'H})(X)$.[41b] The reductive elimination of a partially deuterated solvent, $C_6D_xH_{6-x}$, generates a ruthenium monodeuterium complex, which can catalyse the subsequent C-H activation of the substrate, such as methylcyclohexane, to give the final deuterated product.



Scheme 85. A possible mechanism of the H/D exchange reaction

III.1.5. Computational studies

To better understand the mechanism of sp^3 C-H bond activation under our catalytic conditions, density functional theory (DFT) calculations were performed by our collaborator, Dr. S. Gorelsky (University of Ottawa).[76] Three exchange-correlation (XC) functionals (B3LYP,[81] M06L,[82] and PBE[83]) were used for the model complex $Cp(PMe_3)RuH_3$ (**72**). Since the results obtained by using the M06L and PBE functionals are similar to the results with the B3LYP functional, our discussion will be focused on the latter. Two main scenarios of the catalyst activation were considered: (1) dissociation of dihydrogen from $Cp(PMe_3)RuH_3$ (**72**) and (2) dissociation of the phosphine ligand.

To investigate the pathway of dissociation of dihydrogen, the two lowest energy pathways of oxidative addition of the C-H bond of CH_4 to the ruthenium complex were investigated (Figure 4). The pathway I produced a symmetric ruthenium(IV) product, $Cp(PMe_3)RuH_2(CH_3)$, with the methyl group between two

hydride ligands. On the other hand, pathway II resulted in a nonsymmetric product, $Cp(PMe_3)Ru(H_2)(CH_3)$, with the methyl group next to the dihydrogen ligand. It was found that both pathways I and II start with the formation of a low-energy dihydrogen ruthenium(II) complex, $Cp(PMe_3)RuH(H_2)$ (1.7 kcal mol^{-1}), which loses dihydrogen to give the high-energy ruthenium-monohydride intermediate (ΔG_{298K} of 17.2 kcal mol^{-1}). As the first step of alkane addition, a weak complex featuring a three-centre Ru···HC agostic interaction[84] is formed. This can be characterized by the value of the three-centre bond[85] (0.09) which is about 30% of the maximum theoretically possible value of three-centre orbital interactions (~0.296).[86] The C-H bond showing the agostic interaction with the ruthenium atom is elongated ($d_{C\text{-}H}$ = 1.12 Å compared to 1.086-1.089 Å for the other aliphatic C-H bonds), but the fairly long Ru-C_{CH4} distance indicates a weak interaction. Then, the oxidative cleavage of the C-H bond via the transition state TS_I for the pathway I and TS_{II} for pathway II, having a $\Delta G^{\ddagger}_{298K}$ of 34.5 kcal mol^{-1} and a $\Delta G^{\ddagger}_{298K}$ of 33.6 kcal mol^{-1}, respectively, takes place (Figure 4). The B3LYP functional presents higher $\Delta G^{\ddagger}$ values than the PBE and M06L functionals (~3 kcal mol^{-1} higher). The calculated energy barriers for pathway I and II using the three XC functionals are close to each other and do not allow us to rule out one mechanism at the expense of the other.

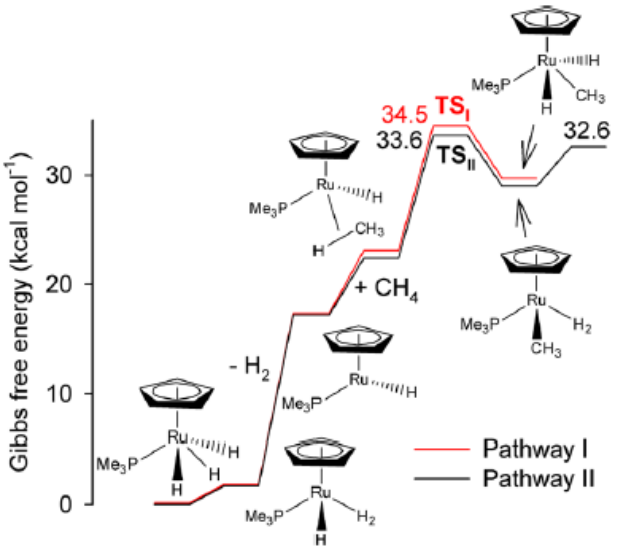


Figure 4. Calculated Gibbs free energies (kcal mol^{-1}) for C-H bond cleavage via pathway I and II

Furthermore, the calculated barriers for substrates other than CH_4 indicate that the reaction may switch from one pathway to another (Table 4). Changing temperature from 25°C to 100°C only slightly increases the $\Delta G^{\ddagger}$ of the barriers for the C-H bond oxidative addition of CH_4 by 0.5 kcal mol^{-1} for both pathways I and II (Table 4, entry 1). The ruthenium(IV) intermediate, $Cp(PMe_3)RuH_2(R)$, having the R group between two hydrides was observed in the pathway I. The internuclear distance between the carbon of the methyl group and the hydride ligand is 2.21 Å (Figure 5). For the pathway II, the intermediate can be described as a ruthenium(II) dihydrogen complex, $Cp(PMe_3)Ru(H_2)(R)$, rather than a ruthenium(IV) dihydride species because of the short internuclear H-H distance of 0.91 Å and the Mayer bond order[87] of 0.59 for the H-H interaction. In addition, there is a three-centre Ru···HH interaction with a three-centre bond order of 0.08 in the intermediate. The TS structure corresponding to the rotation of the H_2 ligand in the species of TS_{II} has a shorter H-H bond (0.84 Å), higher Mayer H-H bond order of 0.66 and a $\Delta G^{\ddagger}$ that is lower than for the C-H

cleavage transition state TS_{II}. The Ru···HH interaction has a three-centre bond order of 0.13 in this structure (Figure 6).

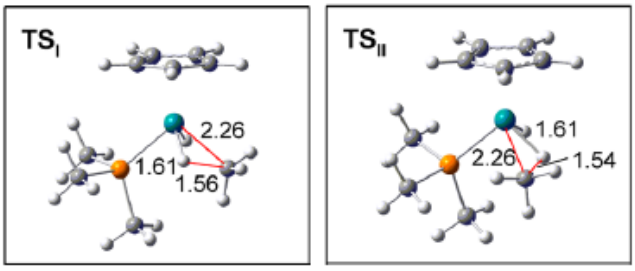


Figure 5. The C-H bond cleavage transition states for pathways I and II

The energy barriers of C-H bond cleavage for several substrates with primary and secondary sp^3 C-H bonds were investigated. In the comparison with methane, the $\Delta G^{\ddagger}$ of ethane increases by 1.5 and 2.1 kcal mol^{-1} for pathways I and II, respectively (Table 4, entry 1 and 2). The methyl group of toluene showed a slightly smaller increase than the values of ethane (Table 4, entry 3). The energy barriers of the cleavage of the methyl group of methylcyclohexane was calculated as 37.7 kcal mol^{-1} for pathway I and 37.3 kcal mol^{-1} for pathway II, indicating that it is the least reactive methyl group in this series (Table 4, entry 6). The energy barriers for secondary C-H bonds were higher than those for primary C-H bonds, with the lowest value being in the 39-40 kcal mol^{-1} range (Table 4, entry 4 and 5). The C-H bonds of cyclohexane were found to be as robust as the methylene positions of methylcyclohexane (Table 4, entry 7 and 8). Therefore, the selectivity for primary C-H bond activation vs secondary C-H bond activation can be explained with this mechanistic model. However, the occurrence of H/D exchange in methyl and methylene positions of methylcyclohexane and the absence of H/D exchange in cyclohexane cannot be explained with this mechanistic model.

Table 4. Calculated Gibbs free energies (kcal mol^{-1}) for C-H bond cleavage via Pathways I and II [a]

Entry	sp^3 C-H substrate	$\Delta G(TS_I)$	$\Delta G(TS_{II})$
1	CH_4	34.5 (35.0) [b]	33.6 (34.1) [b]
2	CH_3CH_3	36.0	35.7
3	$C_6H_5C\underline{H}_3$	35.5	35.4
4	$CH_3C\underline{H}_2CH_3$	39.9	41.2
5	$C_6H_5C\underline{H}_2CH_3$	39.3	39.8
6	$C\underline{H}_3$-C_6H_{11} [c]	37.7	37.3
7	CH_3-$C_6\underline{H}_{11}$ [c]	39.5^{eq}, 41.7^{ax}	41.0^{eq}, 42.4^{ax}
8	cyclohexane, C_6H_{12}	39.5^{eq}, 41.8^{ax}	40.8^{eq}, 42.3^{ax}

[a] $Cp(PMe_3)RuH_3$ as the catalyst at the B3LYP level of theory in the gas phase at 298 K. [b] ΔG at 373 K. [c] Methylcyclohexane with the methyl group in the equatorial position (the lowest energy conformation). TS structures involving methylcyclohexane with the axial methyl group are higher in energy than the corresponding TS structures involving methylcyclohexane with an equatorial methyl group.

Calculations of pathway I and II were repeated using a solvent polarization model to test the influence of solvent on the reaction barriers (Figure 6). The reaction energies of the calculations with benzene as a solvent are similar to those of the gas-phase calculations. For example, the oxidative addition barriers in benzene are only 0.8 kcal mol^{-1} lower than those in the gas phase (pathway I: 34.5 kcal mol^{-1} in gas phase and 33.7 kcal mol^{-1} in benzene, pathway II: 33.6 kcal mol^{-1} in gas phase and 32.8 kcal mol^{-1} in benzene). When water was used as a solvent, the oxidative addition barriers for both pathways increase by 3.5 and 5.0 kcal mol^{-1} for TS_I and TS_{II}, respectively.

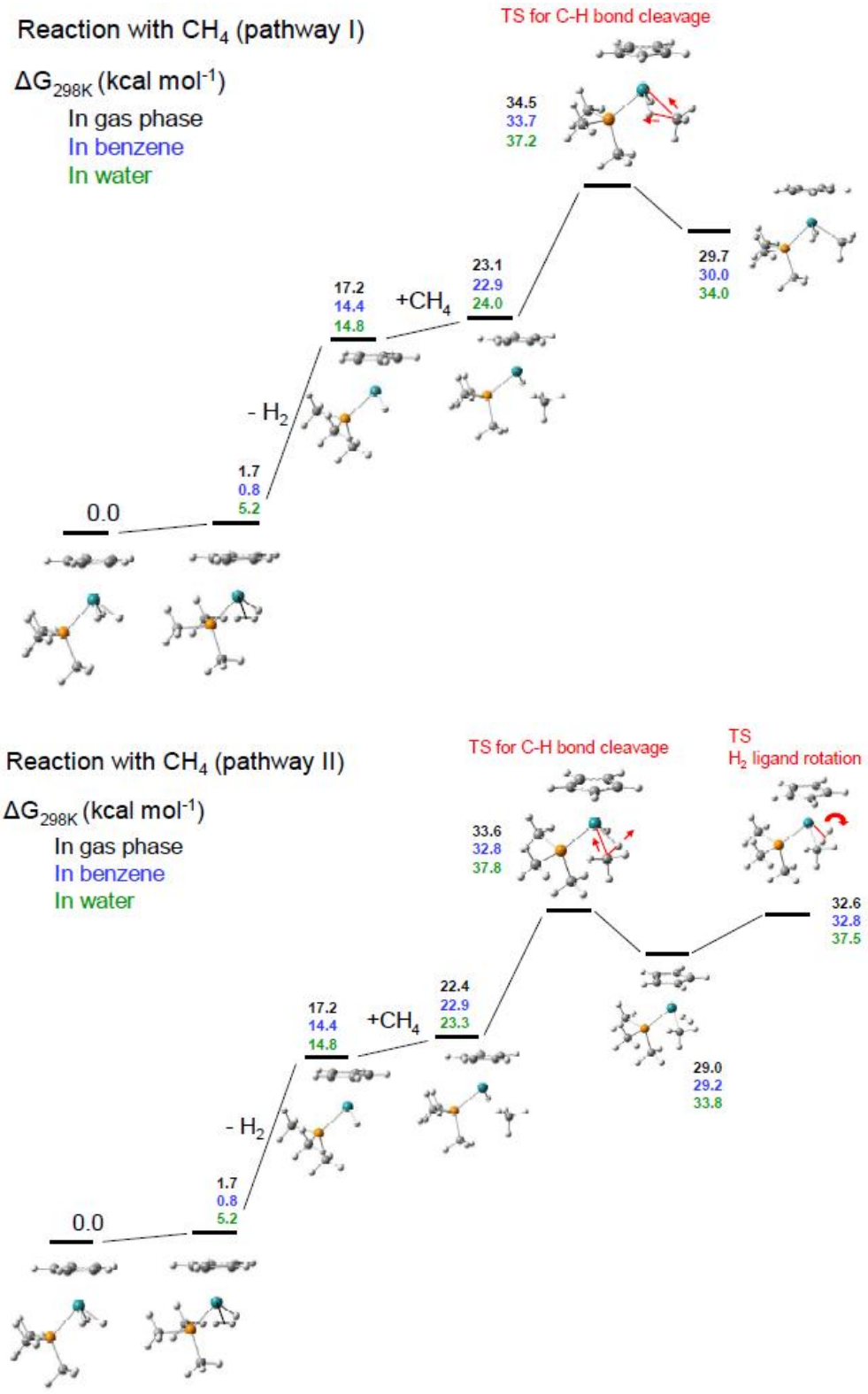


Figure 6. The oxidative addition reaction pathways I and II for C-H bond cleavage of CH_4

The pathway of dissociation of the phosphine ligand turned out to be a higher energy process. Dissociation of PMe_3 from $Cp(PMe_3)RuH_3$ (**72**) to form $CpRuH_3$

requires a ΔG_{278K} of +33.7 kcal mol^{-1} and +30.7 kcal mol^{-1} at 100°C. Then the high-energy intermediate undergoes conversion to the dihydrogen complex CpRuH(H_2) (ΔG_{278K} of 32.1 kcal mol^{-1}, ΔG_{373K} of 29.2 kcal mol^{-1}), featuring a short H-H distance of 0.87 Å. The lowest value of the free energy barrier for the oxidative addition of CH_4 to the complex CpRuH(H_2) was observed as 48.8 kcal mol^{-1}, which is extremely high. We also considered a pathway with dissociation of H_2 from CpRuH(H_2) and oxidative addition of CH_4 to the intermediate CpRu(H). However, the energies of the corresponding species are even higher as the Gibbs free energy of CpRu(H) is 42.3 kcal mol^{-1} at 25°C and 37.2 kcal mol^{-1} at 100°C. Also, the lowest $\Delta G^{\ddagger}$ value for the oxidative addition of CH_4 to CpRu(H) is 55.6 kcal mol^{-1}. Therefore, the pathways with dissociation of phosphine ligand, with and without H_2 dissociation, are not competitive with the pathways I and II (the oxidative addition via the Cp(PMe_3)RuH intermediate).

We studied alternative mechanisms, such as σ-bond metathesis and ring slippage, for the C-H bond cleavage. All our attempts, however, led to transition-state structures corresponding to the oxidative addition.

III.2. Reduction of pyridine derivatives with silanes

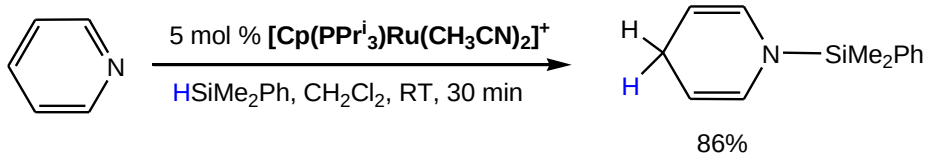
The cationic half-sandwich complex $[Cp(PPr^{i}_{3})Ru(CH_3CN)_2]PF_6$ (**2**) can be easily obtained from the commercially available complex $[CpRu(CH_3CN)_3]^+$ by addition of an equivalent of phosphine. Previously, Nikonov *et al*. have reported various catalytic hydrosilylation reactions mediated by $[Cp(PPr^{i}_{3})Ru(CH_3CN)_2]PF_6$ (**2**).[12] Hydrosilylations of carbonyls, nitriles and pyridines were achieved in good yields under mild reaction conditions in the presence of **2**. Furthermore, due to the poor solubility of the ruthenium complex in non-polar solvents, the catalyst can be easily separated from reaction products by changing the polarity of the media and then reused for further reaction cycles. In this section, our kinetic studies on the hydrosilylation of pyridine catalysed by **2** will be presented. We then discuss further investigation of catalytic activity of Cp^*-substituted analogues of complex **2**.

III.2.1 Hydrosilylation of pyridines and kinetic studies

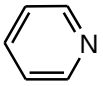
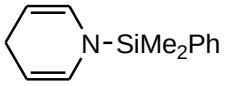
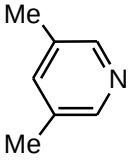
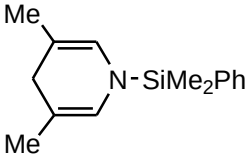
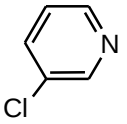
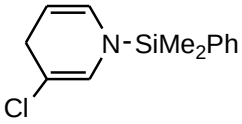
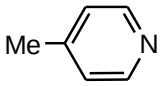
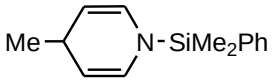
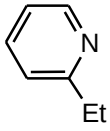
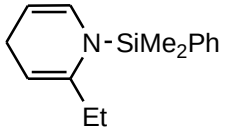
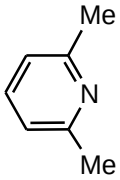
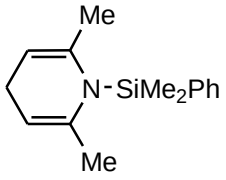
Previously, a highly regioselective hydrosilylation of pyridines was achieved with the catalyst, $[Cp(PPr^{i}_{3})Ru(CH_3CN)_2]PF_6$ (**2**) and $HSiMe_2Ph$.[12c] This complex efficiently catalyses hydrosilylation of pyridine derivatives bearing various substituents. Importantly, the reactions can be carried out at room temperature and result selectively in the formation of 1,4-addition products, *N*-dimethylphenylsilyl-1,4-dihydropyridines. Pyridine was reduced in only 30 min under mild conditions regiospecifically to the 1,4-addition product, *N*-dimethylphenylsilyl-1,4-dihydropyridine (Table 5, entry 1). Pyridine derivatives having substitution in the 3- and 5-positions were also reduced smoothly to the corresponding 1,4-addition products (Table 5, entries 2 and 3). Therefore, it was found that these reductions were 1,4-regiospecific. Substrate having substitution in the 4-positions, however,

completely stopped indicating that access to the 4-position is a prerequisite for reduction (Table 5, entry 4). In addition, substitution in the 2- and 6-positions stopped the reactions, indicating further steric constraints of this system. Attempts at mitigating this problem by heating to 70°C resulted in the formation of $ClSiMe_2Ph$, which comes from the reaction of $HSiMe_2Ph$ and the solvent (Table 5, entry 5 and 6).

Table 5. Hydrosilylation of pyridines catalysed by $[Cp(PPr^i_3)Ru(CH_3CN)_2]^+$ [a]

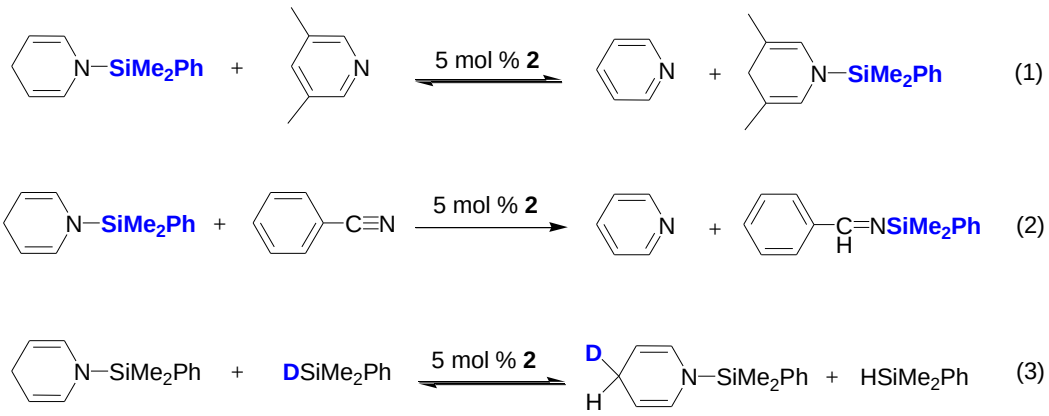


86%

Entry	Substrate	Product	Yield [b]	Time
1			86 % (96 %) [c]	30 min
2			82 %	3 h
3			100 %	15 min
4			NR	24 h
5			NR	3 h
6			NR	24 h

[a] Reaction condition: 5 mol % of $[Cp(PPr^i_3)Ru(CH_3CN)_2]^+$ was added to a solution of substrate and silane in CH_2Cl_2. [b] Based on the ^1H NMR data. [c] Under solvent-free conditions.

It was also found that the reactions of pyridines and silane are reversible. The product of hydrosilylation of pyridine, *N*-dimethylphenylsilyl-1,4-dihydropyridine, can react with 3,5-lutidine and release the free pyridine as well as give the 1,4-hydrosilylated lutidine product (Scheme 86, eq. 1). It also reacts with benzonitrile to generate pyridine and the *N*-silylated imine, $PhCH{=}NSiMe_2Ph$ (Scheme 86, eq. 2). Finally, *N*-dimethylphenylsilyl-1,4-dihydropyridine reacts with $DSiMe_2Ph$ in the presence of the catalyst. The deuteration of the 4-position of *N*-dimethylphenylsilyl-1,4-dihydropyridine was observed and free protonated silane was produced (Scheme 86, eq. 3).



Scheme 86. Reversibility of hydrosilylation of pyridine

Based on these experiments, an ionic hydrosilylation mechanism is suggested.[12a,88] The reaction starts with dissociation of a ligand from **2** to give an intermediate **73** (Figure 7). It is found that this step is reversible and a fast exchange between the coordinated nitrile and the free nitrile was observed in EXSY NMR. Then silane coordination generates a cationic silane σ-complex **74**. Nucleophilic abstraction of the silylium ion by pyridine gives an *N*-silyl pyridinium salt **75** and a neutral ruthenium hydride complex **76**, which has an increased hydridic character.

Hydride transfer from the neutral complex **76** to the 4-position of the pyridinium salt **75** produces the *N*-dimethylphenylsilyl-1,4-dihydropyridine as a sole product. The high selectivity towards the 1,4-addition products is presumably due to the steric hindrance in the 2- and 6-positions.

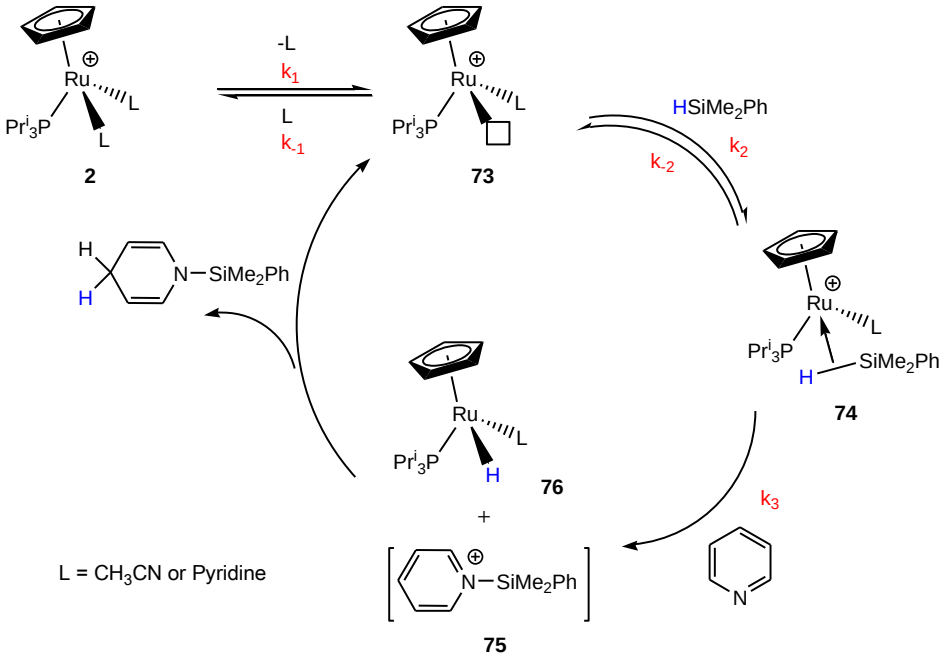


Figure 7. Proposed mechanism of hydrosilylation of pyridine

To support this mechanistic proposal, kinetic studies under catalytic conditions were performed.[89] To minimize the effect of a possible catalyst deactivation, initial rate analysis was performed. First order kinetics in silane concentration was observed by carrying out the hydrosilylation reactions under the pseudo-first-order conditions, with 8- to 12-fold excess pyridine (Figure 8). These experiments allowed us to extract the k^{eff} by using the standard kinetic analysis.[90] Furthermore, it is found that the dependence of k^{eff} on the concentration of pyridine shows a saturation behavior, which indicates that the reaction rate does not depend on the pyridine concentration when the concentration of pyridine is high (Figure 9). Taking into account that **2** and

73 are in fast equilibrium and assuming the steady-state approximation for reactive species shown in the proposed mechanism,

$$\frac{d[\mathbf{74}]}{dt} = k_2[\mathbf{73}][HSiMe_2Ph] - k_{-2}[\mathbf{74}] - k_3[\mathbf{74}][pyr] = 0$$

Hence

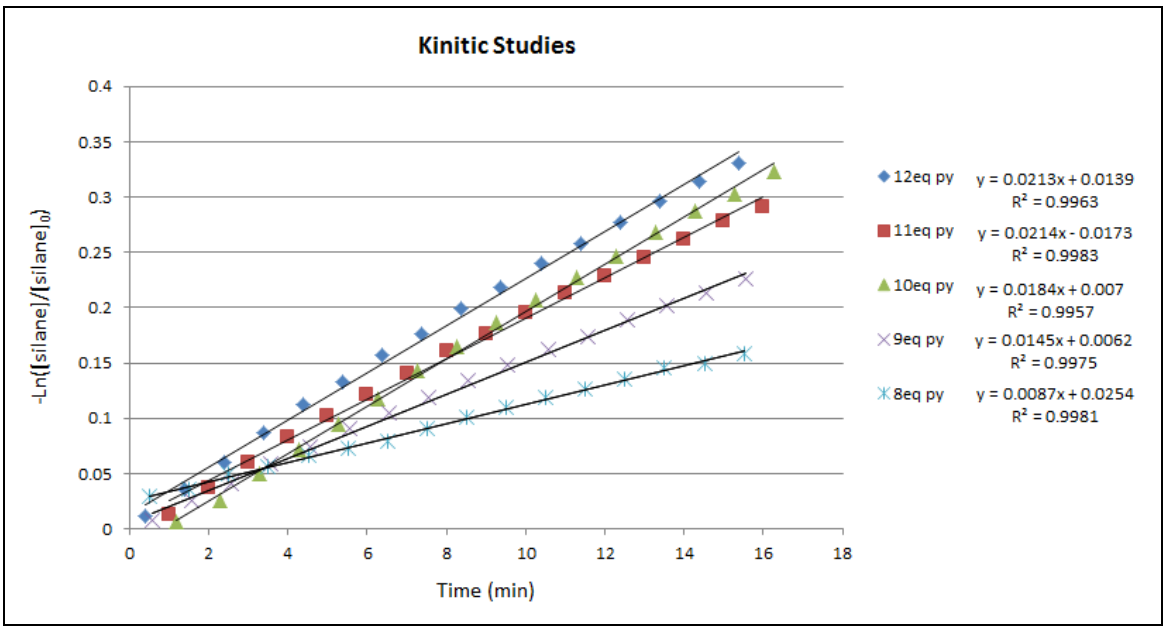
$$k_2[\mathbf{73}][HSiMe_2Ph] = (k_{-2} + k_3[pyr])[\mathbf{74}]$$

And since $k_1[\mathbf{2}] = k_{-1}[\mathbf{73}][NCCH_3]$,

the following kinetic law can be derived:

$$rate = k_3[\mathbf{74}][pyr] = k_3 \frac{k_2[\mathbf{73}][HSiMe_2Ph][pyr]}{k_{-2} + k_3[pyr]}$$
$$= \frac{k_1 k_2 k_3[\mathbf{2}][HSiMe_2Ph][pyr]}{(k_{-1}k_{-2} + k_{-1}k_3[pyr])[NCCH_3]}$$

which is in agreement with our kinetic studies.



0.9 μmol (0.6 mol %) **2**, 0.15 mmol $HSiMe_2Ph$, 1.2-1.8 mmol pyridine, 0.5 mmol CH_2Cl_2, 22°C.

Figure 8. The dependence of $-Ln([silane]/[silane]_0)$ on time at 8- to 12-fold excess of pyridine

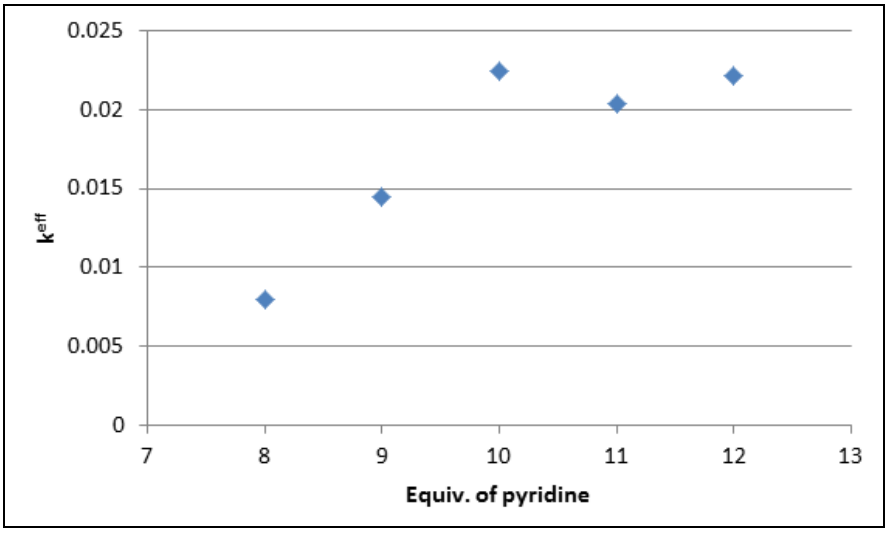


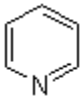
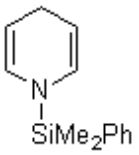
Figure 9. The dependence of k^{eff} on the amount of pyridine

III.2.2 Catalytic hydrosilylation of pyridine with Cp*Ru complexes

To extend our study, different Cp*Ru complexes, which are analogous to the complex $[Cp(PPr^i_3)Ru(CH_3CN)_2]^+$ (**2**), were synthesized and their catalytic activities were investigated.[89,91] Hydrosilylation of pyridine catalysed by Cp*Ru complexes, $[Cp^*(L)Ru(CH_3CN)_2]^+$ (L = PPr^i_2Me (**77**), PPr^i_3 (**4**), PPh_3 (**78**) and phen (**3**)), were studied (Table 6). In comparison with the reactions of the Cp complex **2** discussed above (Table 6, entry 1), a significantly decreased catalytic activity was observed (Table 6, entry 2-5). In the case of catalysis by **2**, the bulky and basic phosphine ligand most likely renders the coordination of silane in the intermediate σ-complex with the η^1-mode, making it accessible for the attack of a nucleophile. The donating phosphine also makes the intermediate hydride complex $CpL(CH_3CN)RuH$ more hydridic, which is a prerequisite for the reduction step.[12a] The bulky triisopropylphosphine was found to be the best ligand in the case of the catalysis by Cp/phosphine complexes. In the case of Cp* complex of ruthenium with the same phosphine ligand, however, the reaction was sluggish (Table 6, entry 3). We believe

that this fact is due to the difficulty of silane coordination to such a sterically loaded environment of complex $[Cp^*(PPr^i_3)Ru(CH_3CN)_2]^+$ (**4**). The reactions of analogous compounds $[Cp^*(PPr^i_2Me)Ru(CH_3CN)_2]^+$ (**77**) and $[Cp^*(PPh_3)Ru(CH_3CN)_2]^+$ (**78**) were also very sluggish (Table 6, entry 2 and 4). In all catalytic runs with the Cp^*Ru phosphine complexes, the reactions did not give further conversion. Compared to the Cp^*Ru phosphine complexes, the phenanthroline supported complex $[Cp^*(phen)Ru(CH_3CN)]^+$ (**3**) showed a much better result, as it gave 40% conversion under solvent-free condition at elevated temperature (Table 6, entry 5).

Table 6. Hydrosilylation of pyridine catalysed by Ru complexes [a]

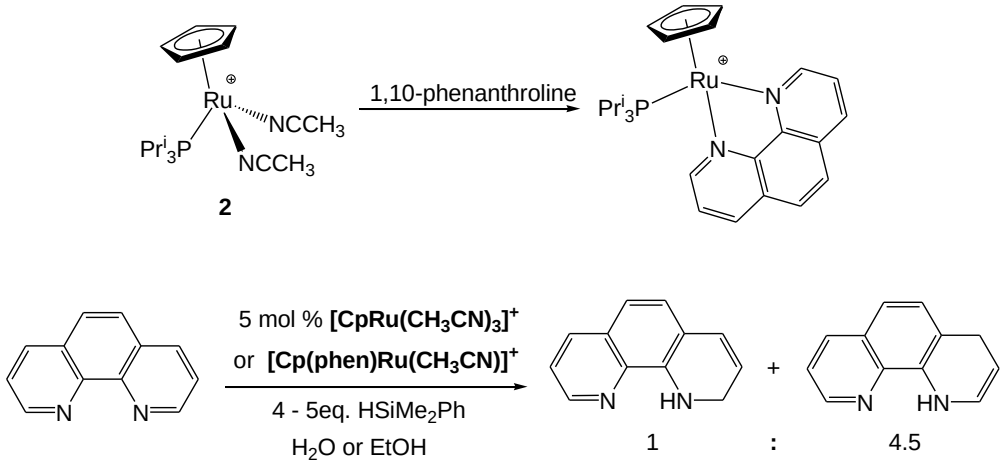
Entry	Catalyst	Substrate	Product	Conv.	Time
1	$[Cp(PPr^i_3)Ru(CH_3CN)_2]^+$ (**2**)			86 % (96 %)[c]	30 min
2	$[Cp^*(PPr^i_2Me)Ru(CH_3CN)_2]^+$(**77**)			20 %	2 d
3	$[Cp^*(PPr^i_3)Ru(CH_3CN)_2]^+$ (**4**)			7 %	1 d
4	$[Cp^*(PPh_3)Ru(CH_3CN)_2]^+$ (**78**)			4 %	5 d
5 [b]	$[Cp^*(phen)Ru(CH_3CN)]^+$ (**3**)			40 % [d]	3 d

[a] Reaction condition: 5 mol % Ru catalyst, $HSiMe_2Ph$ (0.06mmol), pyridine (0.06 mmol), CD_2Cl_2 (0.5 mL), room temperature. [b] 70ºC, [c] under solvent-free conditions, [d] under solvent-free conditions with 0.7 mol % catalyst.

III.2.3 Hydrosilylation of heterocycles catalysed by $[Cp^*(phen)Ru(CH_3CN)]^+$ (3)

Previously, the hydrosilylation of 1,10-phenanthroline by $[Cp(PPr^i_3)Ru(CH_3CN)_2]^+$ (**2**) was studied.[12c] It was found that the addition of

$HSiMe_2Ph$ to 1,10-phenanthroline failed due to the formation of a stable chelate complex $[Cp(PPr^i_3)Ru(phen)]^+$ (Scheme 87, top). We also studied catalysis by $[Cp(phen)Ru(CH_3CN)]^+$ and the commercially available complex $[CpRu(CH_3CN)_3]^+$ (Scheme 87, bottom). Attempted hydrosilylation of 1,10-phenanthroline by both complexes resulted in very sluggish reactions. Nonetheless, it was found that 1,10-phenanthroline can be reduced in the presence of a slight excess (4-5 equiv.) of $HSiMe_2Ph$ and H_2O or alcohol, which act as proton sources. A mixture of 1,2- and 1,4-dihydrophenanthroline products in a 1 : 4.5 ratio was obtained from this reaction.



Scheme 87. Hydrosilylation of 1,10-phenanthroline by CpRu complexes

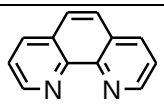
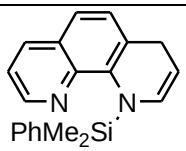
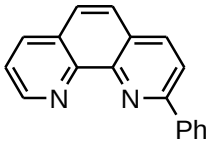
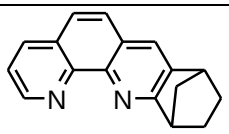
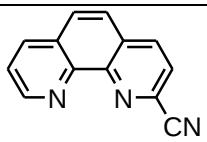
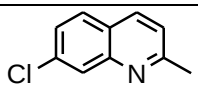
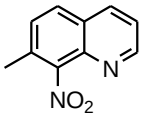
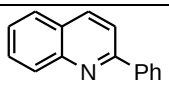
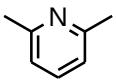
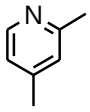
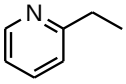
This poor hydrosilylation of 1,10-phenanthroline catalysed by CpRu complexes can be explained by steric reasons. The phenanthroline cannot abstract the silylium ion, $[SiMe_2Ph]^+$, from the intermediate $[Cp(phen)Ru(\eta^1\text{-}HSiMe_2Ph)]^+$, whereas a smaller nucleophile, such as H_2O and EtOH, can. Abstraction of $[SiMe_2Ph]^+$ by water or alcohol leads to the cation $[RO(H)SiMe_2Ph]^+$, deprotonation of which by 1,10-phenanthroline gives an activated form of the substrate, the cation $[phenH]^+$.[89] Abstraction of silylium cation from $[Cp(phen)Ru(\eta^1\text{-}HSiMe_2Ph)]^+$ also affords the neutral complex Cp(phen)RuH. The latter species can transfer hydride to

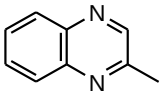
[phenH]$^+$ to furnish the reduced 1,2- or 1,4-dihydrophenanthroilnes in a way similar to the mechanism proposed in Figure 7.

To extend our studies of the catalytic activity of Cp*Ru complexes, we also investigated the hydrosilylation of 1,10-phenanthroline mediated by [Cp*(phen)Ru(CH_3CN)]$^+$ (**3**). To our delight, a highly regioselective hydrosilylation with $HSiMe_2Ph$ was achieved with the complex **3**. The 1,4-addition product, *N*-1,4-silyl-dihydrophenanthroline, was obtained in a quantitative yield by NMR. To the best of our knowledge this reaction presents the first example of catalytic hydrosilylation of phenanthroline, which is a very challenging substrate. It is important to emphasize that the reaction was achieved at room temperature, although a longer reaction time is required (Table 7, entry 1). The difference in the catalytic reactivity of [Cp*(phen)Ru(CH_3CN)]$^+$ (**3**) and [Cp(phen)Ru(CH_3CN)]$^+$ most likely relates to the difference in complexation of silane to the ruthenium centre and the different accessibility of the silylium cation. However, 2-substituted phenanthroline derivatives do not give the corresponding hydrosilylation products even at elevated temperature (Table 7, entry 2-4).

Unfortunately, hydrosilylation of substituted quinolines was unsuccessful (Table 7, entry 5-7). Unlike the reactions with [Cp(PPr^i_3)Ru(CH_3CN)$_2$]PF_6 (**2**), hydrosilylation of 2,6- and 2,4-lutidines and 2-ethylpyridine by **3** did not take place (Table 7, entry 8-10). Reduction of other *N*-heterocycles, such as 2-methylquinoxaline (Table 7, entry 11) and pyrimidine (Table 7, entry 12) also failed.

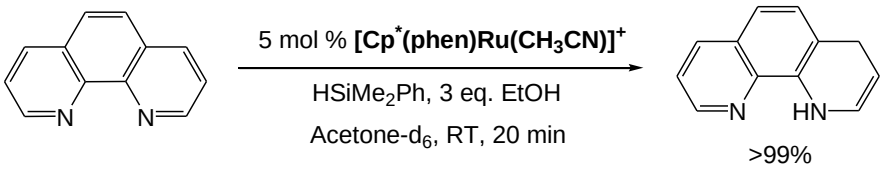
Table 7. Hydrosilylation of phenanthrolines catalysed by $[Cp^*(phen)Ru(CH_3CN)]^+$ (**3**) [a]

Entry	Substrate	Solvent	Temp.	Time	Conv.	Product
1		acetone-d_6	RT	20 h	70%	
2		acetone-d_6	RT	12 h	<5%	
3		CD_2Cl_2	70°C	12 h	<5%	
4		CD_2Cl_2	70°C	12 h	<5%	
5		CD_2Cl_2	70°C	12 h	<5%	
6		CD_2Cl_2	70°C	12 h	<5%	
7		CD_2Cl_2	70°C	12 h	<5%	
8		CD_2Cl_2	70°C	12 h	NR	
9		CD_2Cl_2	70°C	12 h	NR	
10		CD_2Cl_2	70°C	12 h	NR	

11		CD_2Cl_2	70°C	12 h	NR	
12		CD_2Cl_2	70°C	12 h	NR	

[a] Reaction condition: 5 mol % $[Cp^*(phen)Ru(CH_3CN)]^+$, $HSiMe_2Ph$ (0.05 mmol), substrates (0.05 mmol), CD_2Cl_2 (0.5 mL)

Given the success of phenanthroline hydrogenation by the silane/water system discussed above,[89] we also attempted reduction of nitrogen containing compounds in the presence of a mixture of $HSiMe_2Ph$ and EtOH (1 : 3 ratio) and the catalyst $[Cp^*(phen)Ru(CH_3CN)]^+$ (**3**). In the presence of EtOH under the same reaction condition, the 1,4-dihydrophenanthroline product was obtained in high yield and good selectivity (Scheme 88). However, attempted reductions of a quinoline derivative (Table 7, entry 7), as well as 2,6- and 2,4-lutidine, and 2-ethylpyridine by the same reducing mixture did not generate the desired hydrogenated products.

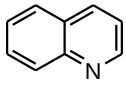
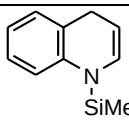
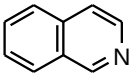
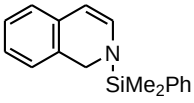
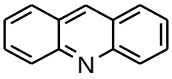
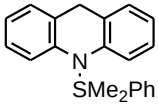
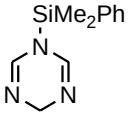


Scheme 88. Reduction of 1,10-phenanthroline in the presence of excess EtOH

Hydrogenation and hydrosilylation of *N*-heterocycles, such as quinoline and isoquinoline, are of great importance for the syntheses of pharmaceutically active ingredients. Therefore, to study further the catalysis by $[Cp^*(phen)Ru(CH_3CN)]^+$ (**3**), we screened its catalytic activity towards reduction of nitrogen containing compounds.[12c,13,47] Interestingly, the hydrosilylation of quinoline was achieved under solvent-free condition in the presence of reduced catalyst loading (0.7 mol %) at elevated temperature (Table 8. entry 1). A very high regioselectivity toward the 1,4-

addition product, *N*-silyl-1,4-dihydroquinoline, was observed, giving a mixture of the 1,2- and 1,4-addition products in the 3 : 97 ratio. Furthermore, the product of reduction can be easily isolated by removing the cationic catalyst by simple filtration due to the changed polarity of the medium during the reaction. The final product is then isolated simply by removal of volatiles under reduced pressure. A high isolated yield (94 %) of *N*-dimethylphenylsilyl-1,4-dihydroquinoline was obtained after this simple work-up. Moreover, isoquinoline, another substrate of biological importance, can be also hydrosilylated efficiently with excellent regioselectivity (Table 8. entry 2). The sole product, the *N*-dimethylphenylsilyl-1,2-dihydroisoquinoline, was obtained in a high isolated yield, although a much longer reaction time was required. We ascribe the sluggishness of the reduction of isoquinoline to the fact that the more activated 8-position is blocked. Even more interestingly, a sterically more hindered substrate, acridine, can be also hydrosilylated at room temperature (Table 8. entry 3). This reaction is driven by the increased aromaticity of the two newly formed non-conjugated benzene rings. Hydrosilylation of 1,3,5-triazine was achieved in a short time, although attempted isolation of the product failed due to its decomposition (Table 8. entry 4). Unfortunately, the reaction of pyrazine does not produce the corresponding product under the same reaction conditions (Table 8. entry 5). For the latter reaction, we found by NMR study that pyrazine adds to **3** to give a stable complex [Cp^*(phen)Ru($_K^1$-N(CHCH)$_2$N)]. We believe that this different reactivity is due to the lack of a carbon atom in the 4-position of pyrazine and more sluggish 1,2-reduction in comparison with the 1,4-reduction.

Table 8. Hydrosilylation of quinoline and related *N*-heterocycles catalysed by $[Cp^*(phen)Ru(CH_3CN)]^+$ (**3**) [a]

Entry	Substrate	Product	Conv.	Time
1[c]		 97  3	95 % (94 %)[e]	1 d
2[d]			99 % (95 %)[e]	18 d
3[b]			100 %	1 d
4			90 %	1.5 h
5			NR	

[a] Reaction condition: 5 mol % $[Cp^*(phen)Ru(CH_3CN)]^+$, $HSiMe_2Ph$ (0.05-0.1 mmol), substrate (0.05-0.1 mmol), CD_2Cl_2 (0.5 mL), 70ºC. [b] room temperature. [c] 0.7 mol % Ru catalyst, 2 mmol quinoline. [d] 1 mmol isoquinoline. [e] Isolated yield.

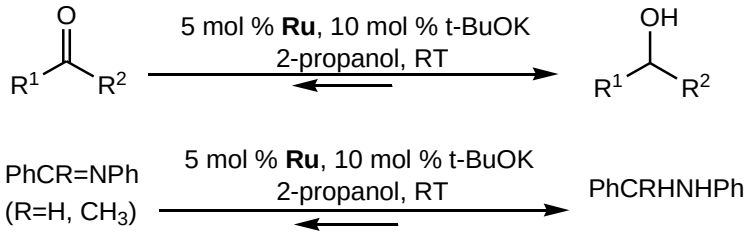
III.3. Transfer hydrogenation of organic compounds

Transfer hydrogenation has attracted much attention as a mild method for reduction of various organic compounds including ketone, aldehyde, imine and nitrile.[60-65] Transfer hydrogenation is a process of formal transfer of an equivalent of hydrogen, H_2, from one organic molecule to another. The usual hydrogenating reagents are alcohols, formates and dihydroarenes. Furthermore, the use of inexpensive and environmentally benign solvents, such as 2-propanol and 2-butanol, as hydrogen sources is a strong advantage.[57,58] In the case of 2-propanol, the only other co-product is acetone, which is easy to remove and which also finds useful applications as a chemical feedstock. Although transfer hydrogenation is considered as a relatively mild process, most catalytic conditions require elevated temperatures to complete the reactions.[57b,60-65]

A series of half-sandwich ruthenium phosphine complexes, previously prepared by us,[91] were used as catalysts for transfer hydrogenation of different organic compounds. The reactions were achieved in the presence of a base in 2-propanol at room temperature. In this section, efficient transfer hydrogenation reactions mediated by ruthenium complexes will be further discussed.

III.3.1 Transfer hydrogenation of ketones and imines

Cationic ruthenium complexes, $[Cp(PPr^i_3)Ru(CH_3CN)_2]PF_6$ (**2**), $[Cp^*Ru(phen)(CH_3CN)]PF_6$ (**3**), $[Cp^*(PPr^i_3)Ru(CH_3CN)]PF_6$ (**4**), and the neutral complex $Cp(PPr^i_3)RuH_3$ (**1**) were used as catalysts for transfer hydrogenation of various ketones and imines. In the presence of 5 mol % of the ruthenium complex and 10 mol % of base, t-BuOK, efficient catalytic transfer hydrogenation was achieved (Scheme 89).



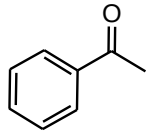
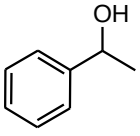
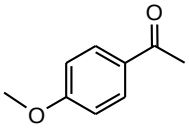
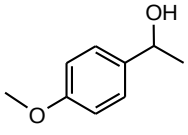
Scheme 89. Transfer hydrogenation of ketones and imines

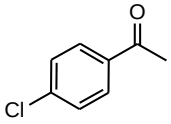
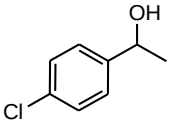
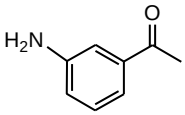
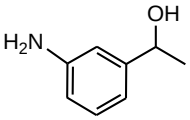
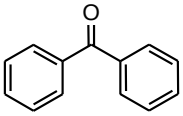
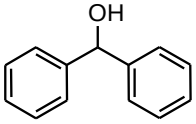
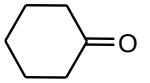
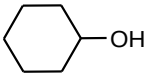
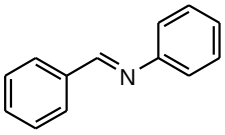
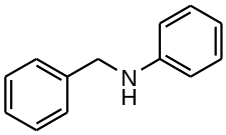
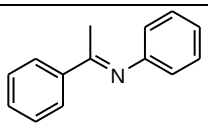
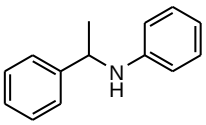
In the case of ketones, the cationic complex $[Cp(PPr^{i}_{3})Ru(CH_3CN)_2]PF_6$ (**2**) showed the best results. It is important to mention that transfer hydrogenation of ketones was achieved at room temperature and the products, secondary alcohols, were isolated with moderate to good yields. In the case of reduction of acetophenone catalysed by **2**, a good conversion was achieved and a relatively high isolated yield (82%) of 1-phenylethanol with high TOF was obtained (Table 9, entry 1). In a blank experiment, a reaction of acetophenone and the base without a ruthenium complex was monitored. As expected, transfer hydrogenation was not observed in the course of 7 days. Ketones bearing electron donating and withdrawing groups, such as methoxy, chloro and amino groups, also produced the corresponding secondary alcohols with good to high yields (Table 9, entry 2-4). The reaction of a more sterically loaded substrate, benzophenone, was also achieved in the presence of the catalyst (Table 9, entry 5). In the case of a cyclic alkyl ketone, cyclohexanone, cyclohexanol was obtained in quantitative NMR yield, although attempted isolation of the product from the ruthenium complex by chromatography failed (Table 9, entry 6). Unfortunately, an aryl ketone bearing the nitro group, 4-nitroacetophenone, was unreactive under these conditions. Finally, the reduction of imines was achieved and the corresponding amines were produced, although it required a longer reaction time (Table 9, entry 7 and 8).

The complex $[Cp^*Ru(phen)(CH_3CN)]PF_6$ (**3**) also showed good results in transfer hydrogenation reactions. Although longer reaction times were required in comparison with the reactions catalysed by **2**, it produced the corresponding secondary alcohols from ketones in high yields (Table 9, entry 1-6). The reduction of *N*-benzylideneaniline was also achieved in high yield after 35 min (Table 9, entry 7). Despite the high catalytic activity of **3** in transfer hydrogenation of the imine, PhN=CHPh, attempted reactions of other imines and ketimines, such as PhCH=NTs, PhCH=NC(O)Ph and 4-$CH_3OC_6H_4C(CH_3)$=NPh, failed to produce the desired amines.

The reactions catalysed by $[Cp^*(PPr^i_3)Ru(CH_3CN)]PF_6$ (**4**) and $Cp(PPr^i_3)RuH_3$ (**1**) were sluggish compared to reactions with **2** and **3**. Also, an elevated temperature was required in the reduction of imine PhN=CHPh (Table 9, entry 7). But it is worth to mention that transfer hydrogenation of ketones takes place with both cationic and neutral ruthenium complexes. More importantly, in almost all cases, the reactions were achieved at room temperature, whereas reflux was required in most literature reports.

Table 9. Transfer hydrogenation of ketones and imines [a]

Entry	Substrate	Product	Catalyst			
			2	**3**	**4**	**1**
			Time/ Yield	Time/ Yield	Time/ Yield	Time/ Yield
1			70 min 90% (82%)[b] (10292)[c]	4.5 h 92% (137)[c]	4 h 95%	4 d 90%
2			2 h 75% (72%)[b]	2 d 75%	3.5 h 75%	5 d 75%

3			3.5 h 98% (86%)[b]	1 d 97%		
4			3 h 95% (67%)[b]	29 h 97%		
5			100 min 97% (60%)[b]	7 h 95%	2 d 85%	
6			1 h 99%	4.5 h 99%	NR	22 h 99%
7			22 h 88% (34%)[b]	35 min 99 %	1 d 35% [d]	7 d 90% [d]
8			24 h 32%			

[a] Reaction condition: 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] TOF per hour. [d] 50°C.

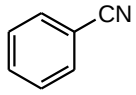
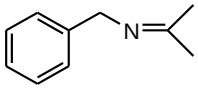
III.3.2 Transfer hydrogenation of nitriles

Transfer hydrogenation of nitriles is a much less developed procedure than transfer hydrogenation of ketones and imines. We therefore became interested in studying the activity of our most efficient catalyst $[Cp(PPr^{i}_{3})Ru(CH_3CN)_2]PF_6$ (**2**) in this reaction. The mild reaction conditions used for other substrates were applied. To our delight, reductions of nitriles were also achieved at room temperature for a range of substrates, except the nicotinonitrile (Table 11, entry 8). Moreover, the initial products of reduction were the corresponding *N*-isopropylidene amines stemming

from condensation of the target amines with acetone produced from 2-propanol. A series of nitriles bearing different functional groups were efficiently reduced in this way (Table 11). The products were then hydrolyzed and the corresponding ammonium salts were obtained in good yields after acidification.

As in reductions of ketones, among various ruthenium catalysts, **2** showed the best result when benzonitrile was used as substrate (Table 10). With this catalyst a quantitative yield was obtained in 5.5 hour at room temperature. On the other hand, benzonitrile remained intact in the presence of $[Cp^*Ru(phen)(CH_3CN)]PF_6$ (**3**) even at elevated temperature. Although good and high yields were obtained in reactions with $[Cp^*(PPr^i_3)Ru(CH_3CN)_2]PF_6$ (**4**) and $Cp(PPr^i_3)RuH_3$ (**1**) (55% and 98%, respectively), a higher reaction temperature (70°C) was required. After the completion of reaction, the imine product was hydrolyzed by acid and the corresponding ammonium salt was isolated in good yield (Table 11, entry 1).

Table 10. Transfer hydrogenation of benzonitrile [a]

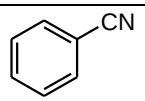
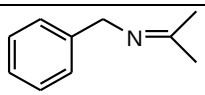
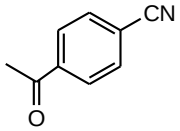
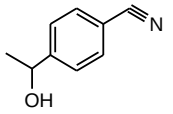
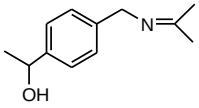
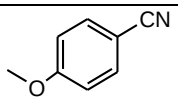
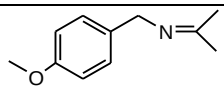
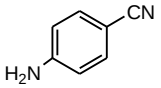
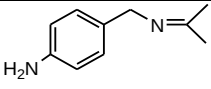
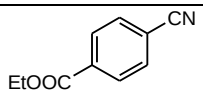
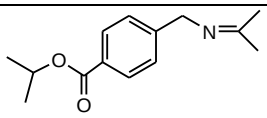
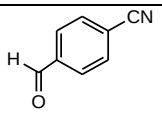
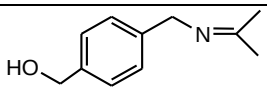
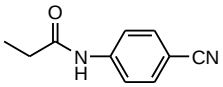
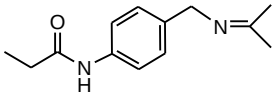
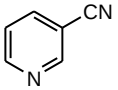
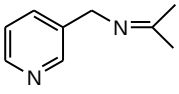
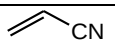
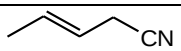
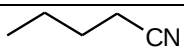
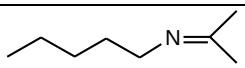
Entry	Substrate	Product	Catalyst			
			2	**3**	**4**	**1**
			Time/ Yield	Time/ Yield	Time/ Yield	Time/ Yield
1			5.5 h 99%	NR [b]	3 h 55% [b]	3 h 99% [b]

[a] Reaction condition: 5 mol % Ru catalyst, 10 mol % t-BuOK, 0.1 mmol substrate, 2-propanol (0.5 mL), room temperature. [b] 70°C.

With these results in hand, we next examined the substrate scope under these conditions. Benzonitrile bearing an acetyl substituent initially showed reduction of the ketone group in a short time and then a fully reduced product was obtained in 18 hours (Table 11, entry 2). The reaction of 4-methoxybenzonitrile also produced the

desired imine in high yield (Table 11, entry 3). Transfer hydrogenation of nitriles tolerates the amino group and full conversion of the para-amino benzonitrile was achieved in only 3 hours (Table 11, entry 4). Similar to the previous report,[64c] transesterification between the ester substituent on the nitrile substrate and 2-propanol as well as the reduction of the nitrile group were observed in the reaction of ethyl 4-cyanobenzoate (Table 11, entry 5). In the latter reaction, the transesterification was achieved first followed by reduction of the nitrile (based on ^{1}H NMR). When 4-cyanobenzaldehyde was used as a substrate, a full conversion was achieved in 24 hours. However, the reaction produced a mixture of several compounds and the fully reduced product was obtained only in 52% yield (Table 11, entry 6). Benzonitrile with an amide group was also selectively reduced under these reaction conditions and produced the corresponding product in high yield (Table 11, entry 7). Although a much longer reaction time and higher temperature were required, the reaction of nicotinonitrile was also achieved (Table 11, entry 8). However, alkyl nitriles bearing a double bond, both conjugated like acrylonitrile (Table 11, entry 9) and non-conjugated like (*E*)-pent-3-enenitrile (Table 11, entry 10), did not give the reduction products, presumably because the chelating azobutadiene poisons the catalyst and because (*E*)-pent-3-enenitrile can isomerize into a conjugated system in the presence of a base. On the other hand, valeronitrile was reduced in high yield (Table 11, entry 11). Unfortunately, attempted isolation of the ammonium salt of the product of the latter reaction did not give the desired product as only uncharacterized decomposition products was observed in ^{1}H NMR.

Table 11. Transfer hydrogenation of nitriles [a]

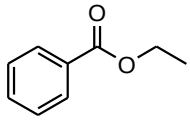
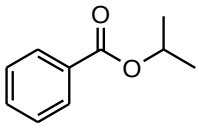
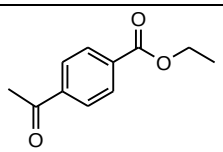
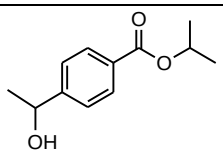
Entry	Substrate	Product	Time	Yield
1			5.5 h	99% (71%)[e]
2		 	30 min 18 h	99% 99% (63%)[e]
3			18 h	99% (65%)[e]
4			3 h	99% (91%)[e]
5			18 h	99% (62%)[e]
6			24 h	52%
7			24 h	99% (91%)[e]
8			3 d	93% [b,c] (79%)[e]
9			NR [b]	
10			NR [d]	
11			2 d	99%

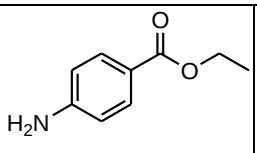
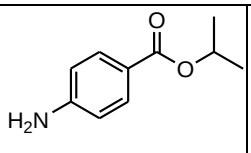
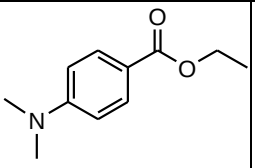
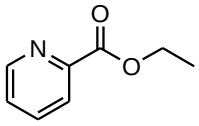
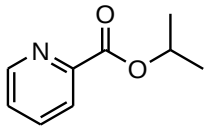
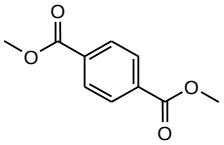
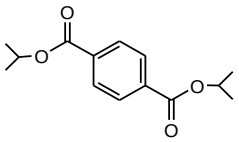
[a] Reaction condition: 5 mol % $[Cp(PPr^{i}_{3})Ru(CH_3CN)_2]PF_6$, 10 mol % t-BuOK, 0.1 mmol substrate, 2-propanol (0.5 mL), room temperature. [b] 70°C. [c] 85% in 2d. [d] 86°C. [e] Isolated yields of the ammonium salts.

III.3.3 Transfer hydrogenation of esters

Given the success of transfer hydrogenation of nitriles, we decided to extend this methodology to the reduction of esters bearing different functional groups. Similar to the reaction of ethyl 4-cyanobenzoate (Table 11, entry 5), in most reactions that we studied the ester group was not reduced but underwent transesterification. Elevated reaction temperature was required to achieve full conversions in most cases. Thus, ethyl benzoate was fully converted into the isopropyl derivative in 2 hours (Table 12, entry 1). For an ester bearing a keto group, like ethyl 4-acetylbenzoate, both transesterification of the ester group and transfer hydrogenation on the ketone group were observed (Table 12, entry 2). Although a longer reaction time was required, the reaction of ethyl 4-aminobenzoate was also achieved (Table 12, entry 3). The corresponding transesterification product was obtained at room temperature in 1 hour from the reaction of ethyl picolinate (Table 12, entry 5). However, the reaction of ethyl 4-(dimethylamino)benzoate did not produce any product, whereas, interestingly, the original cationic Ru catalyst transformed into the neutral complex $Cp(PPr^{i}_{3})RuH_3$ (**1**) (Table 12, entry 4). In addition, attempted reaction of dimethyl terephthalate did not generate reduction products upon monitoring the reactions for several days at room temperature (Table 12, entry 6).

Table 12. Transesterification of substituted alkyl benzoates [a]

Entry	Substrate	Product	Time	Yield
1			2 h	99%
2			1.5 h	99% [b]

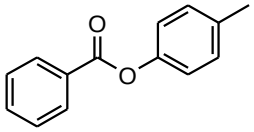
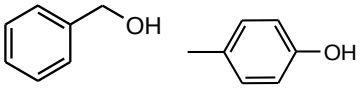
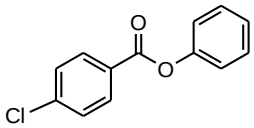
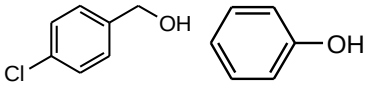
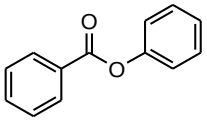
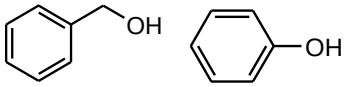
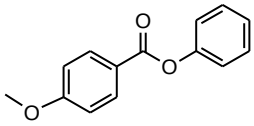
3			44 h	95%
4			2 d	NR
5			1 h	99% [b]
6			20 min	100 %

[a] Reaction condition: 5 mol % $[Cp(PPr^{i}_{3})Ru(CH_3CN)_2]PF_6$, 10 mol % t-BuOK, 0.1 mmol substrate, 2-propanol (0.5 mL), 70°C. [b] room temperature.

In contrast to the lack of reactivity in reduction of alkyl benzoates, attempted transfer hydrogenation of phenyl benzoates resulted in reduction products. The ester group was fully reduced and the product was identified by NMR to be benzyl alcohol compound (Table 13). To the best of our knowledge, this is the first example of reduction of esters by transfer hydrogenation. 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 13, entry 1). Monitoring the formation of *p*-cresol showed full conversion after 3 days. Interestingly, at this point the ratio of benzyl alcohol and *p*-cresol was 0.7 : 1, instead of theoretical 1 : 1, which indicates that there must be (an)other compound(s) formed in the reaction. This result is consistent with the observation of uncharacterized aromatic peaks in the ^{1}H NMR spectrum. Partial reduction of phenyl 4-chlorobenzoate was also achieved at room temperature after one

day, but no further conversion was observed upon monitoring the reaction for 3 days (Table 13, entry 2). Similar to the reaction of 4-methylphenyl benzoate, the ratio of 4-chlorobenzyl alcohol and phenol was 0.5 : 1 suggesting the possibility of formation of other products. Phenyl benzoate was converted into benzyl alcohol in a moderate yield (Table 13, entry 3). In this case, the reaction was achieved at 70°C and no further conversion was observed after one day. The ratio of benzyl alcohol and phenol also indicates the generation of other uncharacterized products. On the other hand, the phenyl benzoate derivative having an electron donating methoxy group was not reduced even after an extended period of time (Table 13, entry 4).

Table 13. Transfer hydrogenation of substituted phenyl benzoates [a]

Entry	Substrate	Product	Time	Conv. [b]
1		 (0.7 : 1) [c]	1 d	48 %
2		 (0.5 : 1) [c]	1 d	15 %
3		 (0.8 : 1) [c]	1 d	45 % [d]
4			3 d	NR [e]

[a] 5 mol % $[Cp(PPr^{i}_{3})Ru(CH_3CN)_2]PF_6$, 10 mol % t-BuOK, 0.1 mmol substrate, 2-propanol (0.5 mL), room temperature. [b] Conversion was calculated based on the formation of phenol derivatives. [c] The ratio of benzyl alcohol and phenol derivatives in 2-propanol solution observed in ^{1}H NMR. [d] 70°C. [e] 84°C.

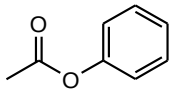
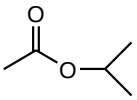
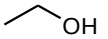
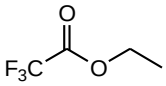
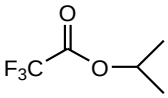
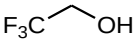
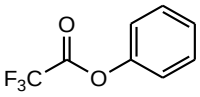
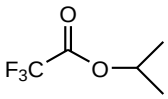
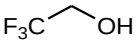
The results shown in Tables 12 and 13 show that, first, only phenyl benzoates can be reduced and, second, the reduction requires the presence of an electrophilically

activated carbonyl centre. We rationalise the greater reactivity of phenyl benzoates to the less donating ability of the phenyl group in comparison with an alkyl group, which can be attributed to the presence of the sp^2 hybridised carbon atom and the mesomeric conjugation of the phenyl π system with the p orbital of the oxygen atom.

With the successful reduction of phenyl benzoates in hand, we decided to study reactions of acetate derivatives. The reaction of phenyl acetate was carried out at room temperature and a mixture of the transesterification and reduction products, isopropylacetate and ethanol, respectively, was obtained with 67% and 13% conversions, respectively (Table 14, entry 1). Unfortunately, no further conversion into the reduction product was observed. Ethyl trifluoroacetate and phenyl trifluoroacetate, which have electron withdrawing groups, were converted into the transesterification products in a shorter time. After monitoring the reaction for one day, a significant amount of the reduction product, 2,2,2-trifluoroethanol, was obtained in 60% yield from the reaction of ethyl trifluoroacetate and in 30% yield from the reaction of phenyl trifluoroacetate, respectively (Table 14, entry 2 and 3).

These results indicate that (i) the reduction is slower than transesterification and (ii) the reduction is facilitated by the presence of an accepting group. Furthermore, these results establish that the reduction of unactivated phenyl esters can take place only before the transesterification is complete. The rate of reduction is slower than transesterification. Also, the entry 2 of Table 14 shows that a strong enough electron-withdrawing group, such as CF_3, can outweigh the donating ability of an alkyl substituent at oxygen. On the other hand, entry 6 of Table 12 shows that the accepting effect of 4-ester substituted phenyl group at the carbonyl centre is not strong enough to compensate for the donating effect of alkyl substituent. Overall, the success of ester reduction is the function of electrophilicity of the carbonyl centre.

Table 14. Transfer hydrogenation of other esters [a]

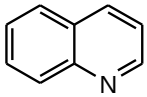
Entry	Substrate	Transesterification Product	Time Conv.	Reduction Product	Time Conv.
1			1 d 67 %		1 d 13 %
2			20 min 100 %		1 d 60 %
3			20 min 100 %		1 d 30 %

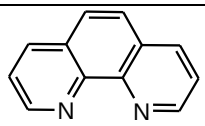
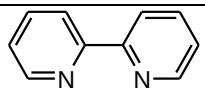
[a] 5 mol % Ru catalyst, 10 mol % t-BuOK, 0.1 mmol substrate, 2-propanol (0.5 mL), room temperature.

III.3.4 Transfer hydrogenation of heterocycles

The cationic complexes $[Cp(PPr^{i}_{3})Ru(NCCH_3)_2]PF_6$ (**2**) and $[Cp^{*}(phen)Ru(NCCH_3)]PF_6$ (**3**) were studied as catalysts for transfer hydrogenation of heteroaromatic compounds. Unfortunately, attempted reactions with quinoline, 1,10-phenanthroline and 2,2'-bipyridine in 2-propanol and in the presence of **3** failed to give any reduction products even at elevated temperatures. To our disappointment, the reactions with **2** did not produce any reduced heterocycles either and the formation of the neutral complex **1** was observed at 70°C (Table 15).

Table 15. Attempted transfer hydrogenation of heterocycles [a]

Entry	Substrate	Catalyst	
		2	**3**
		Time / Yield	Time / Yield
1		NR [b,d]	NR [b]

2		NR [b]	NR [c]
3			NR [c]

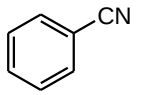
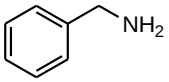
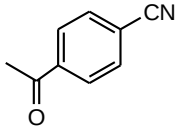
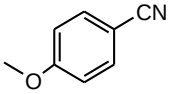
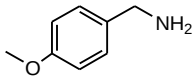
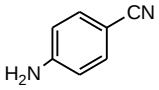
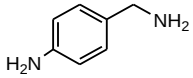
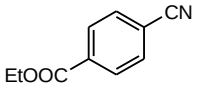
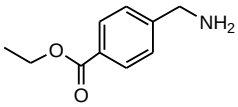
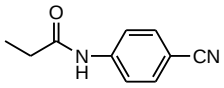
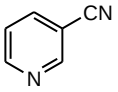
[a] Reaction condition: 5 mol % $[Cp(PPr^{i}_{3})Ru(CH_3CN)_2]PF_6$, 10 mol % t-BuOK, 0.1 mmol substrate, Isopropanol (0.5 mL), room temperature. [b] 70°C. [c] 40°C. [d] NR without t-BuOK.

III.3.5 Transfer hydrogenation with ammonium formate

We further studied transfer hydrogenation by using ammonium formate as the hydrogen source. The advantages of this hydrogen source are the low cost of reagent and the fact that the only other co-product is CO_2. The cationic complexes **2** and **3** were tested in the transfer hydrogenation of acetophenone. The full conversion of acetophenone was achieved in 2 days at 60°C when **2** and excess ammonium formate were used. Unfortunately, no conversion was observed with the complex **3**.

Due to a rather long reaction time of reduction of ketone, we decided to study the transfer hydrogenation of nitriles under the same conditions. To our delight, benzonitrile was successfully reduced to benzylamine in only 2 hours with a high conversion (Table 16, entry 1). Moreover, other nitriles, such as 4-methoxybenzonitrile, 4-aminobenzonitrile and ethyl 4-cyanobenzoate, were also reduced to the corresponding amines (Table 16, entry 3-5). In the latter case, only chemoselective reduction of the cyano group was observed. However, mixtures of undetectable compounds were observed from the reactions of benzonitriles bearing acetyl and amide groups (Table 16, entry 2 and 7). Unfortunately, no reaction was achieved in the case of nicotinonitrile either (Table 16, entry 8). In the case of successful reactions, the amine products were obtained in moderate yields in the form of corresponding ammonium salts upon addition of HCl (Table 16, entry 1, 3 and 5).

Table 16. Transfer hydrogenation of nitriles with ammonium formate [a]

Entry	Substrate	Product	Time	Conv.
1			2 h	95 % (63 %)[b]
2		Mixture	1 h	99 %
3			2 h	99 % (32 %)[b]
4			2 h	99 %
5			2 h	97 % (65 %)[b]
7		Mixture	2 h	97 %
8			2 d	NR

[a] 5 mol % Ru catalyst, 0.05 mmol substrate, 0.2 mmol ammonium formate, methanol (0.5 mL), 60°C. [b] Isolated yields of the ammonium salts.

III.3.6 Stoichiometric reaction

As discussed above, the transfer hydrogenation can occur by several mechanisms. Since our system does not have a cooperative/bifunctional ligand[59e-f], we considered two most likely possibilities. The well-known Meerwein–Ponndorf–Verley-Oppenauer mechanism[58c,d] involves direct hydride transfer from a hydrogen donor to a hydrogen acceptor, when both are attached to the same metal centre (Scheme 50). The hydride mechanism[59b] implies the formation of a metal hydride species, which then coordinates the substrates followed by insertion into the M-H

bond (Scheme 51). A typical MPVO mechanism and a possible hydride route for transfer hydrogenation of ketones by complex **2** are shown in Figure 10 and 11.

To shed light on the intermediate, a reaction of stoichiometric amounts of the ruthenium complex, base and 2-propanol (1:1:1 ratio) in PhCl-d_5 was monitored at low temperature. The ruthenium hydride species **71**, which can be generated by *β*-hydride elimination from an alcoholate precursor, was observed at -15°C (Figure 11). Based on this observation from the stoichiometric reaction, we suggest a possible hydride mechanism for transfer hydrogenation of ketones (Figure 11). Dissociation of the second molecule of CH_3CN can generate a reactive ruthenium monohydride complex **72**. Hydride transfer to the coordinated ketone followed by exchange with 2-propanol will provide the secondary alcohol product and form a reactive alkoxide. The ruthenium hydride species can be regenerated after *β*-hydride shift and dissociation of acetone.

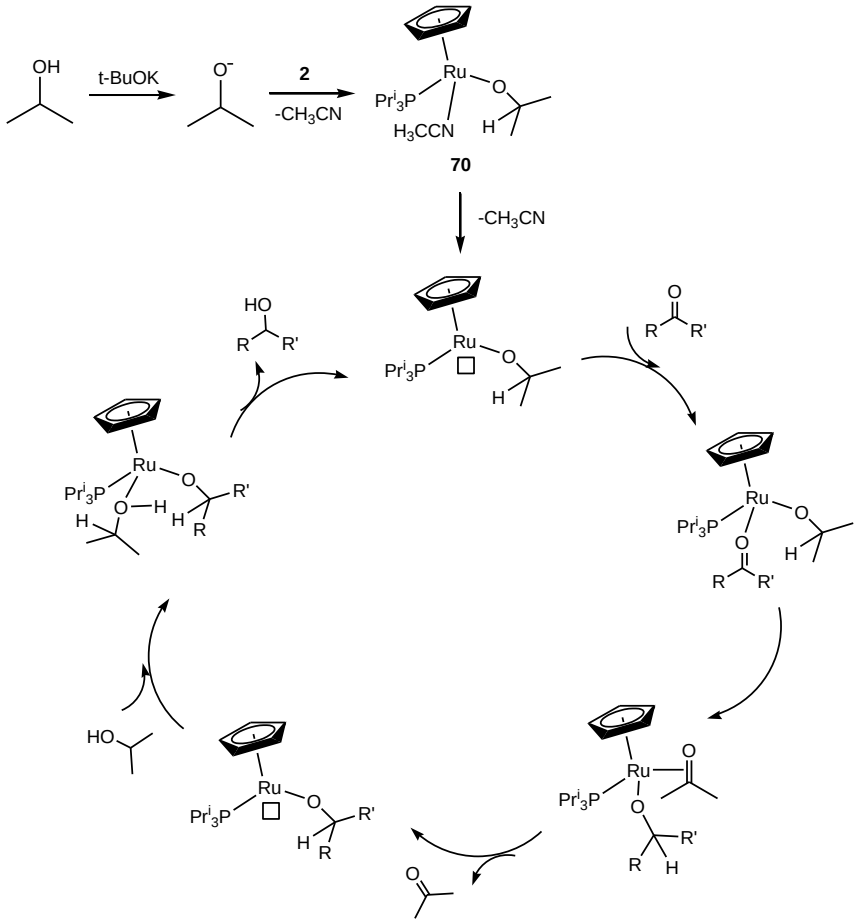


Figure 10. Possible MPVO mechanism of transfer hydrogenation of ketones

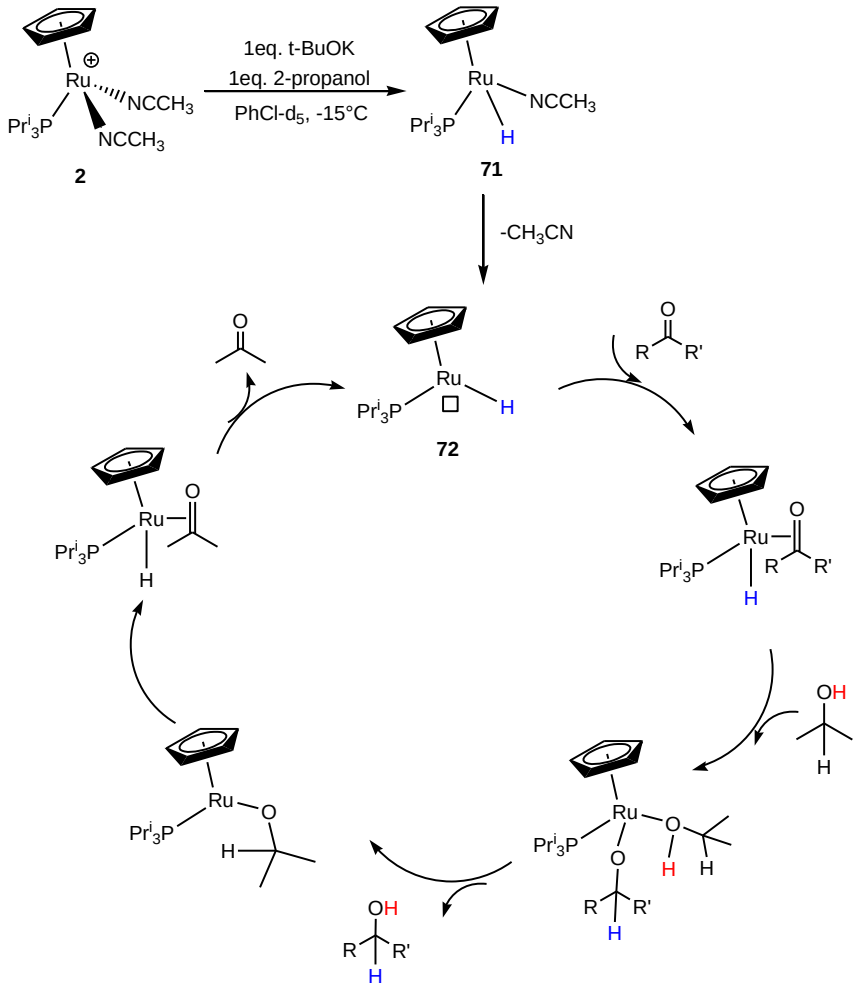
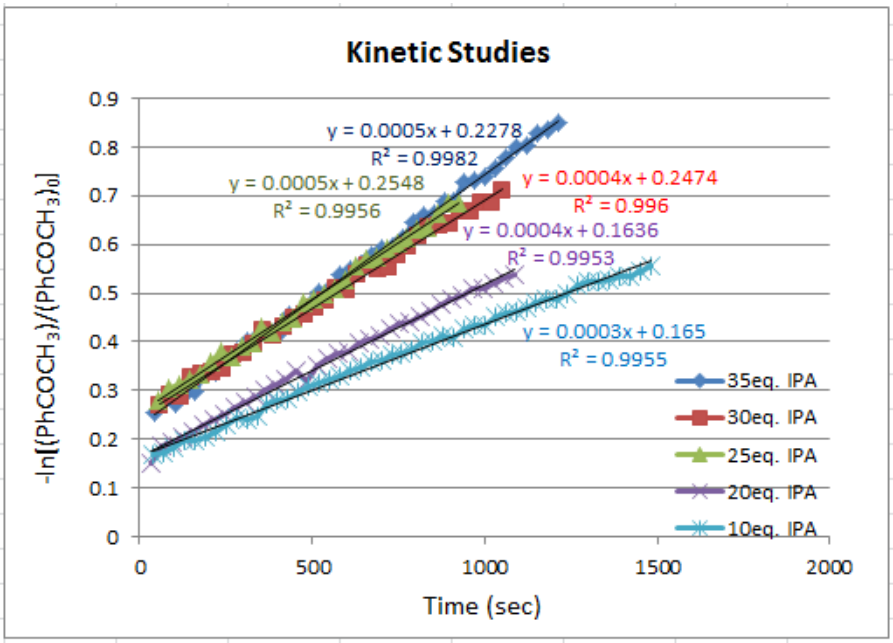


Figure 11. Proposed hydride mechanism of transfer hydrogenation of ketone

III.3.7 Kinetic studies of transfer hydrogenation of acetophenone

The unusual reactivity of nitriles and ketones under mild catalytic conditions prompted a deeper insight into the mechanism of these reactions. We previously showed that catalytic hydrosilylation of nitriles and pyridines can be achieved through an ionic mechanism.[12c-d,89] To understand the mechanism of transfer hydrogenation, initial rate analysis of the catalytic reduction of acetophenone was studied. When the reaction was carried out under pseudo-first order conditions (10- to 35-fold excess of 2-propanol relative to acetophenone), the first-order dependence of the reaction rate on acetophenone was observed (Figure 12). Plotting the variation of the effective rate

constant (K^{eff}*1000) against the amount of 2-propanol showed a linear dependence (Figure 13). This result indicates that the reaction is also first order in 2-propanol.



0.005 mmol (5 mol %) **2** (dissolved in 200 μL PhCl), 0.01 mmol (10 mol %) t-BuOK, 0.1 mmol acetophenone, 1.0-3.5 mmol (10-35 eq.) 2-propanol, 22°C.

Figure 12. The dependence of –Ln(1-[substrate]/[substrate]$_0$) on time at 10- to 35-fold excess of 2-propanol

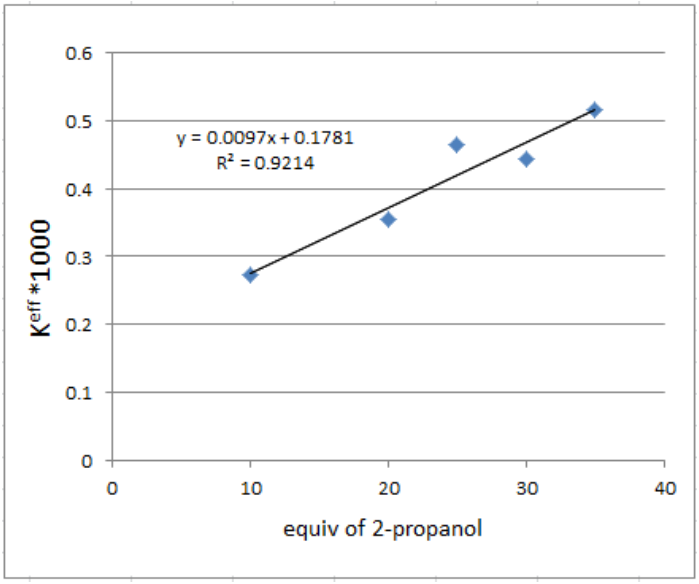
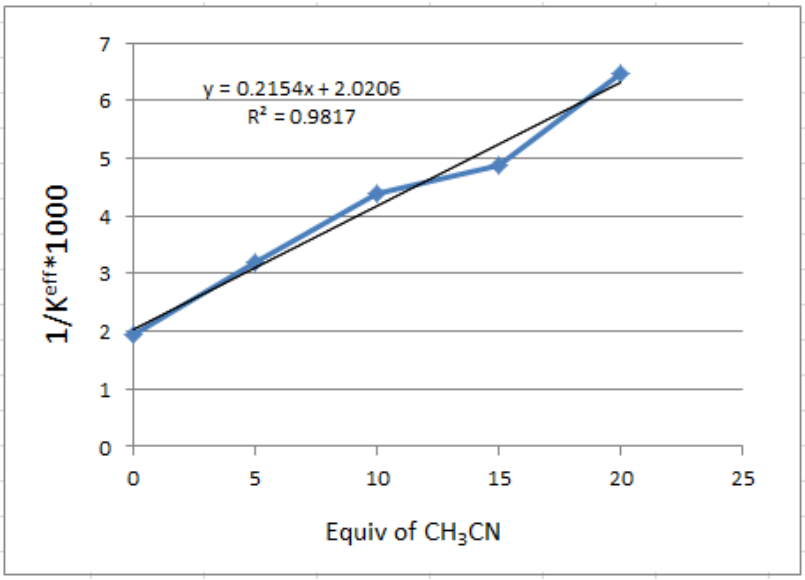


Figure 13. The dependence of k^{eff}*1000 on the amount of 2-propanol (in equivalents of the substrate)

Since any possible mechanism implies dissociation of nitrile ligand as the first step, we decided to investigate the effect of additional CH_3CN on the reaction rate. The reaction was carried out with varying the amount of CH_3CN from 0- to 20-fold excess relative to the ruthenium complex. A linear plot was observed from the plot of $1/k^{eff}*1000$ against the amount of CH_3CN (Figure 14). This result indicates that the reaction rate decreases with increasing amount of extra CH_3CN, which supports the dissociation of CH_3CN in the proposed mechanism (Figure 11).

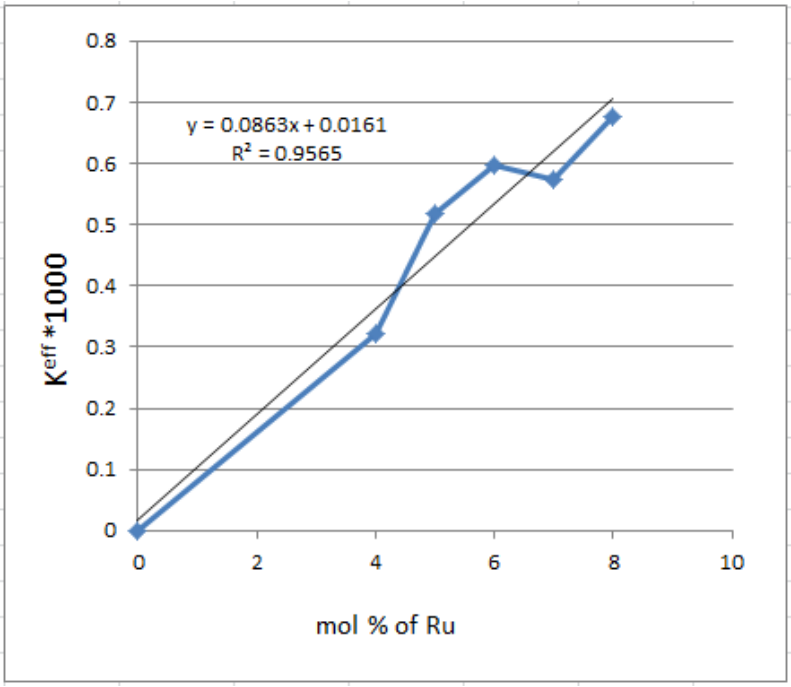


0.005 mmol (5 mol %) **2** (dissolved in 200 μL PhCl), 0.01 mmol (10 mol %) t-BuOK, 0.1 mmol acetophenone, 0-0.1 mmol (0 – 100 mol %) CH_3CN, 1.0-3.5 mmol (10-35 eq.) 2-propanol, 22°C.

Figure 14. The dependence of $1/k^{eff}*1000$ on the equiv. of CH_3CN to the catalyst

We also performed kinetic studies with different amounts of the catalyst. Expectedly, an increase of the reaction rate was observed by varying amounts of the ruthenium complex from 4% to 8% at the fixed amounts of acetophenone and 2-propanol taken in the 1:35 ratio (Figure 15), although we experienced difficulties to correctly dosing the very small amount of the catalyst. Unfortunately, the resulting kinetic law rate = k[Ru][acetophenone][2-propanol]/(A+[H_3CCN]) does not allow us

to determine the exact sequence of key elementary steps and underpin the likely mechanism. However, in the absence of more conclusive experimental data, we speculate that the reaction proceeds via a conventional hydride mechanism.



0.004-0.008 mmol (4-8 mol %) **2** (dissolved in 200 μL PhCl), 0.01 mmol (10 mol %) t-BuOK, 0.1 mmol acetophenone, 1.0-3.5 mmol (10-35 eq.) 2-propanol, 22°C.

Figure 15. The dependence of k^{eff}*1000 on the mol % of the catalyst

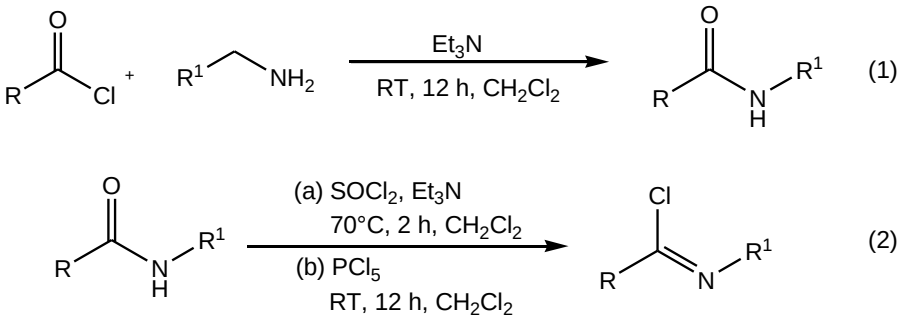
III.4. Reduction of secondary amides to imines and aldehydes

Nitrogen containing compounds, such as amines and imines, are of great importance for pharmaceutical and agrochemical industries and are widely used in organic synthesis. However, the current synthetic repertoire of organic chemistry only allows for the direct reduction of amides to amines. Partial reduction of amides to imines and aldehydes presents a significant challenge and was achieved only very recently by the application of stoichiometric amounts of organometallic reagents. Our research was in progress when the first example of catalytic chemoselective reduction of secondary amides to imines by silane and an iridium catalyst was reported by Brookhart.[67] The development of chemoselective reduction of amides under catalytic conditions is an area of intensive research.[66c,67] While the catalytic reduction of tertiary amides by silanes has been recently studied very well,[69-71] catalytic reduction of secondary amides has not received much attention (vide supra).

Our group has previously developed the chemoselective catalytic reduction of acid chlorides to aldehydes by $[Cp(PPr^{i}_{3})Ru(CH_3CN)_2]PF_6$ (**2**) and $HSiMe_2Ph$, which takes place under mild conditions and is applicable to a wide substrate range.[16] Given the fact that iminoyl chlorides are isoelectronic analogues of acid chlorides, we suggested that a similar reduction to imines can be developed for iminoyl chlorides. Since the latter substrates are just one step away from the respective secondary amides, the overall two step procedure would be a useful semi-catalytic transformation of secondary amides to imines. In this section, catalytic reduction of iminoyl chlorides with $HSiMe_2Ph$ catalysed by the ruthenium complex **2** will be discussed.

III.4.1 Synthesis of secondary amides and iminoyl chlorides

A wide range of secondary amides bearing electron withdrawing and donating groups were synthesized by using known procedures.[93] Moderate to good yields of secondary amides were obtained from the reactions of acyl chlorides with amines in the presence of triethylamine in CH_2Cl_2 except for the case of $C_6H_{11}NHCOC_6H_4CN$ (Scheme 90, eq. 1). Syntheses of various iminoyl chlorides were performed by using literature procedures.[94] Reactions of secondary amides with PCl_5 were carried out at room temperature, whereas an elevated temperature (reflux at 70°C) was required for reactions with thionyl chloride. The corresponding iminoyl chlorides were obtained with good to high yields (60-98%) (Scheme 90, eq. 2).

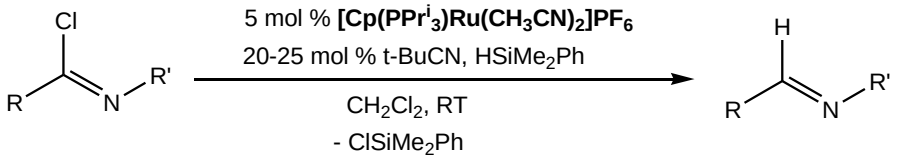


Scheme 90. Synthesis of secondary amides and iminoyl chlorides

III.4.2 Reduction of iminoyl chlorides to imines

Inspired by our earlier work on the chemoselective reduction of acid chlorides to aldehydes catalysed by $[Cp(PPr^i_3)Ru(CH_3CN)_2]^+$ (**2**), we tried to extend this work to the reduction of iminoyl chlorides with silane. To our delight, the complex **2** was found to catalyse efficiently the reduction of iminoyl chlorides into the corresponding imines in high yields (detected by ^1H NMR) at room temperature when $HSiMe_2Ph$ was used as the hydrogen source (Scheme 91). To avoid possible catalyst

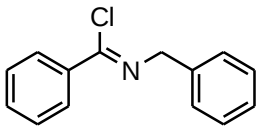
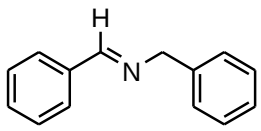
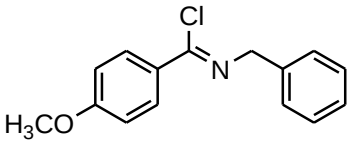
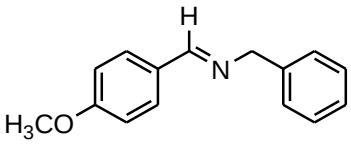
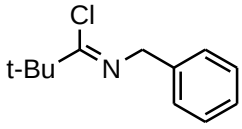
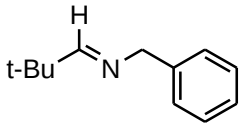
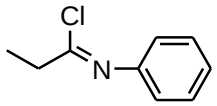
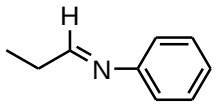
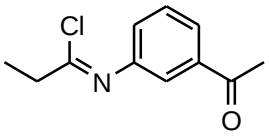
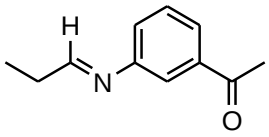
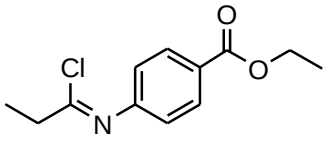
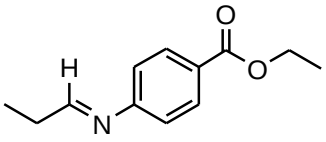
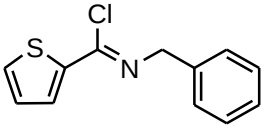
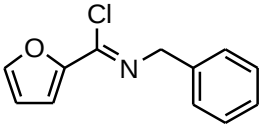
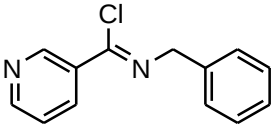
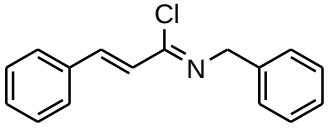
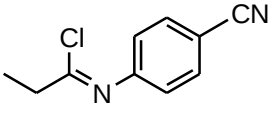
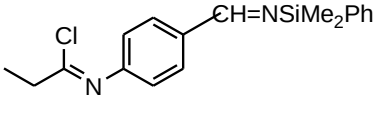
decomposition, excess pivalonitrile was added to the reaction mixture, as this was found previously to be important in the related reductions of acid chlorides.

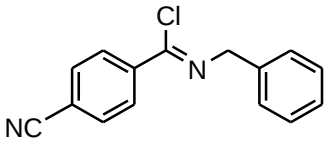
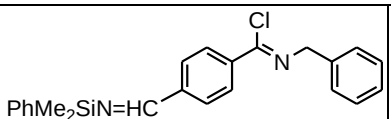
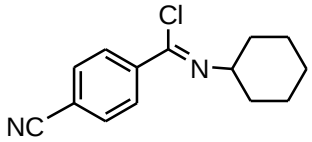
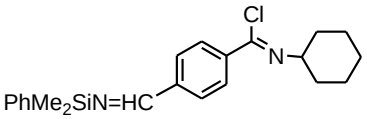
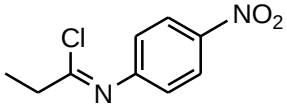
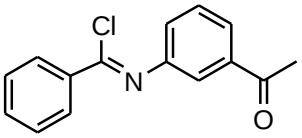
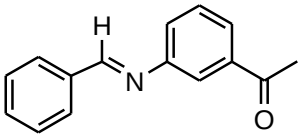
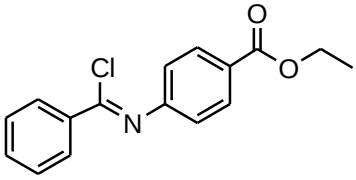


Scheme 91. Reduction of iminoyl chlorides catalysed by ruthenium complex

The full conversion of PhCCl=NCH$_2$Ph was observed in only 15 min, with the imine, PhCH=NCH$_2$Ph, being the product (Table 17, entry 1). The reactions of iminoyl chlorides bearing electron donating substituents, such as methoxy and *tert*-butyl groups, were achieved in high yields, although they required longer reaction times (Table 17, entry 2 and 3). Alkyl substituted iminoyl chlorides also showed good conversions in 30 min (Table 17, entry 4). We observed that these catalytic conditions tolerate the keto- and ester-groups (Table 17, entry 5, 6 and 15). On the other hand, reductions of iminoyl chlorides having heterocyclic substituents were not clean and produced mixtures of uncharacterized products (Table 17, entry 7-9). Unfortunately, a reaction of an alkene-substituted substrate also produced a mixture of different compounds (Table 17, entry 10). Unlike the reactions of acid chlorides mediated by the same catalyst,[16] the reduction of iminoyl chlorides did not tolerate the cyano-group (Table 17, entry 11-13). In these reactions, the products of nitrile hydrosilylation were obtained. A mixture of unidentified products was obtained from the reaction of iminoyl chloride with the nitro substituent (Table 17, entry 14). In summary, the reduction of iminoyl chlorides proceeds similarly to the reduction of acid chlorides but tolerates a much narrower range of functional groups.

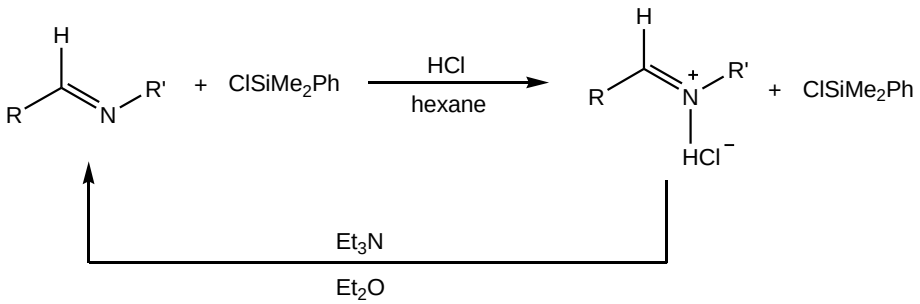
Table 17. NMR scale reduction of iminoyl chlorides to imines [a]

Entry	Substrate	Product	Time	Conv.
1			15 min	100 %
2			2.5 h	90 %
3			1 h	88 %
4			30 min	80 %
5			90 min	93 %
6			3 h	86 %
7		Mixture of products	13 h	90 %
8				NR
9		Mixture of products	24 h	100 %
10		Mixture of products	12 h	100 %
11			2.5 h	30 %

12[b]			40 min	99 %
13[b]			3 h	100 %
14				NR
15			20 h	65 %
16				NR

[a] Reaction condition: 5 mol % $[Cp(PPr^{i}_{3})Ru(CH_3CN)_2]PF_6$, 25 mol % t-BuCN, substrate (0.05-0.1 mmol), $HSiMe_2Ph$ (1.1 eq), CH_2Cl_2 (0.5 mL), room temperature. [b] 1.5 eq. $HSiMe_2Ph$.

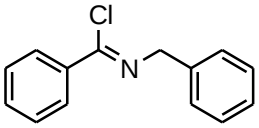
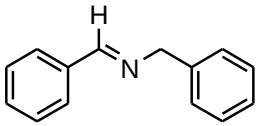
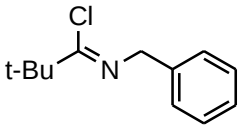
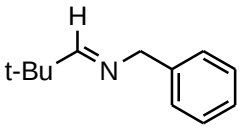
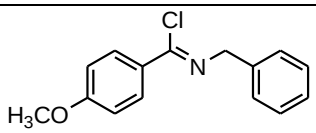
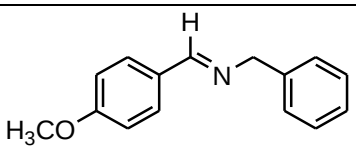
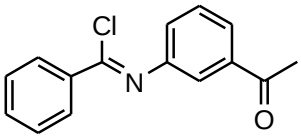
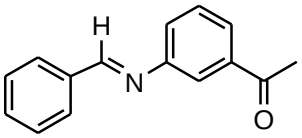
With these results of NMR scale reactions in hand, we studied preparative scale reduction of iminoyl chlorides. The most reactive substrates were used for large scale reactions (1.2-6.0 mmol) of iminoyl chlorides. The reduction of $PhCCl{=}NCH_2Ph$ required a slightly longer time compared to the NMR scale reaction (Table 18, entry 1). Of note, the catalyst can be easily removed from the reaction mixture by filtration after addition of a nonpolar solvent. The target product was separated from the co-product, $ClSiMe_2Ph$, through the formation of an iminium salt by addition of 1 equiv. of dry HCl in ether and extraction with Et_2O. At the last stage the imine was recovered by adding triethylamine (Scheme 92). A modest isolated yield was obtained in the reaction of $PhCCl{=}NCH_2Ph$.

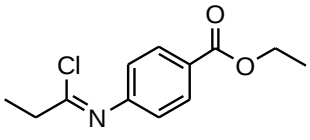
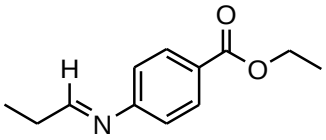


Scheme 92. Isolation of imines from the reaction mixture

The imine t-BuCH=NCH_2Ph was obtained in 57% isolated yield by the same method as described in Scheme 92. The reaction of an iminoyl chloride bearing a keto-group also was achieved and the desired product was obtained in a modest yield (Table 18, entry 4). Unfortunately, although the reductions initially produced the corresponding imines, attempted isolation of 4-$CH_3OC_6H_4CH=NCH_2Ph$ and $CH_3CH_2CH=NC_6H_4COOCH_2CH_3$ failed and only uncharacterized decomposition products were observed (Table 18, entry 3 and 5).

Table 18. Preparative scale reduction of iminoyl chlorides to imines [a]

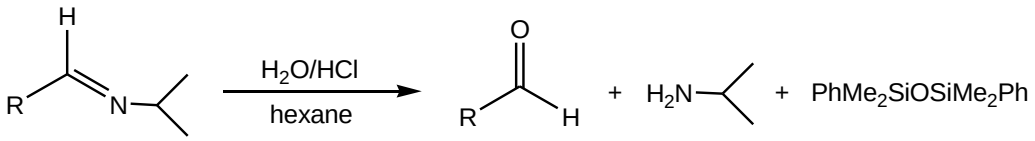
Entry	Substrate	Product	Time	Conv.
1			50 min	100 % (43%)[b]
2			1 h	100 % (57%)[b]
3			5 h	100 %
4			7 d	98 % (40%)[b]

5			3 h	90 %

[a] Reaction condition: 5 mol % $[Cp(PPr^{i}_{3})Ru(CH_3CN)_2]PF_6$, 20 mol % t-BuCN, substrate (1.2-6.0 mmol), $HSiMe_2Ph$ (1 eq), CH_2Cl_2 (12 mL), room temperature. [b] isolated yield.

III.4.3 Reduction of iminoyl chlorides to aldehydes

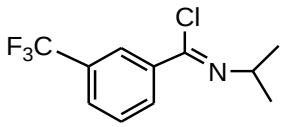
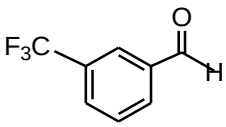
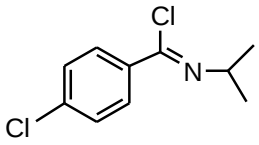
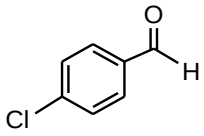
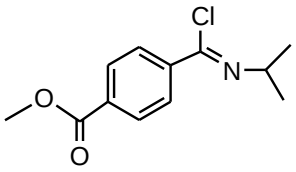
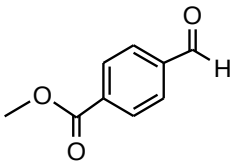
Due to the difficulty of isolation of imines, we decided to reduce the iminoyl chlorides to aldehydes. Aldehydes are useful building blocks for organic synthesis and are widely used in industrial applications. To achieve efficient isolation of aldehydes, *N*-isopropyl substituted amides were used because of the ease of separation from the volatile amine co-product (Scheme 93).



Scheme 93. Isolation of aldehydes from the reaction mixture

The reactions of iminoyl chlorides bearing electron withdrawing and donating substituents were achieved under the same reaction conditions as shown in Scheme 91. In the case of $3\text{-}CF_3C_6H_4CCl{=}NCH(CH_3)_2$, the corresponding imine was obtained as a sole product and the aldehyde, $3\text{-}CF_3C_6H_4CHO$, was isolated in a moderate yield after acid hydrolysis and purification by chromatography over silica (Table 19. entry 1). In the reactions of $4\text{-}ClC_6H_4CCl{=}NCH(CH_3)_2$ and $4\text{-}CH_3OOCC_6H_4CCl{=}NCH(CH_3)_2$, mixtures of both the imine and aldehyde were obtained, although the aldehydes were formed in very small amounts (Table 19. entry 2 and 3). The corresponding aldehydes were separated from the reaction mixtures by following the same isolation procedure.

Table 19. Reduction of iminoyl chlorides to aldehydes [a]

Entry	Substrate	Product	Time	Conv.	Yield [b]
1			70 min	100 %	64 %
2			50 min	100 %	51 %
3			30 min	100 %	46 %

[a] Reaction condition: 5 mol % $[Cp(PPr^{i}_{3})Ru(CH_3CN)_2]PF_6$, 20 mol % t-BuCN, substrate (1.0-1.6 mmol), $HSiMe_2Ph$ (1 eq), CH_2Cl_2 (12 mL), room temperature. [b] Isolated yield of aldehyde after hydrolysis and column chromatography.

IV. Conclusions and Future Work

The main goal of our research was to prepare a series of novel half-sandwich complexes of ruthenium and investigate their catalytic activity in the reduction of various organic substrates.

Most of our research was done with catalyst $[Cp(PPr^{i}_{3})Ru(CH_3CN)_2]PF_6$ (**2**) because previously it was known to be an effective catalyst for hydrosilylation of ketones, nitriles and pyridines. But we were also interested to extend these studies to other catalysts, such the Cp^* analogue of **2**, and therefore a series of Cp^* ruthenium complexes $[Cp^*(phen)Ru(CH_3CN)]^+$ (**3**), $[Cp^*(PPr^{i}_{3})Ru(CH_3CN)_2]^+$ (**4**), $[Cp^*(PPr^{i}_{2}Me)Ru(CH_3CN)_2]^+$ (**74**) and $[Cp^*(PPh_3)Ru(CH_3CN)_2]^+$ (**75**) were synthesized and investigated. In addition, hydrosilylation and transfer hydrogenation of various substrates, such as ketones, nitriles and pyridines were studied.

In the course of our initial studies, we observed an unusual H/D exchange process, which led to investigation of H/D exchange reactions of various organic compounds catalysed by $Cp(PPr^{i}_{3})RuH_3$ (**1**). The advantage of this catalytic reaction is that both C_6D_6 and D_2O can be used as deuterium sources. Another highlight is that a number of substrates showed deuterium incorporation in the usually more inert alkyl groups. Among the latter, the preferential deuteration of methyl groups over activated positions, such as benzylic positions, and methylene positions was observed. The most astounding observation was that methylene and methine positions of alkyl chains were engaged in the H/D exchange only if the substrate contained a donating functionality, including even such weak donors as arene and methyl group.

Back to the main research course of this thesis, we studied the mechanism of chemoselective hydrosilylation of pyridines and nitriles catalysed by $[Cp(PPr^{i}_{3})Ru(CH_3CN)_2]PF_6$ (**2**), and performed kinetic studies on the hydrosilylation

of pyridine. First order kinetics in silane concentration was observed under the pseudo-first-order conditions. Furthermore, we found that the dependence of k^{eff} on the concentration of pyridine shows a saturation behavior, consistent with the first step of the reaction being reversible coordination of silane to the Ru catalyst. We further extended the substrate scope of this reaction by studying different catalysts. Although the Cp^* substituted ruthenium complexes showed more sluggish results in the hydrosilylation of pyridines and nitriles than **2**, the complex $[Cp^*(phen)Ru(CH_3CN)]^+$ (**3**) was found to catalyse efficiently the regioselective hydrosilylation of ring-fused *N*-heteroaromatics, such as quinoline, isoquinoline and acridine under mild conditions, which is a useful addition to the current synthetic repertoire.

We also performed transfer hydrogenation in 2-propanol catalysed by the complexes **2** and **3**. A wide scope of substrates, such as ketones, imines, nitriles and esters were screened and were found to be reactive under mild conditions. Ketones and nitriles were reduced at room temperature to secondary alcohols and *N*-isopropylidene amines, respectively, and the products were obtained with good isolated yields. We also found that phenyl benzoate derivatives can be reduced under the same catalytic conditions.

Extending the previous research by our group on catalytic reduction of acyl chlorides to the corresponding aldehydes, we performed the reduction of iminoyl chlorides to imines and/or aldehydes. Although some useful functionalities were tolerated in this process, the substrate scope was much narrower than in the case of acid chlorides. However, given the fact that iminoyl chlorides can be easily obtained from the corresponding secondary amides, the overall semi-catalytic transformation may be more efficient than alternative multi-step organic methods.

For the nearest future work, transfer hydrogenation by alternative hydrogen sources, such as ammonium formate and hydrogen gas, should be investigated. Also, other potentially more active ruthenium complexes of the type $[CpRu(L)_n(NCCH_3)_m]^+$ and $[Cp^*Ru(L)_n(NCCH_3)_m]^+$ (n = 1, 2 and m = 1, 2) can be envisioned by using the isolobal relationship between phosphines and other two-electron donors (e.g NHC carbenes), and studied in the catalytic hydrosilylation, transfer hydrogenation and hydrogenation of organic substrates.

V. Experimental section

V.1. General methods and instrumentation

All manipulations were carried out using conventional high-vacuum or nitrogen-line Schlenk techniques. All solvents were dried using Grubbs-type purification columns or appropriate drying agents. NMR spectra were obtained with a Bruker DPX-300 (^{1}H 300 MHz, ^{13}C 75.5 MHz, ^{29}Si 59.6 MHz, ^{31}P 121.5 MHz) and/or Bruker DPX-600 (^{1}H 600 MHz, ^{13}C 151 MHz, ^{29}Si 119.2 MHz, ^{31}P 243 MHz) spectrometers at room temperature, unless specified otherwise. IR data were obtained on Perkin-Elmer 1600 FT-IR spectrometer. All organic substrates were purchased from Sigma-Aldrich and Alfa Aesar. These reagents were used without further purification. The silanes were purchased from Gelest.

V.2. H/D exchange reactions catalysed by $Cp(PPr^{i}_{3})RuH_{3}$

V.2.1. The syntheses of ruthenium complexes

Preparation of $Cp(PPr^{i}_{3})RuH_{3}$

$LiAlH_4$ (0.058 g, 1.53 mmol), purified from Et_2O, was added to a solution of $[Cp(PPr^{i}_{3})Ru(CH_3CN)_2]BF_4$ (0.252 g, 0.51 mmol) in 40 mL of THF. The resulting solution was stirred overnight at ambient temperature and then slowly hydrolyzed with degassed water. After evaporation of the solvent, the brown residue was extracted with hexane (3 x 10 mL). Removal of volatiles and recrystallization at -30°C from Et_2O/EtOH (2:1) afforded 0.130 g of $Cp(PPr^{i}_{3})RuH_3$ in the form of dark grey crystals, which deliquesce when brought to room temperature (Yield: 75%).

Preparation of $Cp(PPh_3)RuH_3$

$LiAlH_4$ (0.058 g, 1.53 mmol), purified from Et_2O, was added to a solution of $[Cp(PPh_3)Ru(CH_3CN)_2]BF_4$ (0.220 g, 0.51 mmol) in 40 mL of THF. The resulting solution was stirred overnight at ambient temperature and then slowly hydrolyzed with degassed water. After evaporation of the solvent, the yellow residue was extracted with toluene (3*10 mL). Removal of volatiles and recrystallization at -30°C from concentrated toluene afforded 0.110 g of $Cp(PPh_3)RuH_3$ in the form of yellow powder (Yield: 50%).

V.2.2. Catalytic hydrogen/deuterium exchange reactions

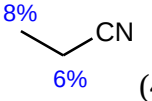
General procedure

The internal standard, ferrocene, was dissolved in a deuterated solvent and transferred into a capillary. Then the capillary was sealed and added to the reaction mixture.

H/D exchange reactions catalysed by $Cp(PPr^i_3)RuH_3$ in C_6D_6

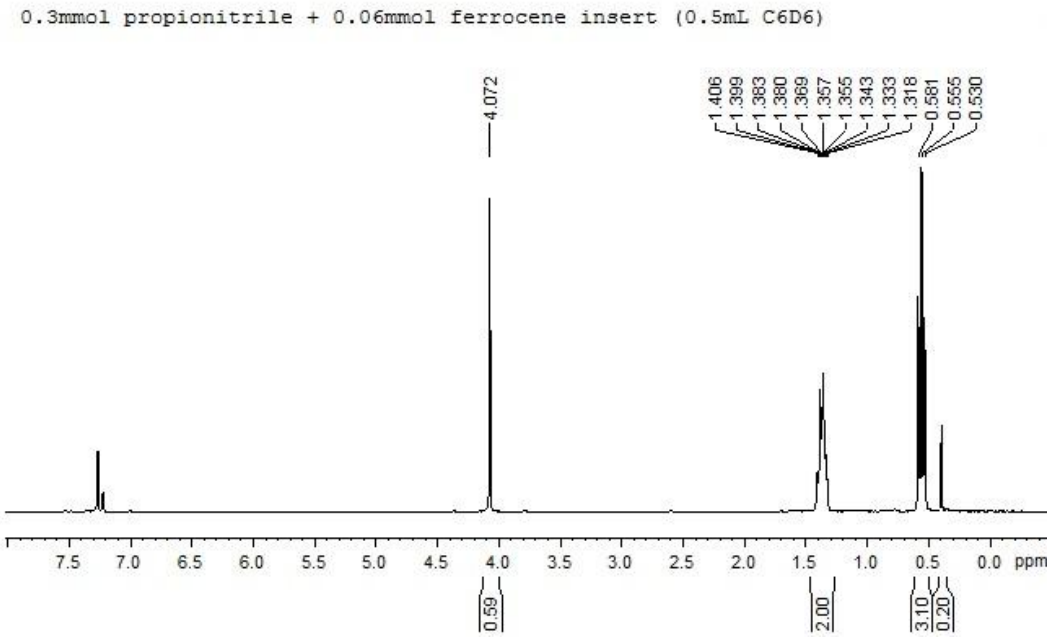
Propionitrile

To a solution of propionitrile (0.017 mL, 0.30 mmol) and internal standard (Cp_2Fe) in C_6D_6 (0.6 mL) was added $Cp(PPr^i_3)RuH_3$ (0.005 g, 5 mol %). The resulting mixture was heated at 100°C and the progress of the reaction was monitored by NMR spectroscopy.



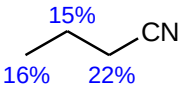
(4 day)

<[1]H NMR spectrum of the reaction of propionitrile in C_6D_6>



Butylnitrile

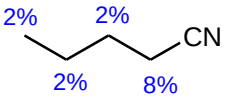
To a solution of butylnitrile (0.021 mL, 0.30 mmol) and internal standard (Cp_2Fe) in C_6D_6 (0.6 mL) was added $Cp(PPr^i_3)RuH_3$ (0.005 g, 5 mol %). The resulting mixture was heated at 100°C and the progress of the reaction was monitored by NMR spectroscopy.



(4 day)

Valeronitrile

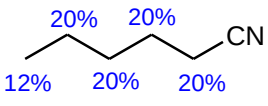
To a solution of valeronitrile (0.025 mL, 0.30 mmol) and internal standard (Cp_2Fe) in C_6D_6 (0.6 mL) was added $Cp(PPr^i_3)RuH_3$ (0.005 g, 5 mol %). The resulting mixture was heated at 100°C and the progress of the reaction was monitored by NMR spectroscopy.



(4 day)

Hexanenitrile

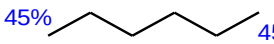
To a solution of hexanenitrile (0.029 mL, 0.30 mmol) and internal standard (Cp_2Fe) in C_6D_6 (0.6 mL) was added $Cp(PPr^i_3)RuH_3$ (0.005 g, 5 mol %). The resulting mixture was heated at 100°C and the progress of the reaction was monitored by NMR spectroscopy.



(4 day)

Hexane

To a solution of hexane (0.026 mL, 0.30 mmol) and internal standard (Cp_2Fe) in C_6D_6 (0.6 mL) was added $Cp(PPr^i_3)RuH_3$ (0.005 g, 5 mol %). The resulting mixture was heated at 100°C and the progress of the reaction was monitored by NMR spectroscopy.



(3 day)

Decane

To a solution of decane (0.043 mL, 0.30 mmol) and internal standard (Cp_2Fe) in C_6D_6 (0.6 mL) was added $Cp(PPr^i_3)RuH_3$ (0.005 g, 5 mol %). The resulting mixture was heated at 100°C and the progress of the reaction was monitored by NMR spectroscopy.

13% $CH_3(CH_2)_8CH_3$ 13% (10 day)

Cyclohexane

To a solution of cyclohexane (0.025 mL, 0.30 mmol) and internal standard (Cp_2Fe) in C_6D_6 (0.6 mL) was added $Cp(PPr^i_3)RuH_3$ (0.005 g, 5 mol %). The resulting mixture was heated at 100°C and the progress of the reaction was monitored by NMR spectroscopy.

(No deuteration) (18 day)

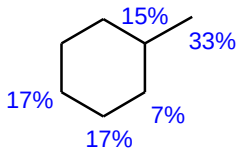
Cyclooctane

To a solution of cyclooctane (0.034 mL, 0.30 mmol) and internal standard (Cp_2Fe) in C_6D_6 (0.6 mL) was added $Cp(PPr^i_3)RuH_3$ (0.005 g, 5 mol %). The resulting mixture was heated at 100°C and the progress of the reaction was monitored by NMR spectroscopy.

(No deuteration) (10 day)

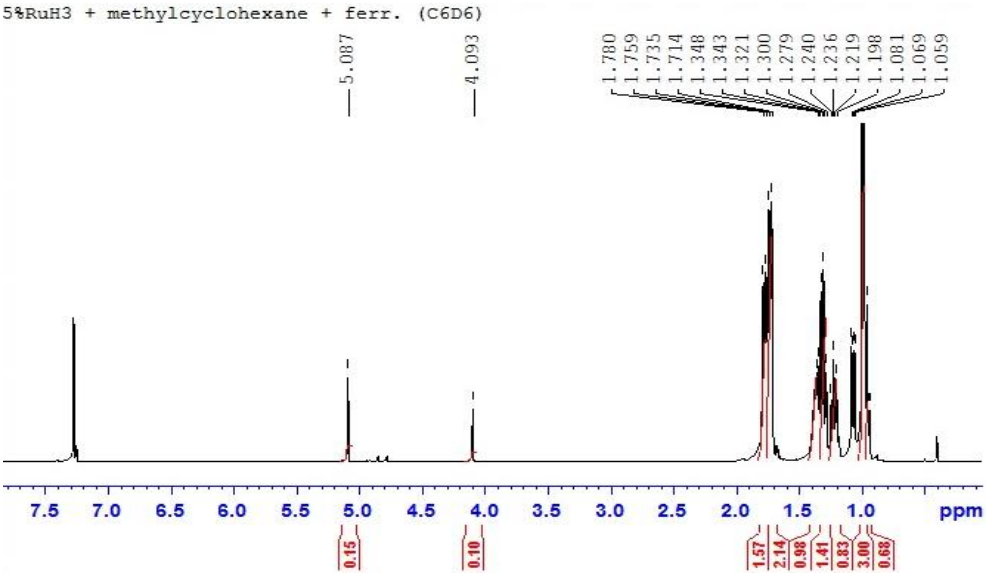
Methyl cyclohexane

To a solution of methyl cyclohexane (0.030 mL, 0.30 mmol) and internal standard (Cp_2Fe) in C_6D_6 (0.6 mL) was added $Cp(PPr^i_3)RuH_3$ (0.005 g, 5 mol %). The resulting mixture was heated at 100°C and the progress of the reaction was monitored by NMR spectroscopy.



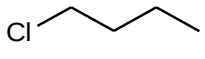
(9 day)

<^{1}H NMR spectrum of the reaction of methyl cyclohexane in C_6D_6>



1-Chlorobutane

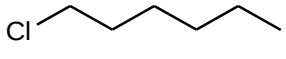
To a solution of 1-chlorobutane (0.028 mL, 0.30 mmol) and internal standard (Cp_2Fe) in C_6D_6 (0.6 mL) was added $Cp(PPr^i_3)RuH_3$ (0.005 g, 5 mol %). The resulting mixture was heated at 100°C and the progress of the reaction was monitored by NMR spectroscopy.



(No deuteration) (4 day)

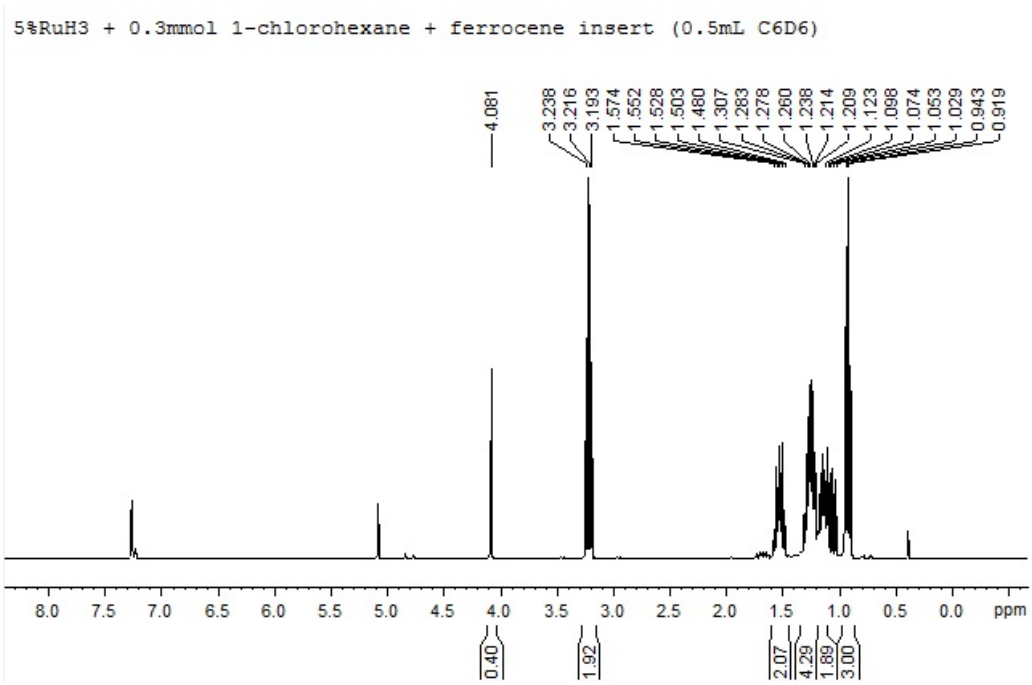
1-Chlorohexane

To a solution of 1-chlorohexane (0.036 mL, 0.30 mmol) and internal standard (Cp_2Fe) in C_6D_6 (0.6 mL) was added $Cp(PPr^i_3)RuH_3$ (0.005 g, 5 mol %). The resulting mixture was heated at 100°C and the progress of the reaction was monitored by NMR spectroscopy.



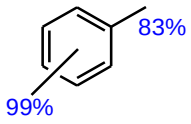
(No deuteration) (7 day)

<^{1}H NMR spectrum of the reaction 1-chlorohexane in C_6D_6>



Toluene

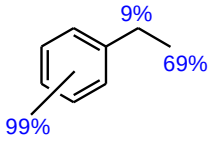
To a solution of toluene (0.028 mL, 0.30 mmol) and internal standard (Cp_2Fe) in C_6D_6 (0.6 mL) was added $Cp(PPr^i_3)RuH_3$ (0.005 g, 5 mol %). The resulting mixture was heated at 100°C and the progress of the reaction was monitored by NMR spectroscopy.



(6 day)

Ethylbenzene

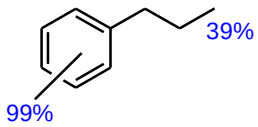
To a solution of ethylbenzene (0.032 mL, 0.30 mmol) and internal standard (Cp_2Fe) in C_6D_6 (0.6 mL) was added $Cp(PPr^i_3)RuH_3$ (0.005 g, 5 mol %). The resulting mixture was heated at 100°C and the progress of the reaction was monitored by NMR spectroscopy.



(33 day)

Propylbenzene

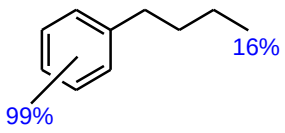
To a solution of propylbenzene (0.036 mL, 0.30 mmol) and internal standard (Cp_2Fe) in C_6D_6 (0.6 mL) was added $Cp(PPr^i_3)RuH_3$ (0.005 g, 5 mol %). The resulting mixture was heated at 100°C and the progress of the reaction was monitored by NMR spectroscopy.



(15 day)

Butylbenzene

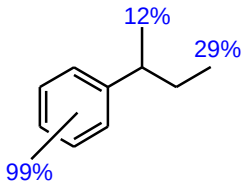
To a solution of butylbenzene (0.047 mL, 0.30 mmol) and internal standard (Cp_2Fe) in C_6D_6 (0.6 mL) was added $Cp(PPr^i_3)RuH_3$ (0.005 g, 5 mol %). The resulting mixture was heated at 100°C and the progress of the reaction was monitored by NMR spectroscopy.



(10 day)

1-sec-butylbenzene

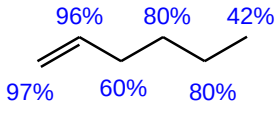
To a solution of 1-*Sec*-butylbenzene (0.047 mL, 0.30 mmol) and internal standard (Cp_2Fe) in C_6D_6 (0.6 mL) was added $Cp(PPr^i_3)RuH_3$ (0.005 g, 5 mol %). The resulting mixture was heated at 100°C and the progress of the reaction was monitored by NMR spectroscopy.



(6 day)

1-Hexene

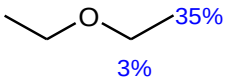
To a solution of 1-hexene (0.031 mL, 0.30 mmol) and internal standard (Cp_2Fe) in C_6D_6 (0.6 mL) was added $Cp(PPr^i_3)RuH_3$ (0.005 g, 5 mol %). The resulting mixture was heated at 100°C and the progress of the reaction was monitored by NMR spectroscopy.



(1 day)

Diethyl ether

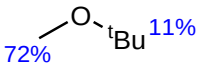
To a solution of diethyl ether (0.022 mL, 0.30 mmol) and internal standard (Cp_2Fe) in C_6D_6 (0.6 mL) was added $Cp(PPr^i_3)RuH_3$ (0.005 g, 5 mol %). The resulting mixture was heated at 100°C and the progress of the reaction was monitored by NMR spectroscopy.



(5 day)

2-methoxy-2-methylpropane

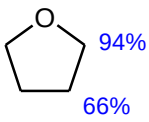
To a solution of 2-methoxy-2-methylpropane (0.026 mL, 0.30 mmol) and internal standard (Cp_2Fe) in C_6D_6 (0.6 mL) was added $Cp(PPr^i_3)RuH_3$ (0.005 g, 5 mol %). The resulting mixture was heated at 100°C and the progress of the reaction was monitored by NMR spectroscopy.



(3 day)

Tetrahydrofuran

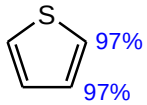
To a solution of tetrahydrofuran (0.022 mL, 0.30 mmol) and internal standard (Cp_2Fe) in C_6D_6 (0.6 mL) was added $Cp(PPr^i_3)RuH_3$ (0.005 g, 5 mol %). The resulting mixture was heated at 100°C and the progress of the reaction was monitored by NMR spectroscopy.



(1 day)

Thiophene

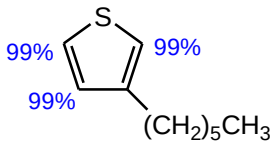
To a solution of thiophene (0.025 mL, 0.30 mmol) and internal standard (Cp_2Fe) in C_6D_6 (0.6 mL) was added $Cp(PPr^i_3)RuH_3$ (0.005 g, 5 mol %). The resulting mixture was heated at 100°C and the progress of the reaction was monitored by NMR spectroscopy.



(1 day)

3-Hexylthiophene

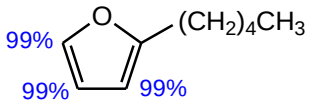
To a solution of 3-hexylthiophene (0.054 mL, 0.30 mmol) and internal standard (Cp_2Fe) in C_6D_6 (0.6 mL) was added $Cp(PPr^i_3)RuH_3$ (0.005 g, 5 mol %). The resulting mixture was heated at 100°C and the progress of the reaction was monitored by NMR spectroscopy.



(3 day)

2-n-pentylfuran

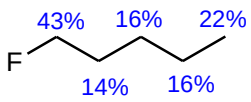
To a solution of 2-*n*-pentylfuran (0.041 mL, 0.30 mmol) and internal standard (Cp_2Fe) in C_6D_6 (0.6 mL) was added $Cp(PPr^i_3)RuH_3$ (0.005 g, 5 mol %). The resulting mixture was heated at 100°C and the progress of the reaction was monitored by NMR spectroscopy.



(1 day)

1-Fluoropentane

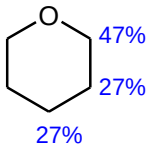
To a solution of 1-fluoropentane (0.027 mL, 0.30 mmol) and internal standard (Cp_2Fe) in C_6D_6 (0.6 mL) was added $Cp(PPr^i_3)RuH_3$ (0.005 g, 5 mol %). The resulting mixture was heated at 100°C and the progress of the reaction was monitored by NMR spectroscopy.



(4 day)

Tetrahydropyran

To a solution of tetrahydropyran (0.026 mL, 0.30 mmol) and internal standard (Cp_2Fe) in C_6D_6 (0.6 mL) was added $Cp(PPr^i_3)RuH_3$ (0.005 g, 5 mol %). The resulting mixture was heated at 100°C and the progress of the reaction was monitored by NMR spectroscopy.



(4 day)

H/D exchange reactions catalysed by $Cp(PPh_3)RuH_3$ in C_6D_6

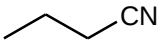
Hexane

To a solution of hexane (0.012 mL, 0.14 mmol) and internal standard (Cp_2Fe) in C_6D_6 (0.6 mL) was added $Cp(PPh_3)RuH_3$ (0.003 g, 5 mol %). The resulting mixture was heated at 100°C and the progress of the reaction was monitored by NMR spectroscopy.


(No deuteration)

Butylnitrile

To a solution of butylnitrile (0.010 mL, 0.14 mmol) and internal standard (Cp_2Fe) in C_6D_6 (0.6 mL) was added $Cp(PPh_3)RuH_3$ (0.003 g, 5 mol %). The resulting mixture was heated at 100°C and the progress of the reaction was monitored by NMR spectroscopy.

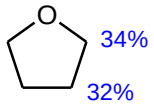


(No deuteration)

H/D exchange reactions catalysed by $Cp(PPr^i_3)RuH_3$ in D_2O

Tetrahydrofuran

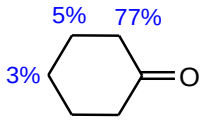
To a solution of tetrahydrofuran (0.024 mL, 0.30 mmol) and internal standard (Cp_2Fe) in D_2O (0.6 mL) was added $Cp(PPr^i_3)RuH_3$ (0.005 g, 5 mol %). The resulting mixture was heated at 100°C and the progress of the reaction was monitored by NMR spectroscopy.



(8 day)

Cyclohexanone

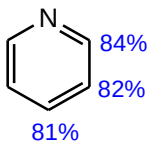
To a solution of cyclohexanone (0.031 mL, 0.30 mmol) and internal standard (Cp_2Fe) in D_2O (0.6 mL) was added $Cp(PPr^i_3)RuH_3$ (0.005 g, 5 mol %). The resulting mixture was heated at 100°C and the progress of the reaction was monitored by NMR spectroscopy.



(3 day)

Pyridine

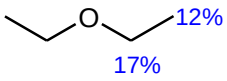
To a solution of pyridine (0.024 mL, 0.30 mmol) and internal standard (Cp_2Fe) in D_2O (0.6 mL) was added $Cp(PPr^i_3)RuH_3$ (0.005 g, 5 mol %). The resulting mixture was heated at 100°C and the progress of the reaction was monitored by NMR spectroscopy.



(1 day)

Diethyl ether

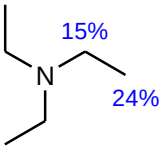
To a solution of diethyl ether (0.032 mL, 0.30 mmol) and internal standard (Cp_2Fe) in D_2O (0.6 mL) was added $Cp(PPr^i_3)RuH_3$ (0.005 g, 5 mol %). The resulting mixture was heated at 100°C and the progress of the reaction was monitored by NMR spectroscopy.



(2 day)

Triethylamine

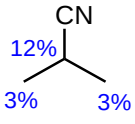
To a solution of triethylamine (0.042 mL, 0.30 mmol) and internal standard (Cp_2Fe) in D_2O (0.6 mL) was added $Cp(PPr^i_3)RuH_3$ (0.005 g, 5 mol %). The resulting mixture was heated at 100°C and the progress of the reaction was monitored by NMR spectroscopy.



(2 day)

2-Cyanopropane

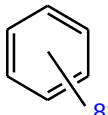
To a solution of 2-cyanopropane (0.021 mL, 0.30 mmol) and internal standard (Cp_2Fe) in D_2O (0.6 mL) was added $Cp(PPr^i_3)RuH_3$ (0.005 g, 5 mol %). The resulting mixture was heated at 100°C and the progress of the reaction was monitored by NMR spectroscopy.



(4 day)

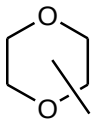
Benzene

To a solution of benzene (0.027 mL, 0.30 mmol) and internal standard (Cp_2Fe) in D_2O (0.6 mL) was added $Cp(PPr^i_3)RuH_3$ (0.005 g, 5 mol %). The resulting mixture was heated at 100°C and the progress of the reaction was monitored by NMR spectroscopy.


82% (1 day)

1,4-Dioxane

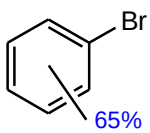
To a solution of 1,4-dioxane (0.026 mL, 0.30 mmol) and internal standard (Cp_2Fe) in D_2O (0.6 mL) was added $Cp(PPr^i_3)RuH_3$ (0.005 g, 5 mol %). The resulting mixture was heated at 100°C and the progress of the reaction was monitored by NMR spectroscopy.



5% (6 day)

1-Bromobenzene

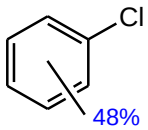
To a solution of 1-bromobenzene (0.032 mL, 0.30 mmol) and internal standard (Cp_2Fe) in D_2O (0.6 mL) was added $Cp(PPr^i_3)RuH_3$ (0.005 g, 5 mol %). The resulting mixture was heated at 100°C and the progress of the reaction was monitored by NMR spectroscopy.



65% (1 day)

1-Chlorobenzene

To a solution of 1-chlorobenzene (0.031 mL, 0.30 mmol) and internal standard (Cp_2Fe) in D_2O (0.6 mL) was added $Cp(PPr^i_3)RuH_3$ (0.005 g, 5 mol %). The resulting mixture was heated at 100°C and the progress of the reaction was monitored by NMR spectroscopy.



48% (1 day)

Synthesis of ruthenium styrene complex

To a solution of styrene (0.021 mL, 0.2 mmol) in C_6H_6 was added $Cp(PPr^i_3)RuH_3$ (0.033 g, 0.1 mmol). The mixture was heated at 100°C and the progress of the reaction was monitored by NMR spectroscopy. The Ru-styrene complex, $Cp(PPr^i_3)RuH(\eta^2\text{-}H_2C{=}CHPh)$, was obtained in 5 days as brown oil.

^{1}H NMR (C_6D_6): δ 7.48 (d, J(H-H) = 7.56 Hz, 2, $H_2C{=}CH\mathit{Ph}$), 7.28 (m, 2, $H_2C{=}CH\mathit{Ph}$), 7.03 (t, 1, $H_2C{=}CH\mathit{Ph}$), 4.55 (s, 5, $C_5\mathit{H}_5(PPr^i_3)RuH$), 3.56 (dd, J(H-H) = 2.78 and 10.62 Hz, 1, $H_2C{=}C\mathit{H}Ph$), 3.11 (dd, J(H-H) = 2.18 and 10.88 Hz, 1, $\mathit{H}_2C{=}CHPh$), 1.53 (m, 3, $RuP(C\mathit{H}(CH_3)_2)_3$), 1.43 (m, 1, $\mathit{H}_2C{=}CHPh$), 1.10 (dd, J(H-H) = 5.34 and 7.20 Hz, 18, $RuP(CH(C\mathit{H}_3)_2)_3$), -10.24 (d, J(P-H) = 35.74 Hz, 1, $Ru\mathit{H}$). $^{31}P\{^1H\}$ NMR (C_6D_6): δ 84.0 (s). ^1H-^{13}C HSQC (C_6D_6): δ 127.9 (s, $H_2C{=}CH\mathit{Ph}$), 126.4 (s, $H_2C{=}CH\mathit{Ph}$), 122.8 (s, $H_2C{=}CH\mathit{Ph}$), 83.9 (s, $\mathit{C}_5H_5(PPr^i_3)RuH$), 41.5 (s, $H_2C{=}\mathit{C}HPh$), 26.5 (s, $RuP(\mathit{C}H(CH_3)_2)_3$), 20.1 (s, $RuP(CH(\mathit{C}H_3)_2)_3$), 16.8 (s, $H_2\mathit{C}{=}CHPh$). IR (neat): υ (Ru-H) = 1988 cm^{-1}.

V.3. Reduction of pyridine derivatives catalysed by [Cp*(phen)Ru(CH3CN)]PF6

V.3.1. The syntheses of ruthenium complexes

Preparation of $[Cp^*RuCl_2]_n$

The synthesis of $[Cp^*RuCl_2]_n$ was performed based on a previously reported procedure under inert atmosphere. Pentamethylcyclopentadiene (7 mL, 50.3 mmol) was added to a solution of $RuCl_3 \cdot nH_2O$ (4.98 g, 22.1 mmol) in CH_3OH (100 mL). Refluxing the solution for 7 h resulted in color change of reaction mixture from green to brown-red. The brown-red solution was kept for 12 h at -80 ℃. The solution was filtered and the residue was washed with hexane to remove Cp^*_2Ru. The residue was dried under vacuum to afford $[Cp^*RuCl_2]_n$ as a brown solid. Yield 4.70 g (70 %).

Preparation of $[Cp^*Ru(CH_3CN)_3]PF_6$

The solution of $[Cp^*RuCl_2]_n$ (2 g, 6.52 mmol) in CH_3CN was added Zn dust (0.8 g, 12.76 mmol) and KPF_6 (1.68 g, 9.14 mmol). The reaction mixture was stirred for 15 h and the color of the reaction mixture changed from brown to green. The brown solution was filtered using a cannular with filter paper and the yellow solid was obtained by evaporating. The solid was extracted with dichloromethane. Then dichloromethane was evaporated to afford a yellow solid which was dried under vacuum. The solid was washed with hexane using ultrasonic for 20 min and hexane was filtered. The residue was dried under vacuum to afford $[Cp^*Ru(CH_3CN)_3]PF_6$ as yellow solid. Yield 3.05 g (92 %).

^1H NMR ($CDCl_3$): δ 2.30 (s, 9, C*H*$_3$CN), 1.50 (s, 15, Cp^*). $^{31}P\{^1H\}$ NMR ($CDCl_3$): δ -144 (m, PF_6).

Preparation of $[Cp^*Ru(PPr^i_2Me)(CH_3CN)_2]PF_6$

The solution of $[Cp^*Ru(CH_3CN)_3]PF_6$ (0.5 g, 1 mmol) in CH_3CN (60 mL) was added to PPr^i_2Me (0.13 mL, 1 mmol). The reaction mixture was stirred for 15 h at room temperature. The solvent was evaporated and the residue was washed with hexane (3*20 mL). The yellow solid was dried under vacuum. Yield 0.45 g (75 %).

^{1}H NMR (Acetone-d_6): δ 2.61 (s, 6, C*H*$_3$CN), 2.19 (m, 2, C*H*$(CH_3)_2$), 1.69 (s, 15, Cp^*), 1.12 (m, 12, CH(C*H*$_3)_2$), 1.12 (d, 3, C*H*$_3$). ^{31}P{^{1}H} NMR (Acetone-d_6): δ 35.6 (s). ^{1}H-^{13}C HSQC (Ace-d_6): δ 26.1 (d, *C*H$(CH_3)_2$), 16.3 (br s, CH(*C*H$_3)_2$), 9.4 (s, Cp^*), 4.7 (*C*H$_3$), 2.5 (s, *C*H$_3$CN). IR (neat): υ (CH_3CN) = 2228 cm^{-1}.

Preparation of $[Cp^*Ru(PPr^i_2Me)(CH_3CN)_2]BAF$

The solution of $[Cp^*Ru(PPr^i_2Me)(CH_3CN)_2]PF_6$ (0.25 g, 0.42 mmol) in CH_2Cl_2 was added LiBAF·Et_2O (0.32 g, 0.42 mmol). The solution was stirred for 12 h at room temperature. The solvent was evaporated under vacuum and then complex $[Cp^*Ru(PPr^i_2Me)(CH_3CN)_2]BAF$ was extracted with Et_2O (3*40 mL). The product was obtained as yellow powder after removal of Et_2O under vacuum. Yield 0.30 g (63 %).

^{1}H NMR (CD_2Cl_2): δ 2.35 (s, 6, C*H*$_3$CN), 2.07 (m, 2, C*H*$(CH_3)_2$), 1.61 (d, J(P-H) = 1.24 Hz, 15, Cp^*), 1.03 (m, 12, CH(C*H*$_3)_2$), 1.03-1.17 (d, 3, C*H*$_3$). ^{31}P{^{1}H} NMR (CD_2Cl_2): δ 35.2 (s).

Preparation of $[Cp^*Ru(PPr^i_3)(CH_3CN)_2]PF_6$

The solution of $[Cp^*Ru(CH_3CN)_3]PF_6$ (0.30 g, 0.6 mmol) in CH_3CN (60 mL) was added to PPr^i_3 (0.10 mL, 0.6 mmol). The reaction mixture was stirred for 30 min at room temperature. The solvent was evaporated and the residue was washed with hexane (3*20 mL). The yellow solid was dried under vacuum. Yield 0.27 g (72 %).

^{1}H NMR (CD_2Cl_2): δ 2.41 (s, 6, C*H*$_3$CN), 2.28 (m, 3, C*H*(CH_3)$_2$), 1.57 (s, 15, Cp^*), 1.17 (m, 18, CH(C*H*$_3$)$_2$), ^{31}P{^{1}H} NMR (CD_2Cl_2): δ 49.4 (s). ^{1}H-^{13}C HSQC (Ace-d_6): δ 29.3 (d, *C*H(CH_3)$_2$), 19.3 (br s, CH(*C*H$_3$)$_2$), 9.05 (s, Cp^*), 3.02 (s, *C*H$_3$CN). IR (neat): υ (CH_3CN) = 2265 cm^{-1}.

Preparation of [Cp^*Ru(PPr^i_3)(CH_3CN)$_2$]BAF

The solution of [Cp^*Ru(PPr^i_3)(CH_3CN)$_2$]PF_6 (0.15 g, 0.27 mmol) in CH_2Cl_2 was added to LiBAF·Et_2O (0.21 g, 0.27 mmol). The solution was stirred for 12 h at room temperature. The solvent was evaporated under vacuum and then complex [Cp^*Ru(PPr^i_3)(CH_3CN)$_2$]BAF was extracted with Et_2O (3*40 mL). The product was obtained as dark green powder after removal of Et_2O under vacuum. Yield 0.17 g (55 %).

^{1}H NMR (CD_2Cl_2): δ 2.36 (s, 6, C*H*$_3$CN), 2.25 (m, 3, C*H*(CH_3)$_2$), 1.56 (s, 15, Cp^*), 1.16 (m, 18, CH(C*H*$_3$)$_2$), ^{31}P{^{1}H} NMR (CD_2Cl_2): δ 49.2 (s).

Preparation of [Cp^*Ru(PPh_3)(CH_3CN)$_2$]PF_6

The solution of [Cp^*Ru(CH_3CN)$_3$]PF_6 (0.30 g, 0.6 mmol) in CH_3CN (60 mL) was added to PPh_3 (0.16 g, 0.6 mmol). The reaction mixture was stirred for 3 h at room temperature. The solvent was evaporated and the residue was washed with hexane (3*20 mL). The yellow solid was dried under vacuum. Yield 0.38 g (88 %).

^{1}H NMR (CD_2Cl_2): δ 7.17 (m, 15, Ph_3), 2.13 (s, 6, C*H*$_3$CN), 1.40 (d, J(H-P) = 0.9 Hz, 15, Cp^*). ^{31}P{^{1}H} NMR (CD_2Cl_2): δ 48.3 (s). IR (neat): υ (CH_3CN) = 2268 cm^{-1}.

Preparation of [Cp^*Ru(PPh_3)(CH_3CN)$_2$]BAF

The solution of [Cp^*Ru(PPh_3)(CH_3CN)$_2$]PF_6 (0.20 g, 0.28 mmol) in CH_2Cl_2 was added to LiBAF·Et_2O (0.21 g, 0.28 mmol). The solution was stirred for 12 h at room temperature. The solvent was evaporated under vacuum and then complex [Cp^*Ru(PPh_3)(CH_3CN)$_2$]BAF was extracted with Et_2O (3*40 mL). The product was

obtained as bright yellow powder after removal of Et_2O under vacuum. Yield 0.25 g (71 %).

^1H NMR (CD_2Cl_2): δ 7.27 (m, 15, Ph_3), 2.06 (s, 6, C*H*$_3$CN), 1.39 (d, J(H-P) = 1.5 Hz, 15, Cp^*). $^{31}P\{^1H\}$ NMR (CD_2Cl_2): δ 48.4 (s). ^1H-^{13}C HSQC (Ace-d_6): δ 9.1 (s, Cp^*), 3.4 (s, *C*H_3CN).

Preparation of [Cp^*(phen)Ru(CH_3CN)]PF_6

The solution of [$Cp^*Ru(CH_3CN)_3$]PF_6 (0.30 g, 0.6 mmol) in CH_3CN (60 mL) was added to 1,10-phenanthroline (0.11 g, 0.6 mmol). The reaction mixture was stirred for 12 h at room temperature. The solvent was evaporated and the residue was washed with hexane (3*20 mL). The yellow solid was dried under vacuum. Yield 0.34 g (94 %).

^1H NMR (Acetone-d_6): δ 9.68 (m, 2, 1, o-phen), 8.72 (m, 2, 1, p-phen), 8.23 (m, 2, phen), 8.13 (m, 2, m-phen), 2.13 (s, 3, C*H*$_3$CN), 1.70 (s, 15, Cp^*). $^{31}P\{^1H\}$ NMR (Acetone-d_6): δ -144.2 (septet, PF_6). ^1H-^{13}C HSQC (Acetone-d_6): δ 209.0 (CH_3*C*N), 152.5 (o-phen), 135.4 (p-phen), 127.2 (phen), 125.6 (m-phen), 8.65 (Cp), 2.34 (*C*H_3CN). IR (neat): υ (CH_3CN) = 2339 cm^{-1}. Mp: 217 °C dec. Anal. Calcd for $C_{24}H_{26}F_6N_3PRu$: C, 47.84; H, 4.35; N, 6.97. Found: C, 47.20; H, 4.19; N, 6.72.

Preparation of [Cp^*(phen)Ru (CH_3CN)]BAF

The solution of [Cp^*(phen)Ru(CH_3CN)]PF_6 (0.15 g, 0.25 mmol) in CH_2Cl_2 was added LiBAF·Et_2O (0.19 g, 0.25 mmol). The solution was stirred for 2 h at room temperature. The solvent was evaporated under vacuum and then complex [$Cp^*Ru(PPh_3)(CH_3CN)_2$]BAF was extracted with Et_2O (2*40 mL). The product was obtained as bright yellow powder after removal of Et_2O under vacuum. Yield 0.27 g (95 %).

^{1}H NMR (Acetone-d_6): δ 9.68 (d, 2, 1, o-phen), 8.73 (d, 2, 1, p-phen), 8.24 (s, 2, phen), 8.13 (m, 2, m-phen), 2.15 (s, 3, C*H*$_3$CN), 1.70 (s, 15, Cp*). ^{11}B NMR (Acetone-d_6): δ -16.62 (s, BAF). ^{1}H-^{13}C HSQC (Ace-d_6): δ 152.4 (o-phen), 135.5 (p-phen), 127.3 (phen), 125.4 (m-phen), 8.5 (Cp), 2.0 (*C*H$_3$CN). IR (neat): υ (CH$_3$CN) = 2337 cm^{-1}. Mp: 223 °C dec. Anal. Calcd for $C_{48}H_{26}BF_{20}N_3PRu$: C, 50.72; H, 2.31; N, 3.70. Found: C, 49.76; H, 2.34; N, 2.84.

V.3.2. Catalytic reduction of pyridine derivatives

Hydrosilylation catalysed by [Cp*(phen)Ru(CH$_3$CN)]PF$_6$

1,10-Phenanthroline

To a solution of HSiMe$_2$Ph (15.4 μL, 0.1 mmol) and 1,10-phenanthroline (18.0 mg, 0.1 mmol) in Acetone-d_6 was added [Cp*(phen)Ru(CH$_3$CN)]PF$_6$ (3 mg, 0.005 mmol). The reaction was periodically monitored by NMR spectroscopy. 70% conversion was achieved after 20 h at room temperature and 1,4-hydrosilylated phenanthroline was obtained. After 70% conversion, the reaction does not give further conversion because of the equilibrium.

N-dimethylphenylsilyl 1,4-dihydrophenanthroline

^{1}H NMR (Ace-d_6): δ 8.64 (dd, *J*(H-H) = 3.8 Hz and 1.1 Hz, 1, NCHC*H*CH), 8.12 (d, *J*(H-H) = 7.3 Hz, 1, NC*H*CHCH), 7.62 (m, 2, SiMe$_2$*Ph*(*o*)), 7.29 (m, 1, NCHCHC*H*), 7.22 (m, 3, SiMe$_2$*Ph*(*m, p*)), 7.10 (d, *J*(H-H) = 7.9 Hz, 1, C*H*CH), 6.93 (d, *J*(H-H) = 7.9 Hz, 1, CHC*H*), 6.55 (d, *J*(H-H) = 7.6 Hz, 1, Si-NC*H*CHCH$_2$), 4.82 (m, 1, Si-NCHC*H*CH$_2$), 3.66 (m, 2, Si-NCHCHC*H*$_2$), 0.54 (s, 6, Si*Me*$_2$Ph).

2-Cyano-1,10-phenanthroline

To a solution of HSiMe$_2$Ph (3.9 μL, 0.025 mmol) and 2-cyano-1,10-phenanthroline (5.1 mg, 0.025 mmol) in CD_2Cl_2 was added [Cp*(phen)Ru(CH$_3$CN)]PF$_6$ (0.8 mg,

0.0013 mmol). The reaction was periodically monitored by NMR spectroscopy. A very little conversion was achieved at 70ºC and a mixture of products was obtained.

Quinoline

To a mixture of $HSiMe_2Ph$ (338.8.0 μL, 2.20 mmol) and quinoline (260.0 μL, 2.00 mmol) was added $[Cp^*(phen)Ru(CH_3CN)]PF_6$ (8.4 mg, 0.014 mmol). The reaction was periodically monitored by NMR spectroscopy. 80% conversion was achieved after 5 h at 70ºC. 97% of 1,4-hydrosilylated quinoline and 3% of 1,2-hydrosilylated quinoline were obtained. Full conversion was achieved for overnight. The mixture of 1,4-hydrosilylated quinoline and 1,2-hydrosilylated quinoline was isolated by extraction with hexane (94 %).

N-dimethylsilyl-1,4-dihydroquinoline

^1H NMR ($CDCl_3$): δ 7.66 (m, 2, $SiMe_2$*Ph*), 7.44 (m, 3, $SiMe_2$*Ph*), 7.02 (dd, 1, quin), 6.87 (m, 2, quin), 6.77 (dd, 1, quin), 6.36 (m, 1, quin), 4.82 (m, 1, quin), 3.59 (d, 2, C*H*$_2$), 0.68 (s, 6, Si*Me*$_2$Ph). ^1H-^{13}C HSQC ($CDCl_3$): 133.1, 129.0, 127.9 ($SiMe_2$*Ph*), 130.4, 129.2, 125.6, 121.2, 117.6, 99.8 (quin), 27.0 (*C*H_2), -0.9 (Si*Me*$_2$Ph). Isolated yield 0.52 g (98 %).

Quinoline with $DSiMe_2Ph$

To a mixture of $DSiMe_2Ph$ (174.3 μL, 1.27 mmol) and quinoline (150.0 μL, 1.27 mmol) was added $[Cp^*(phen)Ru(CH_3CN)]PF_6$ (5.5 mg, 0.0089 mmol). The reaction was periodically monitored by NMR spectroscopy. 75% conversion was achieved after 5 h at 70ºC and 1,4-hydrosilylated quinoline was obtained. The product was confirmed by ^2H and ^1H-^{13}C HSQC NMR.

Acridine

To a solution of $HSiMe_2Ph$ (7.7 μL, 0.05 mmol) and acridine (8.9 mg, 0.05 mmol) in CD_2Cl_2 was added $[Cp^*(phen)Ru(CH_3CN)]PF_6$ (1.5 mg, 0.0025 mmol). The reaction

was periodically monitored by NMR spectroscopy. Full conversion was achieved after 24 h at 70ºC and hydrosilylated acridine was obtained.

9,10-dihydro-10-(dimethylphenylsilyl)acridine

^{1}H NMR (CD_2Cl_2): δ 7.67 (m, 2, $SiMe_2$*Ph*), 7.45 (m, 3, $SiMe_2$*Ph*), 7.10 (m, 4, acridine), 6.87 (t, 2, acridine), 6.72 (d, 2, acridine), 4.07 (s, 2, C*H*$_2$), 0.73 (s, 6, Si*Me*$_2$Ph). ^{1}H-^{13}C HSQC (CD_2Cl_2): δ 133.1, 129.7, 128.1 ($SiMe_2$*Ph*), 128.5, 126.9, 120.5, 113.2 (acridine), 31.4 (*C*H$_2$), 1.7 (Si*Me*$_2$Ph).

Pyrazine

To a solution of $HSiMe_2Ph$ (7.7 μL, 0.05 mmol) and pyrazine (4.0 mg, 0.05 mmol) in CD_2Cl_2 was added $[Cp^*(phen)Ru(CH_3CN)]PF_6$ (1.5 mg, 0.0025 mmol). The reaction was periodically monitored by NMR spectroscopy. No reaction was observed at 70 ºC.

Triazine

To a solution of $HSiMe_2Ph$ (15.4 μL, 0.1 mmol) and triazine (8.1 mg, 0.1 mmol) in CD_2Cl_2 was added $[Cp^*(phen)Ru(CH_3CN)]PF_6$ (3.0 mg, 0.005 mmol). The reaction was periodically monitored by NMR spectroscopy. 90% conversion was achieved after 1.5 h at 70ºC and hydrosilylated triazine was obtained.

1,2-dihydro-1-(dimethylphenylsilyl)-1,3,5-triazine

^{1}H NMR (CD_2Cl_2): δ 7.61 (m, 2, $SiMe_2$*Ph*), 7.46 (m, 3, $SiMe_2$*Ph*), 7.09 (s, 2, C*H*), 4.93 (s, 2, C*H*$_2$), 0.62 (s, 6, Si*Me*$_2$Ph). ^{1}H-^{13}C HSQC (CD_2Cl_2): δ 145.4 (*C*H), 128.4, 133.5, 134.0 ($SiMe_2$*Ph*), 62.4 (*C*H$_2$), -2.83 (Si*Me*$_2$Ph).

Isoquinoline

To a mixture of $HSiMe_2Ph$ (200.2 μL, 1.30 mmol) and isoquinoline (130.0 μL, 1.00 mmol) was added $[Cp^*(phen)Ru(CH_3CN)]PF_6$ (30.0 mg, 0.05 mmol). The reaction was periodically monitored by NMR spectroscopy. 90% conversion was achieved

after 9 days at 70ºC. Hydrosilylated isoquinoline were obtained. The hydrosilylated isoquinoline was isolated by extraction with hexane (95 %).

1,2-dihydro-2-(dimethylphenylsilyl)isoquinoline

^{1}H NMR ($CDCl_3$): δ 7.56 (m, 2, $SiMe_2$*Ph*), 7.37 (m, 3, $SiMe_2$*Ph*), 7.09 (m, 1, quin), 6.98-7.04 (td, 1, quin), 6.84 (t, 2, quin), 6.38-6.41 (d, 1, quin), 5.53 (d, 1, quin), 4.28 (s, 2, C*H*$_2$), 0.50 (s, 6, Si*Me*$_2$Ph). ^{1}H-^{13}C HSQC ($CDCl_3$): 102.3, 125.3, 125.4, 127.6, 136.3 (quin), 127.9, 129.3, 133.5 ($SiMe_2$*Ph*), 47.3 (*C*H_2), -2.5 (Si*Me*$_2$Ph). Isolated yield 0.25 g (95 %).

2,6-Lutidine

To a solution of $HSiMe_2Ph$ (7.7 μL, 0.05 mmol) and 2,6-lutidine (5.4 μL, 0.05 mmol) in CD_2Cl_2 was added $[Cp^*(phen)Ru(CH_3CN)]PF_6$ (1.5 mg, 0.0025 mmol). The reaction was periodically monitored by NMR spectroscopy. No reaction was observed at 70ºC.

2,4-Lutidine

To a solution of $HSiMe_2Ph$ (7.7 μL, 0.05 mmol) and 2,4-lutidine (5.4 μL, 0.05 mmol) in CD_2Cl_2 was added $[Cp^*(phen)Ru(CH_3CN)]PF_6$ (1.5 mg, 0.0025 mmol). The reaction was periodically monitored by NMR spectroscopy. No reaction was observed at 70ºC.

7-Chloroquinaldine

To a solution of $HSiMe_2Ph$ (3.9 μL, 0.025 mmol) and 7-chloroquinaldine (4.5 mg, 0.025 mmol) in CD_2Cl_2 was added $[Cp^*(phen)Ru(CH_3CN)]PF_6$ (0.8 mg, 0.0013 mmol). The reaction was periodically monitored by NMR spectroscopy. No reaction was observed at 70ºC.

2-Phenylquinoline

To a solution of $HSiMe_2Ph$ (7.7 μL, 0.05 mmol) and 2-phenylquinoline (10.3 mg, 0.05 mmol) in CD_2Cl_2 was added $[Cp^*(phen)Ru(CH_3CN)]PF_6$ (1.5 mg, 0.0025 mmol). The reaction was periodically monitored by NMR spectroscopy. No reaction was observed at 70ºC.

7-Methyl-8-nitroquinoline

To a solution of $HSiMe_2Ph$ (7.7 μL, 0.05 mmol) and 7-Methyl-8-nitroquinoline (9.4 mg, 0.05 mmol) in CD_2Cl_2 was added $[Cp^*(phen)Ru(CH_3CN)]PF_6$ (1.5 mg, 0.0025 mmol). The reaction was periodically monitored by NMR spectroscopy. No reaction was observed at 70ºC.

2-Ethylpyridine

To a solution of $HSiMe_2Ph$ (7.7 μL, 0.05 mmol) and 2-ethylpyridine (5.4 μL, 0.05 mmol) in CD_2Cl_2 was added $[Cp^*(phen)Ru(CH_3CN)]PF_6$ (1.5 mg, 0.0025 mmol). The reaction was periodically monitored by NMR spectroscopy. No reaction was observed at 70ºC.

2-Methylquinoxaline

To a solution of $HSiMe_2Ph$ (7.7 μL, 0.05 mmol) and 2-methylquinoxaline (7.2 μL, 0.05 mmol) in CD_2Cl_2 was added $[Cp^*(phen)Ru(CH_3CN)]PF_6$ (1.5 mg, 0.0025 mmol). The reaction was periodically monitored by NMR spectroscopy. No reaction was observed at 70ºC.

Reduction catalysed by $[Cp^*(phen)Ru(CH_3CN)]PF_6$

1,10-Phenanthroline

To a solution of $HSiMe_2Ph$ (15.4 μL, 0.1 mmol), 1,10-phenanthroline (18.0 mg, 0.1 mmol) and EtOH (4.6 μL, 0.3 mmol)in Acetone-d_6 was added

[Cp^*(phen)Ru(CH_3CN)]PF_6 (3 mg, 0.005 mmol). The reaction was periodically monitored by NMR spectroscopy. Full conversion was achieved after 20 m at room temperature. 1,4-reduced phenanthroline and $CH_3CH_2OSiMe_2Ph$ were obtained.

1,4-Dihydro-1,10-phenanthroline

^{1}H NMR (Acetone-d_6): δ 8.71 (d, 1, phen), 8.14 (d, 1, phen), 7.72 (s, br, 1, N*H*), 7.38 (m, 1, phen), 7.25 (d, 1, phen), 7.11 (d, 1, phen), 6.40 (m, 1, phen), 4.51 (m, 1, phen), 3.75 (s, 2, C*H*$_2$).

Acridine

To a solution of $HSiMe_2Ph$ (9.24 μL, 0.6 mmol), acridine (8.9 mg, 0.05 mmol) and EtOH (6.9 μL, 0.15 mmol) in Acetone-d_6 was added [Cp^*(phen)Ru(CH_3CN)]PF_6 (1.5 mg, 0.0025 mmol). The reaction was periodically monitored by NMR spectroscopy. Full conversion was achieved after 10 m at room temperature. Reduced acridine and $CH_3CH_2OSiMe_2Ph$ were obtained.

9,10-Dihydroacridine

^{1}H NMR (CD_2Cl_2): δ 7.86 (s, br, 1, NH), 7.08 (d, 2, acridine), 7.03 (t, 2, acridine), 6.77 (m, 4, acridine), 4.02 (s, 2, C*H*$_2$).^{1}H-^{13}C HSQC (CD_2Cl_2): δ 113.6, 120.1, 126.9, 128.5 (acridine), 31.4 (*C*H_2).

Pyrazine

To a solution of $HSiMe_2Ph$ (15.4 μL, 0.1 mmol), pyrazine (8.0 mg, 0.1 mmol) and EtOH (13.8 μL, 0.3 mmol) in Acetone-d_6 was added [Cp^*(phen)Ru(CH_3CN)]PF_6 (3.0 mg, 0.005 mmol). The reaction was periodically monitored by NMR spectroscopy at room temperature. Cp^*Ru(phen)(pyrazine) complex was obtained.

2,6-Lutidine

To a solution of $HSiMe_2Ph$ (7.7 μL, 0.05 mmol), 2,6-lutidine (5.4 μL, 0.05 mmol) and EtOH (6.9 μL, 0.15 mmol) in Acetone-d_6 was added [Cp^*(phen)Ru(CH_3CN)]PF_6 (1.5

mg, 0.0025 mmol). The reaction was periodically monitored by NMR spectroscopy at room temperature. Formation of $EtOSiMe_2Ph$ and H_2 was observed.

2,4-Lutidine

To a solution of $HSiMe_2Ph$ (7.7 μL, 0.05 mmol), 2,4-lutidine (5.4 μL, 0.05 mmol) and EtOH (6.9 μL, 0.15 mmol) in Acetone-d_6 was added $[Cp^*(phen)Ru(CH_3CN)]PF_6$ (1.5 mg, 0.0025 mmol). The reaction was periodically monitored by NMR spectroscopy at room temperature. Formation of $EtOSiMe_2Ph$ and H_2 was observed.

2-Phenylquinoline

To a solution of $HSiMe_2Ph$ (7.7 μL, 0.05 mmol) and 2-phenylquinoline (10.3 mg, 0.05 mmol) and EtOH (6.9 μL, 0.15 mmol) in Acetone-d_6 was added $[Cp^*(phen)Ru(CH_3CN)]PF_6$ (1.5 mg, 0.0025 mmol). The reaction was periodically monitored by NMR spectroscopy at room temperature. Formation of $EtOSiMe_2Ph$ and H_2 was observed.

2-Ethylpyridine

To a solution of $HSiMe_2Ph$ (7.7 μL, 0.05 mmol) and 2-ethylpyridine (5.4 μL, 0.05 mmol) and EtOH (6.9 μL, 0.15 mmol) in Acetone-d_6 was added $[Cp^*(phen)Ru(CH_3CN)]PF_6$ (1.5 mg, 0.0025 mmol). The reaction was periodically monitored by NMR spectroscopy at room temperature. Formation of $EtOSiMe_2Ph$ and H_2 was observed.

V.4.Transfer hydrogenation of organic compounds catalysed by Ru complexes

V.4.1. The synthesis of ruthenium complex

Preparation of $[Cp^*(PPr^i_3)Ru(CH_3CN)_2]PF_6$

The solution of $[Cp^*Ru(CH_3CN)_3]PF_6$ (0.30 g, 0.6 mmol) in CH_3CN (60 mL) was added PPr^i_3 (0.10 mL, 0.6 mmol). The reaction mixture was stirred for 30 min at room temperature. The solvent was evaporated and the residue was washed with hexane (3*20 mL). The yellow solid was dried under vacuum. Yield 0.27 g (72 %).

^1H NMR (CD_2Cl_2): δ 2.41 (s, 6, C*H*$_3$CN), 2.28 (m, 3, C*H*$(CH_3)_2$), 1.57 (s, 15, Cp^*), 1.17 (m, 18, CH(C*H*$_3)_2$), $^{31}P\{^1H\}$ NMR (CD_2Cl_2): δ 49.4 (s). ^1H-^{13}C HSQC (Ace-d_6): δ 29.3 (d, *C*H$(CH_3)_2$), 19.3 (br s, CH(*C*H$_3)_2$), 9.1 (s, Cp^*), 3.0 (s, *C*H$_3$CN). IR (neat): υ (CH_3CN) = 2265 cm^{-1}.

V.4.2. Transfer hydrogenation of ketones and an imine

Acetophenone

In a representative procedure, to a solution of $PhCOCH_3$ (12.0 μL, 0.1 mmol) and t-BuOK (1.12 mg, 0.01 mmol) in 2-propanol was added the Ru complex (5 mol %). The reaction was periodically monitored by NMR spectroscopy at room temperature. $PhCH(OH)CH_3$ was obtained as a corresponding product.

Preparative scale reaction

To a solution of $PhCOCH_3$ (120.2 μL, 1.0 mmol) and t-BuOK (11.2 mg, 0.1 mmol) in 2-propanol was added the Ru complex (2.5 mol %).

Purification

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 brown oil. The compound $PhCH(OH)CH_3$ was isolated by chromatography over silica using 3:1 hexane : ethyl acetate as eluent to afford the product as a yellow oil. (100 mg, 82% yield)

$PhCH(OH)CH_3$

^{1}H NMR ($CH_3CH(OH)CH_3$): δ 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 (d, J(H-H) = 6.37 Hz, 3, C*H*$_3$). ^{1}H-^{13}C HSQC ($CH_3CH(OH)CH_3$): δ 128.1 (s, *Ph*), 126.7 (s, *Ph*), 125.4 (s, *Ph*), 69.1 (s, Ph*C*H(OH)CH_3), 25.1 (s, PhCH(OH)*C*H$_3$).

Turnover Frequency

(Mole of ketone converted into alcohol per mole of catalyst per hour)

Substrate	Product	$[Cp(PPr^i_3)Ru(CH_3CN)_2]PF_6$		$[Cp^*Ru(phen)(CH_3CN)]PF_6$	
		Time	Conv.	Time	Conv.
$PhCOCH_3$	$PhCH(OH)CH_3$	10s	35%	15s	-
		20s	46%	45s	-
		25s	50%	5m	12%
		40s	66%	15m	30%
		60s	74%	35m	56%
		90s	80%	70m	80%
				100m	85%
		TOF 0.5/0.007/0.00694(25s) = 10292		TOF 0.56/0.007/0.58333(35m) = 137	

Ru catalyst (0.7 mol %), t-BuOK (1 mol %, 0.01 mmol), $PhCOCH_3$ (1.0 mmol), 2-propanol (0.5 mL), 84°C.

4-Methoxyacetophenone

To a solution of 4-$CH_3OC_6H_4COCH_3$ (15.2 μL, 0.1 mmol) and t-BuOK (1.12 mg, 0.01 mmol) in 2-propanol was added the Ru complex (5 mol %). The reaction was periodically monitored by NMR spectroscopy at room temperature. 4-$CH_3OC_6H_4CH(OH)CH_3$ was obtained as a corresponding product.

Preparative scale reaction

To a solution of 4-$CH_3OC_6H_4COCH_3$ (150.2 μL, 1.0 mmol) and t-BuOK (11.2 mg, 0.1 mmol) in 2-propanol was added the Ru complex (2.5 mol %).

Purification

After the reaction was completed, the mixture was concentrated. The compound 4-$CH_3OC_6H_4CH(OH)CH_3$was isolated by chromatography over silica using 3:1 hexane : ethyl acetate as eluent to afford the product as a transparent oil. (110 mg, 72% yield)

4-$CH_3OC_6H_4CH(OH)CH_3$

^{1}H NMR ($CH_3CH(OH)CH_3$): δ 7.57 (d, J(H-H) = 8.63 Hz, 2, C_6H_4), 7.12 (d, J(H-H) = 8.63 Hz, 2, C_6H_4), 5.07 (m, 1, C*H*), 4.06 (s, 3, OCH_3), 1.73 (d, J(H-H) = 6.57 Hz, 3, CH_3). ^{1}H-^{13}C HSQC (CH_2Cl_2): δ 125.7 (s, 4-$CH_3OC_6H_4CH$), 112.9 (s, 4-$CH_3OC_6H_4CH$), 55.4 (s, 4-$CH_3OC_6H_4$), 53.1 (s, 4-$CH_3OC_6H_4CH(OH)CH_3$), 24.7 (s, 4-$CH_3OC_6H_4CH(OH)CH_3$).

3-Aminoacetophenone

To a solution of 3-$NH_2C_6H_4COCH_3$ (13.5 mg, 0.1 mmol) and t-BuOK (1.12 mg, 0.01 mmol) in 2-propanol was added the Ru complex (5 mol %). The reaction was periodically monitored by NMR spectroscopy at room temperature. 3-$NH_2C_6H_4CH(OH)CH_3$ was obtained as a corresponding product.

Preparative scale reaction

To a solution of 3-$NH_2C_6H_4COCH_3$ (135.2 mg, 1.0 mmol) and t-BuOK (11.2 mg, 0.1 mmol) in 2-propanol was added the Ru complex (2.5 mol %).

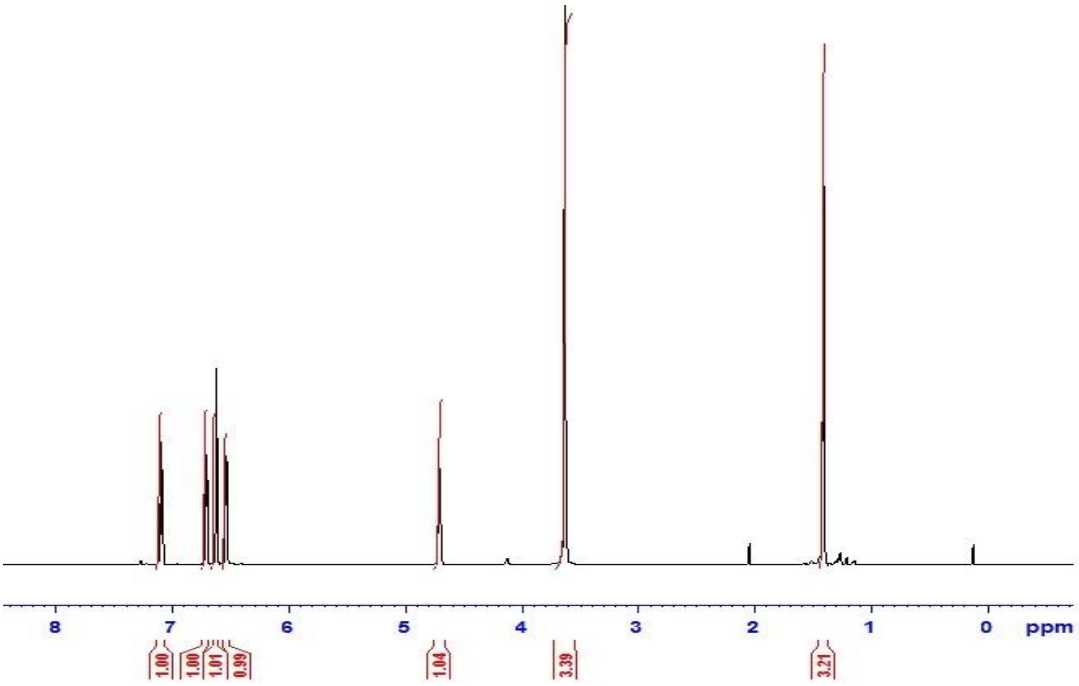
Purification

After the reaction was completed, volatile was removed and the mixture was dissolved in the 1:1 mixture of hexane and ethyl acetate. The compound 3-$NM_2C_6H_4CH(OH)CH_3$ was isolated by chromatography over silica using 1:1 hexane : ethyl acetate as eluent to afford the product as a pink oil. (92 mg, 67% yield).

3-$NH_2C_6H_4CH(OH)CH_3$

^{1}H NMR ($CH_3CH(OH)CH_3$): δ 7.28 (t, J(H-H) = 7.65 Hz, 1, 3-$NH_2C_6H_4$ *(5)*), 7.06 (s, 1, 3-$NH_2C_6H_4$ *(2)*), 6.97 (d, J(H-H) = 7.65 Hz, 1, 3-$NH_2C_6H_4$ *(4)*), 6.87 (dd, J(H-H) = 1.77 and 7.65 Hz, 1, 3-$NH_2C_6H_4$ *(6)*), 5.01 (q, 1, Ph*C*H(OH)CH_3), 4.75 (s, br, 2, 3-$NH_2C_6H_4$), 1.71 (d, J(H-H) = 6.73 Hz, 3, $C_6H_4CH(OH)CH_3$). ^{1}H-^{13}C HSQC ($CDCl_3$): δ 129.1 (s, C_6H_4), 115.8 (s, C_6H_4), 114.0 (s, C_6H_4), 112.3 (s, C_6H_4), 69.3 (s, $C_6H_4CH(OH)$), 26.2 (s, $C_6H_4CH(OH)CH_3$).

<^{1}H NMR spectrum of 3-$NH_2C_6H_4CH(OH)CH_3$ in $CDCl_3$>



4-Chloroacetophenone

To a solution of 4-chloroacetophenone (15.5 μL, 0.1 mmol) and t-BuOK (1.12 mg, 0.01 mmol) in 2-propanol was added the Ru complex (5 mol %). The reaction was periodically monitored by NMR spectroscopy at room temperature. 4-$ClC_6H_4CH(OH)CH_3$ was obtained as a corresponding product.

Preparative scale reaction

To a solution of 4-chloroacetophenone (154.6 μL, 1.0 mmol) and t-BuOK (11.2 mg, 0.1 mmol) in 2-propanol was added the Ru complex (2.5 mol %).

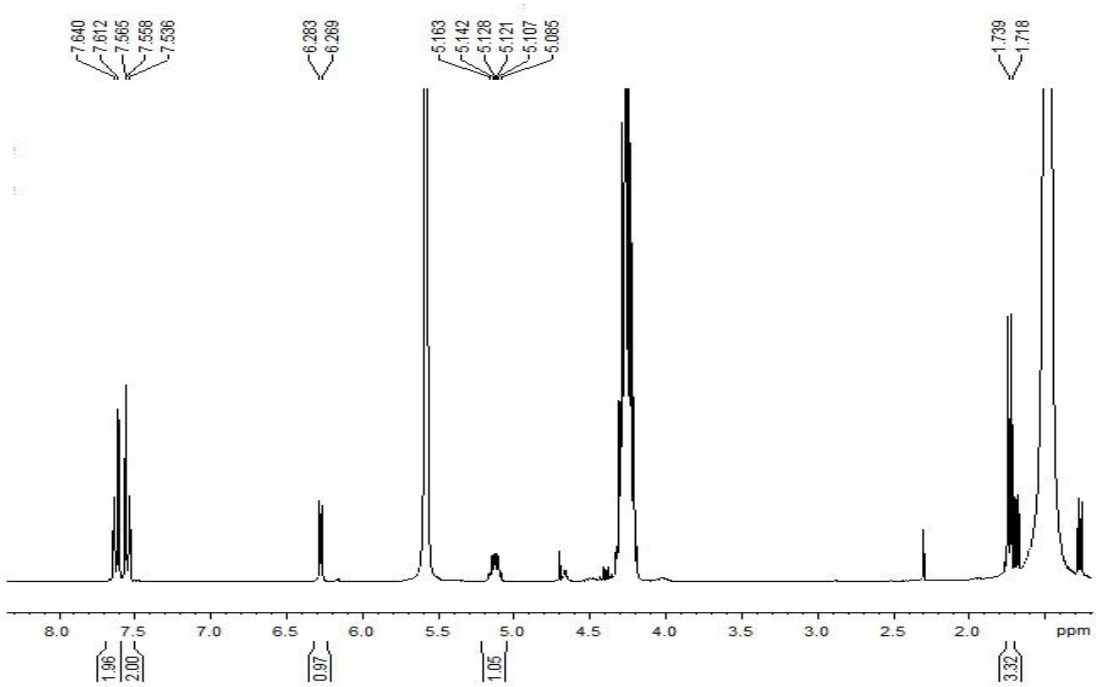
Purification

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 brown oil. The compound 4-$ClC_6H_4CH(OH)CH_3$ was isolated by chromatography over silica using 3:1 hexane : ethyl acetate as eluent to afford the product as a transparent oil. (134 mg, 86% yield)

4-$ClC_6H_4CH(OH)CH_3$

^{1}H NMR ($CH_3CH(OH)CH_3$): δ 7.61 (d, J(H-H) = 8.72 Hz, 2, 4-ClC_6H_4), 7.53 (d, J(H-H) = 8.36 Hz, 2, 4-ClC_6H_4), 5.08 (q, 1, 4-$ClC_6H_4CH(OH)CH_3$), 1.71 (d, J(H-H) = 6.65 Hz, 3, 4-$ClC_6H_4CH(OH)CH_3$). ^{1}H-^{13}C HSQC ($CH_3CH(OH)CH_3$): δ 128.2 (s, 4-ClC_6H_4(*o*)CH), 127.1 (s, 4-ClC_6H_4(*o*)CH), 68.5(s, 4-$ClC_6H_4CH(OH)CH_3$), 25.2 (s, 4-$ClC_6H_4CH(OH)CH_3$).

<^{1}H NMR spectrum of 4-$ClC_6H_4CH(OH)CH_3$ in 2-propanol with D_2O insert>



Benzophenone

To a solution of PhCOPh (18.2 mg, 0.1 mmol) and t-BuOK (1.12 mg, 0.01 mmol) in 2-propanol was added the Ru complex (5 mol %). The reaction was periodically monitored by NMR spectroscopy at room temperature. PhCH(OH)Ph was obtained as a corresponding product.

Preparative scale reaction

To a solution of PhCOPh (182.2 mg, 1.0 mmol) and t-BuOK (11.2 mg, 0.1 mmol) in 2-propanol was added the Ru complex (2.5 mol %).

Purification

After the reaction was completed, volatile was removed and the mixture was dissolved in ethyl acetate. The compound PhCH(OH)Ph was isolated by chromatography over silica using 15:1 hexane : ethyl acetate as eluent to afford the product as a white oil. (110 mg, 60% yield)

PhCH(OH)Ph

^{1}H NMR ($CH_3CH(OH)CH_3$): δ 7.64 (d, J(H-H) = 7.10 Hz, 4, *Ph*), 7.52 (t, J(H-H) = 6.76 Hz, 4, *Ph*), 7.43 (t, J(H-H) = 7.10 Hz, 2, *Ph*), 6.07 (s, 1, C*H*). ^{1}H-^{13}C HSQC (CH_2Cl_2): δ 128.2 (s, *Ph*(*m*)), 127.2 (s, *Ph*(*p*)), 126.0 (s, *Ph*(*o*)), 75.9 (Ph*C*H).

Cyclohexanone

To a solution of $C_6H_{10}O$ (9.8 μL, 0.1 mmol) and t-BuOK (1.12 mg, 0.01 mmol) in 2-propanol was added the Ru complex (5 mol %). The reaction was periodically monitored by NMR spectroscopy at room temperature (at 70°C with $[Cp^*(phen)Ru(CH_3CN)]PF_6$). $C_6H_{11}OH$ was obtained as a corresponding product.

$C_6H_{11}OH$

^{1}H NMR ($CH_3CH(OH)CH_3$): δ 3.86 (m, br, 1, C*H*), 2.20 (m, br, 4, CH_2), 2.08 (m, br, 4, CH_2), 1.89 (m, br, 2, CH_2).

PhCH=NPh

To a solution of PhCH=NPh (18.3 mg, 0.1 mmol) and t-BuOK (1.12 mg, 0.01 mmol) in 2-propanol was added the Ru complex (5 mol %). The reaction was periodically monitored by NMR spectroscopy at room temperature (at 50°C with $[Cp^*(PPr^i_3)Ru(CH_3CN)_2]PF_6$ and $Cp(PPr^i_3)RuH_3$). $PhCH_2NHPh$ was obtained as a corresponding product.

Preparative scale reaction

To a solution of PhCH=NPh (183.3 mg, 1.0 mmol) and t-BuOK (11.2 mg, 0.1 mmol) in 2-propanol was added the Ru complex (2.5 mol %).

Purification

After the reaction was completed, the mixture was concentrated. Initially, the 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 eluent.

Then benzaldehyde was removed under vacuum to afford the product $PhCH_2NHPh$ as a yellow oil. (62 mg, 34% yield)

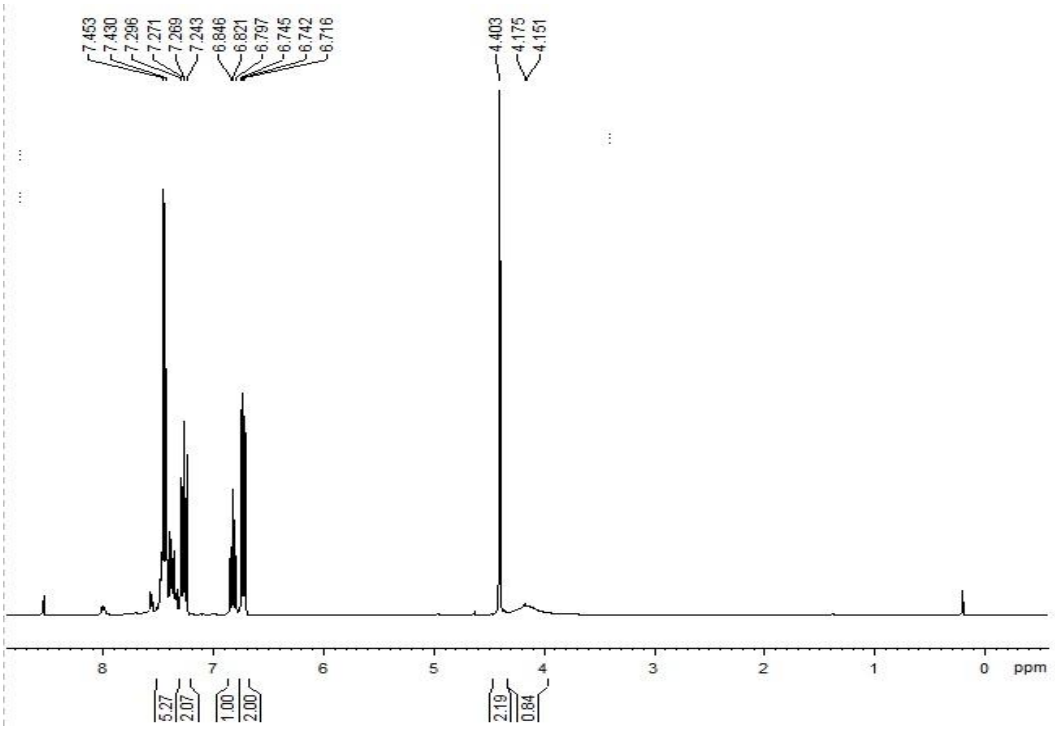
$PhCH_2NHPh$

^{1}H NMR ($CH_3CH(OH)CH_3$): δ 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 (d, J(H-H) = 5.82 Hz, 2, C*H*$_2$). ^{1}H-^{13}C HSQC ($CDCl_3$): δ 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 (Ph*C*H$_2$).

PhCHO

^{1}H NMR ($CDCl_3$): δ 10.09 (s, 1, PhC*H*O), 7.96 (m, 2, *Ph*), 7.69 (m, 1, *Ph*), 7.56 (m, 2, *Ph*). ^{1}H-^{13}C HSQC ($CDCl_3$): δ 192.3 (s, Ph*C*HO), 134.6 (s, *Ph*), 129.9 (s, *Ph*), 128.8 (s, *Ph*).

<^{1}H NMR spectrum of $PhCH_2NHPh$ in $CDCl_3$>



V.4.3. Transfer hydrogenation of nitriles

Benzonitrile

In a representative procedure, to a solution of PhCN (10.3 μL, 0.1 mmol) and t-BuOK (1.12 mg, 0.01 mmol) in 2-propanol was added the Ru complex (5 mol %). The reaction was periodically monitored by NMR spectroscopy at 70°C (at room temperature with $[Cp(PPr^{i}_{3})Ru(CH_3CN)_2]PF_6$). The imine, $PhCH_2N{=}C(CH_3)_2$, was obtained as a corresponding product. Also, the formation of $Cp(PPr^{i}_{3})RuH_3$ and $Cp(PPr^{i}_{3})_2RuH(CH_3CN)$ was observed in the ^1H NMR spectrum.

Preparative scale reaction

To a solution of PhCN (82.5 μL, 0.8 mmol) and t-BuOK (4.48 mg, 0.04 mmol) in 2-propanol was added the Ru complex (2.5 mol %). The reaction was periodically monitored by NMR spectroscopy at room temperature. The imine, $PhCH_2N{=}C(CH_3)_2$, was obtained as a corresponding product.

Purification

Attempted isolation of the product by chromatography over silica using 15:1 hexane : ethyl acetate as eluent and over alumina using ethyl acetate as eluent failed as it produced mixtures of undetectable compounds.

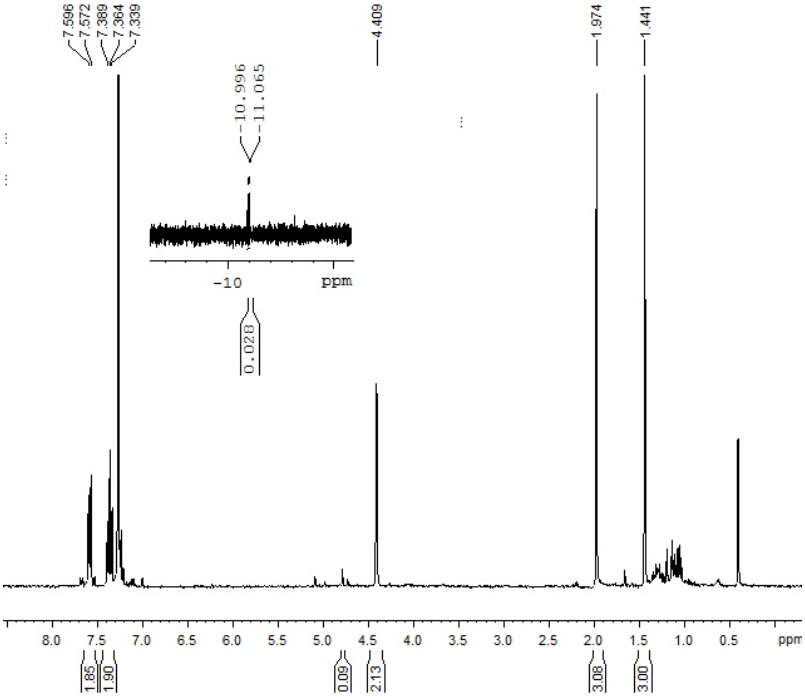
To isolate the imine product, the 2-propanol solution of the imine and Ru complex was filtered through celite. Based on ^1H NMR, the filtrate contains 2 mol % of Ru complex.

To the 2-propanol solution of $PhCH_2N{=}C(CH_3)_2$ (0.8 mmol) and the Ru complex, 1 M HCl (1.8 mL) was added. The mixture was stirred for 1 hour to hydrolyze the imine. After removing volatile, slightly pink solid was obtained. The solid was washed with hexane and CH_2Cl_2 respectively, and the solid was dried. The ammonium salt, $PhCH_2NH_3^+$ was obtained as a pale yellow solid. (81 mg, 71% yield)

PhCH$_2$N=C(CH$_3$)$_2$

^{1}H NMR (CH$_3$CH(OH)CH$_3$): δ 7.51 (m, 5, Ph), 4.80 (s, 2, C*H$_2$*), 2.42 (s, 3, C*H$_3$*), 2.27 (s, 3, C*H$_3$*). ^{1}H NMR (C$_6$D$_6$): δ 7.57 (d, J(H-H) = 6.89 Hz, 2, *Ph(o)*), 7.35 (t, J(H-H) = 7.16Hz, 2, *Ph(m)*), 7.24 (t, J(H-H) = 7.42Hz, 1, *Ph(p)*), 4.41 (s, 2, PhC*H$_2$*N), 1.97 (s, 3, NC(C*H$_3$*)$_2$), 1.44 (s, 3, NC(C*H$_3$*)$_2$). ^{1}H-^{13}C HSQC (C$_6$D$_6$): δ 166.0 (s, N*C*(CH$_3$)$_2$), 141.1 (s, *Ph*), 128.3 (s, *Ph(m)*), 127.9 (s, *Ph(o)*), 126.2 (s, *Ph(p)*), 55.1 (s, PhCH$_2$), 28.7 (s, NC(*C*H$_3$)$_2$), 17.6 (s, NC(*C*H$_3$)$_2$). IR (neat): υ (C=N) = 1666 cm^{-1}.

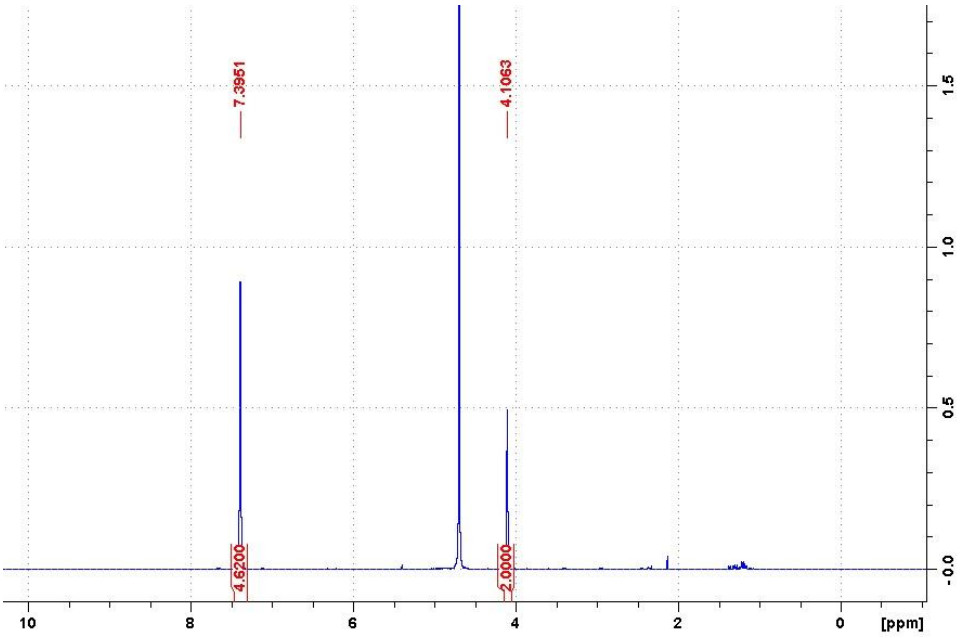
<^{1}H NMR spectrum of PhCH$_2$N=C(CH$_3$)$_2$ and 2 mol % Ru complex in C$_6$D$_6$>



PhCH$_2$NH$_3^+$Cl$^-$

^{1}H NMR (D$_2$O): δ 7.39 (m, 5, *Ph*), 4.10 (s, 2, PhC*H$_2$*). ^{1}H-^{13}C HSQC (D$_2$O): δ 129.4 (s, *Ph*), 43.3 (s, PhC*H$_2$*). IR (neat): υ (NH$_3$) = 3391 cm^{-1}.

<^{1}H NMR spectrum of $PhCH_2NH_3^+Cl^-$ in D_2O>



4-acetylbenzonitrile

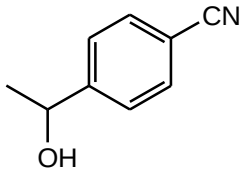
To a solution of 4-acetylbenzonitrile (14.5 mg, 0.1 mmol) and t-BuOK (1.12 mg, 0.01 mmol) in 2-propanol was added the Ru complex (5 mol %). The reaction was periodically monitored by NMR spectroscopy at room temperature. Initially, the reduction product of the ketone group, 4-(1-hydroxyethyl)benzonitrile, was produced in 30 m. The final reduction product, 1-(4-((propan-2-yildeneamino)methyl)-phenyl)ethanol, was produced in 18 hours.

Preparative scale reaction

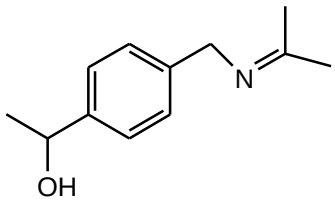
To a solution of 4-acetylbenzonitrile (145.2 mg, 1.0 mmol) and t-BuOK (5.6 mg, 0.05 mmol) in 2-propanol was added the Ru complex (2.5 mol %). The reaction was periodically monitored by NMR spectroscopy at room temperature. The imine was obtained as a corresponding product.

Purification

To the 2-propanol solution of 4-$CH_3CH(OH)C_6H_4CH_2N{=}C(CH_3)_2$ (1.0 mmol) and the Ru complex, 1 M HCl (2.0 mL) was added. The mixture was stirred for 1 hour to hydrolyze the imine. After removing volatile, a grey-brown powder was obtained. The solid was washed with CH_2Cl_2 three times and the solid was dried. The ammonium salt, 4-$CH_3CH(OH)C_6H_4CH_2NH_3^+$ was obtained as a brown solid. (118mg, 63% yield)



^{1}H NMR ($CH_3CH(OH)CH_3$): δ 7.89 (dd, J(H-H) = 8.16 and 20.18 Hz, 2, 4-$CH_3CH(OH)C_6H_4$), 7.58 (dd, J(H-H) = 8.16 and 17.82 Hz, 2, 4-$CH_3CH(OH)C_6H_4$), 5.13 (dq, J(H-H) = 6.51 and 22.31 Hz, 1, 4-$CH_3CH(OH)C_6H_4$), 4.10 (s, br, 1, 4-$CH_3CH(OH)C_6H_4$), 1.75 (dd, J(H-H) = 3.23 and 6.46 Hz, 3, 4-$CH_3CH(OH)C_6H_4$).



^{1}H NMR ($CH_3CH(OH)CH_3$): δ 7.62 (d, J(H-H) = 8.01 Hz, 2, 4-$CH_3CH(OH)C_6H_4$), 7.49 (d, J(H-H) = 8.01 Hz, 2, 4-$CH_3CH(OH)C_6H_4$), 5.11 (q, 1, 4-$CH_3CH(OH)C_6H_4$), 4.79 (s, 2, $C_6H_4CH_2N{=}C(CH_3)_2$), 2.41 (s, 3, $C_6H_4CH_2N{=}C(CH_3)_2$), 2.27 (s, 3, $C_6H_4CH_2N{=}C(CH_3)_2$), 1.73 (d, J(H-H) = 6.45 Hz, 3, 4-$CH_3CH(OH)C_6H_4$). ^{1}H-^{13}C HSQC ($CH_3CH(OH)CH_3$): δ 127.7 (s, 4-$CH_3CH(OH)C_6H_4$), 125.4 (s, 4-$CH_3CH(OH)C_6H_4$), 69.1 (s, 4-$CH_3CH(OH)C_6H_4$), 54.6 (s, $C_6H_4CH_2N{=}C(CH_3)_2$), 28.2 (s, $C_6H_4CH_2N{=}C(CH_3)_2$), 25.7 (s, 4-$CH_3CH(OH)C_6H_4$), 19.1 (s, $C_6H_4CH_2N{=}C(CH_3)_2$). IR (neat): υ (C=N) = 1662 cm^{-1}.

4-$CH_3CH(OH)C_6H_4CH_2NH_3^+Cl^-$

^{1}H NMR (D_2O): δ 7.35 (s, br, 2, 4-$CH_3CH(OH)C_6H_4$), 4.79 (q, 1, 4-$CH_3CH(OH)C_6H_4$), 4.07 (s, 2, $C_6H_4CH_2$), 1.35 (d, J(H-H) = 6.44 Hz, 3, 4-$CH_3CH(OH)C_6H_4$). ^{1}H-^{13}C HSQC (D_2O): δ 129.1, 126.1 (s, 4-$CH_3CH(OH)C_6H_4$), 68.8 (s, 4-$CH_3CH(OH)C_6H_4$), 42.7 (s, $C_6H_4CH_2$), 23.4 (s, 4-$CH_3CH(OH)C_6H_4$). IR (neat): υ (NH_3) = 3342 cm^{-1}, υ (OH) = 3245 cm^{-1}.

4-methoxybenzonitrile

To a solution of 4-methoxybenzonitrile (13.3 mg, 0.1 mmol) and t-BuOK (1.12 mg, 0.01 mmol) in 2-propanol was added the Ru complex (5 mol %). The reaction was periodically monitored by NMR spectroscopy at room temperature. The imine, 4-$CH_3OC_6H_4CH_2N=C(CH_3)_2$, was obtained as a corresponding product.

Preparative scale reaction

To a solution of 4-methoxybenzonitrile (133.2 mg, 1.0 mmol) and t-BuOK (5.6 mg, 0.05 mmol) in 2-propanol was added the Ru complex (2.5 mol %). The reaction was periodically monitored by NMR spectroscopy at room temperature. The imine, 4-$CH_3OC_6H_4CH_2N=C(CH_3)_2$, was obtained as a corresponding product.

Purification

To the 2-propanol solution of 4-$CH_3OC_6H_4CH_2N=C(CH_3)_2$ (1.0 mmol) and the Ru complex, 1 M HCl (2.0 mL) was added. The mixture was stirred for 1 hour to hydrolyze the imine. After removing volatile, a yellow solid was obtained. The solid was washed with CH_2Cl_2 three times and the solid was dried. The ammonium salt, 4-$CH_3OC_6H_4CH_2NH_3^+$ was obtained as a beige solid. (122 mg, 65% yield)

4-$CH_3OC_6H_4CH_2N=C(CH_3)_2$

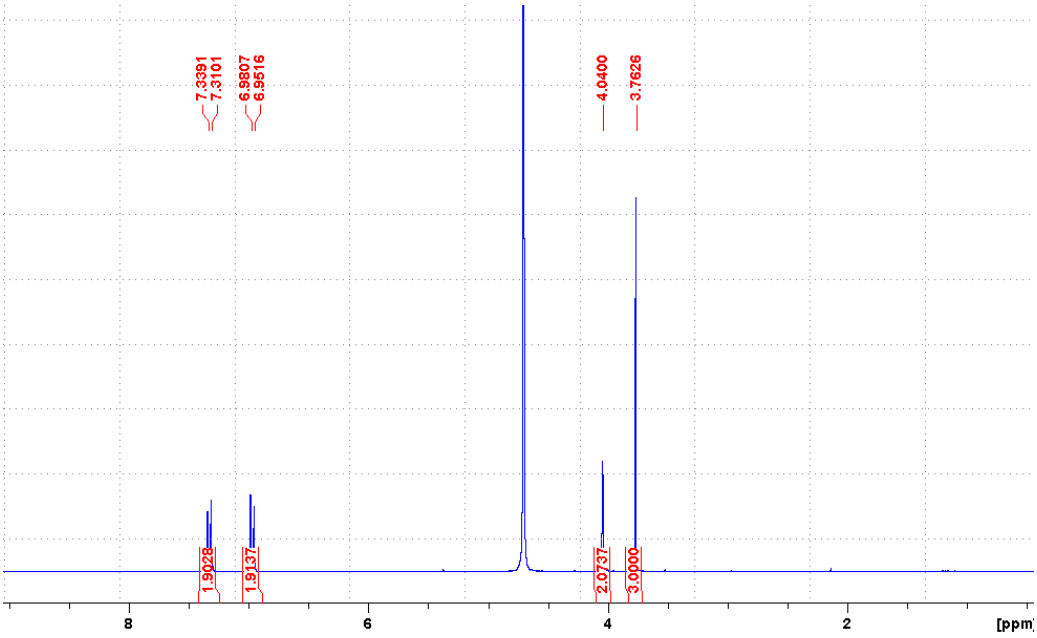
^{1}H NMR ($CH_3CH(OH)CH_3$): δ 7.49 (d, J(H-H) = 8.54 Hz, 2, 4-$CH_3OC_6H_4$), 7.14 (d, J(H-H) = 8.54 Hz, 2, 4-$CH_3OC_6H_4$), 4.73 (s, br, 2, 4-$CH_3OC_6H_4CH_2N$), 4.07 (s, 3, 4-

C*H*$_3$OC$_6$H$_4$), 2.40 (s, 3, CH$_2$N=C(C*H*$_3$)$_2$), 2.27 (s, 3, CH$_2$N=C(C*H*$_3$)$_2$). ^{1}H-^{13}C HSQC (CH$_3$CH(OH)CH$_3$): δ 129.2 (s, 4-CH$_3$O*C*$_6$H$_4$), 113.8 (s, 4-CH$_3$O*C*$_6$H$_4$), 54.8 (s, 4-*C*H$_3$OC$_6$H$_4$), 54.2 (s, *C*H$_2$N=C(CH$_3$)$_2$), 28.4 (s, CH$_2$N=C(*C*H$_3$)$_2$), 18.9 (s, CH$_2$N=C(*C*H$_3$)$_2$).

4-CH$_3$OC$_6$H$_4$CH$_2$NH$_3^+$Cl$^-$

^{1}H NMR (D$_2$O): δ 7.31 (d, J(H-H) = 8.57 Hz, 2, 4-CH$_3$OC$_6$*H*$_4$), 6.95 (d, J(H-H) = 8.57 Hz, 2, 4-CH$_3$OC$_6$*H*$_4$), 4.04 (s, 2, C$_6$H$_4$C*H*$_2$), 3.76 (s, 3, 4-C*H*$_3$OC$_6$H$_4$). ^{1}H-^{13}C HSQC (D$_2$O): δ 130.6 (s, 4-CH$_3$O*C*$_6$H$_4$), 114.4 (s, 4-CH$_3$O*C*$_6$H$_4$), 55.1 (s, 4-*C*H$_3$OC$_6$H$_4$), 42.7 (s, C$_6$H$_4$*C*H$_2$). IR (neat): υ (NH$_3$) = 3418 cm^{-1}.

<^{1}H NMR spectrum of 4-CH$_3$OC$_6$H$_4$CH$_2$NH$_3^+$Cl$^-$ in D$_2$O>



4-aminobenzonitrile

To a solution of 4-aminobenzonitrile (11.8 mg, 0.1 mmol) and t-BuOK (1.12 mg, 0.01 mmol) in 2-propanol was added the Ru complex (5 mol %). The reaction was periodically monitored by NMR spectroscopy at room temperature. The imine, 4-NH$_2$C$_6$H$_4$CH$_2$N=C(CH$_3$)$_2$, was obtained as a corresponding product.

Preparative scale reaction

To a solution of 4-aminobenzonitrile (118.1 mg, 1.0 mmol) and t-BuOK (5.6 mg, 0.05 mmol) in 2-propanol was added the Ru complex (2.5 mol %). The reaction was periodically monitored by NMR spectroscopy at room temperature. The imine, 4-$H_2NC_6H_4CH_2N=C(CH_3)_2$, was obtained as a corresponding product.

Purification

To the 2-propanol solution of 4-$H_2NC_6H_4CH_2N=C(CH_3)_2$ (1.0 mmol) and the Ru complex, 1 M HCl (2.0 mL) was added. The mixture was stirred for 1 hour to hydrolyze the imine. After removing volatile, a yellow solid was obtained. The solid was washed with CH_2Cl_2 three times and the solid was dried. The ammonium salt, 4-$H_2NC_6H_4CH_2NH_3^+$ was obtained as a yellow solid. (144 mg, 91% yield)

4-$NH_2C_6H_4CH_2N=C(CH_3)_2$

^{1}H NMR ($CH_3CH(OH)CH_3$): δ 7.25 (d, J(H-H) = 8.24 Hz, 2, 4-$NH_2C_6H_4$), 6.96 (d, J(H-H) = 8.40 Hz, 2, 4-$NH_2C_6H_4$), 4.77 (s, br, 2, 4-$NH_2C_6H_4$), 4.66 (s, 2, 4-$NH_2C_6H_4CH_2N$), 2.38 (s, 3, $CH_2N=C(CH_3)_2$), 2.24 (s, 3, $CH_2N=C(CH_3)_2$). ^{1}H-^{13}C HSQC ($CH_3CH(OH)CH_3$): δ 128.8 (s, 4-$NH_2C_6H_4$), 115.2 (s, 4-$NH_2C_6H_4$), 54.4 (s, $CH_2N=C(CH_3)_2$), 28.3 (s, $CH_2N=C(CH_3)_2$), 24.8 (s, $CH_2N=C(CH_3)_2$).

4-$NH_2C_6H_4CH_2NH_3^+Cl^-$

^{1}H NMR (D_2O): δ 7.50 (d, J(H-H) = 8.66 Hz, 2, 4-$NH_2C_6H_4$), 7.37 (d, J(H-H) = 8.66 Hz, 2, 4-$NH_2C_6H_4$), 4.15 (s, 2, $C_6H_4CH_2$). ^{1}H-^{13}C HSQC (D_2O): δ 130.8 (s, 4-$NH_2C_6H_4$), 123.3 (s, 4-$NH_2C_6H_4$), 42.3 (s, $C_6H_4CH_2$).

Ethyl-4-cyanobenzoate

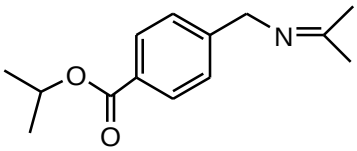
To a solution of 4-aminobenzonitrile (17.5 mg, 0.1 mmol) and t-BuOK (1.12 mg, 0.01 mmol) in 2-propanol was added the Ru complex (5 mol %). The reaction was periodically monitored by NMR spectroscopy at room temperature. The imine was obtained as a corresponding product.

Preparative scale reaction

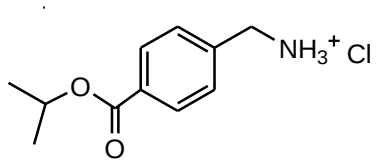
To a solution of ethyl 4-cyanobenzoate (175.2 mg, 1.0 mmol) and t-BuOK (5.6 mg, 0.05 mmol) in 2-propanol was added the Ru complex (2.5 mol %). The reaction was periodically monitored by NMR spectroscopy at room temperature. The imine was obtained as a corresponding product.

Purification

To the 2-propanol solution of the corresponding imine (1.0 mmol) and the Ru complex, 1 M HCl (2.0 mL) was added. The mixture was stirred for 1 hour to hydrolyze the imine. After removing volatile, a pale beige solid was obtained. The solid was washed with CH_2Cl_2 three times and the solid was dried. The ammonium salt was obtained as a pale beige solid. (143 mg, 62% yield)



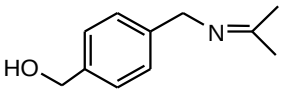
^{1}H NMR (C_6D_6): δ 8.38 (d, J(H-H) = 8.36 Hz, 2, $(CH_3)_2CHOOCC_6H_4$), 7.53 (d, J(H-H) = 7.72 Hz, 2, $(CH_3)_2CHOOCC_6H_4$), 5.29 (m, 1, $(CH_3)_2CHOOCC_6H_4$), 4.27 (s, 2, $CH_2N=C(CH_3)_2$), 1.95 (s, 3, $CH_2N=C(CH_3)_2$), 1.39 (s, 3, $CH_2N=C(CH_3)_2$), 1.21 (d, J(H-H) = 6.34 Hz, 6, $(CH_3)_2CHOOCC_6H_4$). ^{1}H-^{13}C HSQC (C_6D_6): δ 129.8 (s, $(CH_3)_2CHOOCC_6H_4$), 127.6 (s, $(CH_3)_2CHOOCC_6H_4$), 67.5 (s, $(CH_3)_2CHOOCC_6H_4$), 54.5 (s, $CH_2N=C(CH_3)_2$), 28.9 (s, $CH_2N=C(CH_3)_2$), 21.7 (s, $(CH_3)_2CHOOCC_6H_4$). IR (neat): υ (C=N) = 1667 cm^{-1}, υ (C=O) = 1720 cm^{-1}.



^{1}H NMR (D_2O): δ 7.97 (d, J(H-H) = 8.03 Hz, 2, $(CH_3)_2CHOOCC_6H_4$), 7.45 (d, J(H-H) = 8.38 Hz, 2, $(CH_3)_2CHOOCC_6H_4$), 5.05 (m, 1, $(CH_3)_2CHOOCC_6H_4$), 4.17 (s, 2, $C_6H_4CH_2$), 1.27 (d, J(H-H) = 6.33 Hz, 6, $(CH_3)_2CHOOCC_6H_4$). ^{1}H-^{13}C HSQC (D_2O): δ 130.4 (s, $(CH_3)_2CHOOCC_6H_4$), 129.0 (s, $(CH_3)_2CHOOCC_6H_4$), 69.6 (s, $(CH_3)_2CHOOCC_6H_4$), 42.7 (s, $C_6H_4CH_2$), 21.0 (s, $(CH_3)_2CHOOCC_6H_4$). IR (neat): υ (C=O) = 1713 cm^{-1}, υ (NH_3) = 3308 cm^{-1}.

4-Cyanobenzaldehyde

To a solution of 4-aminobenzonitrile (13.1 mg, 0.1 mmol) and t-BuOK (1.12 mg, 0.01 mmol) in 2-propanol was added the Ru complex (5 mol %). The reaction was periodically monitored by NMR spectroscopy at room temperature. The imine, 4-$HOCH_2C_6H_4CH_2N=C(CH_3)_2$, was obtained as a corresponding product.



^{1}H NMR ($CH_3CH(OH)CH_3$): δ 7.60 (d, J(H-H) = 8.08 Hz, 2, $HOCH_2C_6H_4$), 7.50 (d, J(H-H) = 7.85 Hz, 2, $HOCH_2C_6H_4$), 4.92 (s, 2, $HOCH_2C_6H_4$), 4.80 (s, 2, $C_6H_4CH_2N=C(CH_3)_2$), 2.42 (s, 3, $N=C(CH_3)_2$), 2.26 (s, 3, $N=C(CH_3)_2$). ^{1}H-^{13}C HSQC ($CH_3CH(OH)CH_3$): δ 127.7 (s, $HOCH_2C_6H_4$), 127.0 (s, $HOCH_2C_6H_4$), 63.4 (s, $HOCH_2C_6H_4$), 54.6 (s, $C_6H_4CH_2N=C(CH_3)_2$), 28.3 (s, $N=C(CH_3)_2$), 18.6 (s, $N=C(CH_3)_2$). IR (neat): υ (C=N) = 1664 cm^{-1}, υ (OH) = 3410 cm^{-1}.

***N*-(4-cyanophenyl)propionamide**

To a solution of *N*-(4-cyanophenyl)propionamide (17.4 mg, 0.1 mmol) and t-BuOK (1.12 mg, 0.01 mmol) in 2-propanol was added the Ru complex (5 mol %). The

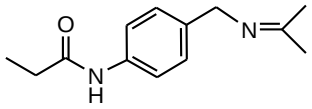
reaction was periodically monitored by NMR spectroscopy at room temperature. The corresponding imine was obtained as a corresponding product.

Preparative scale reaction

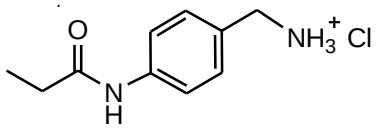
To a solution of *N*-(4-cyanophenyl)propionamide (174.1 mg, 1.0 mmol) and t-BuOK (5.6 mg, 0.05 mmol) in 2-propanol was added the Ru complex (2.5 mol %). The reaction was periodically monitored by NMR spectroscopy at room temperature. The imine was obtained as a corresponding product.

Purification

To the 2-propanol solution of the corresponding imine (1.0 mmol) and the Ru complex, 1 M HCl (2.0 mL) was added. The mixture was stirred for 1 hour to hydrolyze the imine. After removing volatile, a yellow solid was obtained. The solid was washed with CH_2Cl_2 three times and the solid was dried. The ammonium salt was obtained as a yellow solid. (195 mg, 91% yield)



^{1}H NMR (C_6D_6): δ 7.75 (m, 2, $C_6H_4CH_2N=C(CH_3)_2$), 7.47 (d, J(H-H) = 8.54 Hz, 2, $C_6H_4CH_2N=C(CH_3)_2$), 4.34 (s, 1, $C_6H_4CH_2N=C(CH_3)_2$), 5.36 (s, br, 1, CH_3CH_2CONH), 1.98 (q, 2, CH_3CH_2CONH), 1.94 (s, 3, $C_6H_4CH_2N=C(CH_3)_2$), 1.44 (s, 3, $C_6H_4CH_2N=C(CH_3)_2$), 1.15 (t, 3, CH_3CH_2CONH). ^{1}H-^{13}C HSQC (C_6D_6): δ 128.4 (s, $C_6H_4CH_2N=C(CH_3)_2$), 119.7 (s, $C_6H_4CH_2N=C(CH_3)_2$), 54.4 (s, $C_6H_4CH_2N=C(CH_3)_2$), 30.2 (s, CH_3CH_2CONH), 29.1 (s, $C_6H_4CH_2N=C(CH_3)_2$), 17.4 (s, $C_6H_4CH_2N=C(CH_3)_2$), 9.4 (s, CH_3CH_2CONH). IR (neat): υ (C=O) = 1662 cm^{-1}, υ (N-H) = 3242 cm^{-1}.



^{1}H NMR (D_2O): δ 7.39 (d, J(H-H) = 8.84 Hz, 2, 4-$CH_3CH_2CONHC_6H_4$), 7.34 (d, J(H-H) = 8.55 Hz, 2, 4-$CH_3CH_2CONHC_6H_4$), 4.07 (s, 2, $C_6H_4CH_2$), 2.31 (q, 2, 4-$CH_3CH_2CONHC_6H_4$), 1.07 (q, 2, 4-$CH_3CH_2CONHC_6H_4$). ^{1}H-^{13}C HSQC (D_2O): δ 129.9 (s, 4-$CH_3CH_2CONHC_6H_4$), 123.1 (s, 4-$CH_3CH_2CONHC_6H_4$), 42.7 (s, $C_6H_4CH_2$), 28.7 (s, 4-$CH_3CH_2CONHC_6H_4$), 9.2 (s, 4-$CH_3CH_2CONHC_6H_4$). IR (neat): υ (N-H) = 1416, 1595 cm^{-1}, υ (C=O) = 1665 cm^{-1}, υ (NH_3) = 3319 cm^{-1}.

Nicotinonitrile

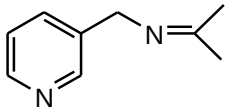
To a solution of nicotinonitrile (10.4 μL, 0.1 mmol) and t-BuOK (1.12 mg, 0.01 mmol) in 2-propanol was added the Ru complex (5 mol %). The reaction was periodically monitored by NMR spectroscopy at 70°C. The corresponding imine was obtained as a corresponding product.

Preparative scale reaction

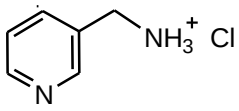
To a solution of nicotinonitrile (104.1 mg, 1.0 mmol) and t-BuOK (5.6 mg, 0.05 mmol) in 2-propanol was added the Ru complex (2.5 mol %). The reaction was periodically monitored by NMR spectroscopy at room temperature. The imine was obtained as a corresponding product.

Purification

To the 2-propanol solution of the corresponding imine (1.0 mmol) and the Ru complex, 1 M HCl (2.0 mL) was added. The mixture was stirred for 1 hour to hydrolyze the imine. After removing volatile, a brown solid was obtained. The solid was washed with CH_2Cl_2 three times and the solid was dried. The ammonium salt was obtained as a brown solid. (114 mg, 79% yield)



^{1}H NMR ($CH_3CH(OH)CH_3$): δ 8.83 (dd, J(H-H) = 1.41 and 7.52 Hz, 1, $C_5H_4NCH_2N$), 8.73 (td, J(H-H) = 1.04 and 4.85 Hz, 1, $C_5H_4NCH_2N$), 8.09 (m, 1, $C_5H_4NCH_2N$), 7.67 (dt, J(H-H) = 5.23 and 7.85 Hz, 1, $C_5H_4NCH_2N$), 4.85 (s, 2, $CH_2N=C(CH_3)_2$), 2.44 (s, 3, $CH_2N=C(CH_3)_2$), 2.34 (s, 3, $CH_2N=C(CH_3)_2$). ^{1}H-^{13}C HSQC ($CH_3CH(OH)CH_3$): δ 148.4 (s, $C_5H_4NCH_2N$), 147.2 (s, $C_5H_4NCH_2N$), 137.0 (s, $C_5H_4NCH_2N$), 124.0 (s, $C_5H_4NCH_2N$), 52.4 (s, $CH_2N=C(CH_3)_2$), 28.4 (s, $CH_2N=C(CH_3)_2$), 19.1 (s, $CH_2N=C(CH_3)_2$). IR (neat): υ (C=N) = 1670 cm^{-1}.



^{1}H NMR (D_2O): δ 8.86 (s, 1, $C_5H_4NCH_2$), 8.78 (d, J(H-H) = 5.02 Hz, 1, $C_5H_4NCH_2$), 8.62 (d, J(H-H) = 8.03 Hz, 1, $C_5H_4NCH_2$), 8.07 (dd, J(H-H) = 5.07 and 7.98 Hz, 1, $C_5H_4NCH_2$), 4.40 (s, 1, $C_5H_4NCH_2$). ^{1}H-^{13}C HSQC (D_2O): δ 146.8 (s, $C_5H_4NCH_2$), 142.1 (s, $C_5H_4NCH_2$), 141.5 (s, $C_5H_4NCH_2$), 127.7 (s, $C_5H_4NCH_2$), 39.4 (s, $C_5H_4NCH_2$). IR (neat): υ (NH_3) = 3380 cm^{-1}.

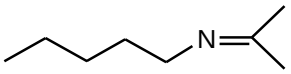
Valeronitrile

To a solution of valeronitrile (8.3 μL, 0.1 mmol) and t-BuOK (1.12 mg, 0.01 mmol) in 2-propanol was added the Ru complex (5 mol %). The reaction was periodically monitored by NMR spectroscopy at room temperature. The corresponding imine was obtained as a corresponding product. Decomposition products were observed by NMR after removing volatile under vacuum.

Preparative scale reaction

To a solution of valeronitrile (83.1 μL, 1.0 mmol) and t-BuOK (5.6 mg, 0.05 mmol) in 2-propanol was added the Ru complex (2.5 mol %). The reaction was periodically

monitored by NMR spectroscopy at room temperature. The imine was obtained as a corresponding product.

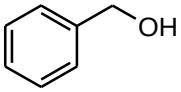


^{1}H NMR ($CH_3CH(OH)CH_3$): δ 3.56 (t, J(H-H) = 7.40 Hz, 2, $CH_3(CH_2)_3CH_2$), 2.36 (s, 3, $CH_2N=C(CH_3)_2$), 2.21 (s, 3, $CH_2N=C(CH_3)_2$), 1.91 (m, 2, $CH_3(CH_2)_2CH_2CH_2$), 1.62 (m, 4, $CH_3(CH_2)_2CH_2CH_2$ (overlap)), 1.25 (t, J(H-H) = 6.94 Hz, 3, $CH_3(CH_2)_3CH_2$). ^{1}H-^{13}C HSQC ($CH_3CH(OH)CH_3$): δ 51.2 (s, $CH_3(CH_2)_3CH_2$), 30.4 (s, $CH_3(CH_2)_2CH_2CH_2$), 29.7 (s, $CH_3(CH_2)_2CH_2CH_2$ (overlap)), 28.1 (s, $CH_2N=C(CH_3)_2$), 18.1 (s, $CH_2N=C(CH_3)_2$), 13.9 (s, $CH_3(CH_2)_3CH_2$).

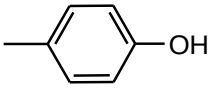
V.4.4. Transfer hydrogenation of esters

4-Methylphenyl benzoate

In a representative procedure, to a solution of 4-methylphenyl benzoate (21.0 mg, 0.1 mmol) and t-BuOK (1.12 mg, 0.01 mmol) in 2-propanol was added the Ru complex (5 mol %). The reaction was periodically monitored by NMR spectroscopy at room temperature. The product was obtained as a corresponding product.



^{1}H NMR ($CH_3CH(OH)CH_3$): δ 7.62 (d, J(H-H) = 7.21 Hz, 2, $PhCH_2OH$), 7.56 (t, J(H-H) = 7.59 Hz, 2, $PhCH_2OH$), 7.48 (t, J(H-H) = 7.40 Hz, 1, $PhCH_2OH$, overlap), 4.91 (s, 2, $PhCH_2OH$). ^{1}H-^{13}C HSQC ($CH_3CH(OH)CH_3$): δ 128.0 (s, $PhCH_2OH$), 127.0 (s, $PhCH_2OH$), 126.6 (s, $PhCH_2OH$), 64.3 (s, $PhCH_2OH$).



^{1}H NMR ($CH_3CH(OH)CH_3$): δ 7.20 (d, J(H-H) = 8.30 Hz, 2, $CH_3C_6H_4OH$), 7.03 (d, J(H-H) = 8.30 Hz, 2, $CH_3C_6H_4OH$), 2.52 (s, 3, $CH_3C_6H_4OH$). ^{1}H-^{13}C HSQC ($CH_3CH(OH)CH_3$): δ 129.9 (s, $CH_3C_6H_4OH$), 115.9 (s, $CH_3C_6H_4OH$), 20.9 (s, $CH_3C_6H_4OH$).

Phenyl 4-methoxybenzoate

Synthesis of Phenyl 4-methoxybenzoate

To a solution of phenol (0.47 g, 5 mmol) and Et_3N (1.01 mL, 10 mmol) in CH_2Cl_2 was added to 4-methoxybenzoyl chloride (1.02 g, 6 mmol). The mixture was stirred for overnight and the solvent was removed under vacuum. Then the solid was extracted with Et_2O. Phenyl 4-methoxybenzoate was obtained as a white powder (1.01g, 89%).

^{1}H NMR (CH_2Cl_2): δ 7.97 (d, J(H-H) = 8.47 Hz, 2, 4-$CH_3OC_6H_4COO$), 7.26 (t, 2, PhCOO*Ph*), 7.10 (t, 1, PhCOO*Ph*), 7.03 (d, J(H-H) = 7.47 Hz, 2, PhCOO*Ph*), 6.84 (d, J(H-H) = 8.96 Hz, 2, 4-$CH_3OC_6H_4COO$), 3.73 (s, 3, 4-$CH_3OC_6H_4COO$).

To a solution of phenyl 4-methoxybenzoate (23.1 mg, 0.1 mmol) and t-BuOK (1.12 mg, 0.01 mmol) in 2-propanol was added the Ru complex (5 mol %). The reaction was periodically monitored by NMR spectroscopy at 70°C.

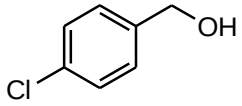
Phenyl 4-chlorobenzoate

Synthesis of Phenyl 4-chlorobenzoate

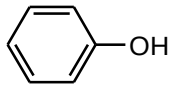
To a solution of phenol (0.47 g, 5 mmol) and Et_3N (1.01 mL, 10 mmol) in CH_2Cl_2 was added to 4-chlorobenzoyl chloride (1.05 mL, 6 mmol). The mixture was stirred for overnight and the solvent was removed under vacuum. Then the solid was extracted with Et_2O. Phenyl 4-chlorobenzoate was obtained as a yellow powder (1.00g, 86%).

^{1}H NMR (CH_2Cl_2): δ 7.94 (d, J(H-H) = 8.13 Hz, 2, 4-ClC_6*H*$_4$COO), 7.32 (d, J(H-H) = 8.51 Hz, 2, 4-ClC_6*H*$_4$COO), 7.24 (t, 2, PhCOO*Ph*), 7.09 (t, 2, PhCOO*Ph*), 7.02 (d, J(H-H) = 7.81 Hz, 2, PhCOO*Ph*).

To a solution of phenyl 4-chlorobenzoate (23.3 mg, 0.1 mmol) and t-BuOK (1.12 mg, 0.01 mmol) in 2-propanol was added the Ru complex (5 mol %). The reaction was periodically monitored by NMR spectroscopy at 70°C. The corresponding acetal derivative was obtained as a corresponding product.



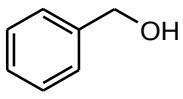
^{1}H NMR ($CH_3CH(OH)CH_3$): δ 7.64 (m, 4, 4-ClC_6*H*$_4$C*H*$_2$OH, overlap), 4.90 (s, 2, 4-ClC_6H$_4$C*H*$_2$OH).



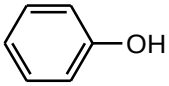
^{1}H NMR ($CH_3CH(OH)CH_3$): δ 7.41 (t, J(H-H) = 7.34 Hz, 2, *Ph*OH), 7.13 (d, J(H-H) = 7.68 Hz, 2, *Ph*OH), 7.05 (t, J(H-H) = 7.34 Hz, 1, *Ph*OH).

Phenyl benzoate

To a solution of phenyl benzoate (19.8 mg, 0.1 mmol) and t-BuOK (1.12 mg, 0.01 mmol) in 2-propanol was added the Ru complex (5 mol %). The reaction was periodically monitored by NMR spectroscopy at 70°C. The corresponding acetal derivative was obtained as a corresponding product.



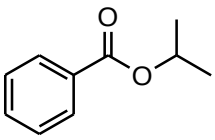
^{1}H NMR ($CH_3CH(OH)CH_3$): δ 7.62 (d, J(H-H) = 7.28 Hz, 2, *Ph*CH_2OH), 7.57 (t, J(H-H) = 7.28 Hz, 2, *Ph*CH_2OH), 4.92 (s, 2, PhC*H*$_2$OH). ^{1}H-^{13}C HSQC ($CH_3CH(OH)CH_3$): δ 128.0 (s, *Ph*CH_2OH), 126.8 (s, *Ph*CH_2OH), 126.6 (s, *Ph*CH_2OH), 63.9 (s, Ph*C*H_2OH).



^{1}H NMR ($CH_3CH(OH)CH_3$): δ 7.40 (t, J(H-H) = 7.97 Hz, 2, *Ph*OH), 7.12 (d, J(H-H) = 7.69 Hz, 2, *Ph*OH), 7.04 (t, J(H-H) = 7.14 Hz, 1, *Ph*OH). ^{1}H-^{13}C HSQC ($CH_3CH(OH)CH_3$): δ 129.3 (s, *Ph*OH), 119.1 (s, *Ph*OH), 115.7 (s, *Ph*OH).

Ethyl benzoate

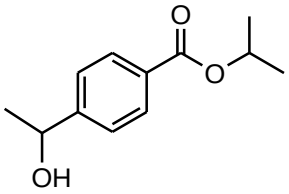
To a solution of ethylbenzoate (15.0 μL, 0.1 mmol) and t-BuOK (1.12 mg, 0.01 mmol) in 2-propanol was added the Ru complex (5 mol %). The reaction was periodically monitored by NMR spectroscopy at 70°C. The transesterification product was obtained as a corresponding product.



^{1}H NMR ($CH_3CH(OH)CH_3$): δ 8.31 (d, J(H-H) = 7.16 Hz, 2, *Ph*C(O)OCH$(CH_3)_2$), 7.85 (t, 1, *Ph*C(O)OCH$(CH_3)_2$), 7.73 (t, 2, *Ph*C(O)OCH$(CH_3)_2$), 5.50 (m, 1, PhC(O)OC*H*$(CH_3)_2$), 1.68 (d, J(H-H) = 6.35 Hz, 6, PhC(O)OCH(C*H*$_3)_2$). ^{1}H-^{13}C HSQC ($CH_3CH(OH)CH_3$): δ 132.6 (s, *Ph*C(O)OCH$(CH_3)_2$), 130.1 (s, *Ph*C(O)OCH$(CH_3)_2$), 128.5 (s, *Ph*C(O)OCH$(CH_3)_2$), 68.0 (s, PhC(O)O*C*H$(CH_3)_2$), 22.3 (s, PhC(O)OCH(*C*H$_3)_2$).

Ethyl 4-acetylbenzoate

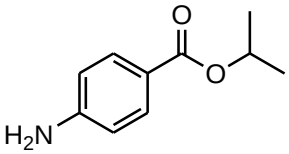
To a solution of ethylbenzoate (10.1 mg, 0.05 mmol) and t-BuOK (0.56 mg, 0.005 mmol) in 2-propanol was added the Ru complex (5 mol %). The reaction was periodically monitored by NMR spectroscopy at room temperature. The transesterification product was obtained as a corresponding product.



^{1}H NMR ($CH_3CH(OH)CH_3$): δ 8.27 (d, J(H-H) = 8.21 Hz, 2, 4-$CH_3CH(OH)C_6H_4$), 7.77 (d, J(H-H) = 8.54 Hz, 2, 4-$CH_3CH(OH)C_6H_4$), 5.50 (m, 1, $C_6H_4C(O)OCH(CH_3)_2$), 5.20 (q, 1, 4-$CH_3CH(OH)C_6H_4$), 1.76 (d, J(H-H) = 6.49 Hz, 3, 4-$CH_3CH(OH)C_6H_4$), 1.69 (d, J(H-H) = 6.35 Hz, 6, $C_6H_4C(O)OCH(CH_3)_2$). ^{1}H-^{13}C HSQC ($CH_3CH(OH)CH_3$): δ 130.6 (s, 4-$CH_3CH(OH)C_6H_4$), 125.3 (s, 4-$CH_3CH(OH)C_6H_4$), 69.4 (s, $C_6H_4C(O)OCH(CH_3)_2$), 67.9 (s, 4-$CH_3CH(OH)C_6H_4$), 24.4 (s, 4-$CH_3CH(OH)C_6H_4$), 21.6 (s, $C_6H_4C(O)OCH(CH_3)_2$). IR (neat): υ (CH_3) = 1276 cm^{-1}, υ (CH_2) = 1455 cm^{-1}, υ (CH) = 2925 cm^{-1}, υ (OH) = 3415 cm^{-1}, υ (C=O) = 1714 cm^{-1}.

Ethyl 4-aminobenzoate

To a solution of ethyl 4-aminobenzoate (16.5 mg, 0.05 mmol) and t-BuOK (0.56 mg, 0.005 mmol) in 2-propanol was added the Ru complex (5 mol %). The reaction was periodically monitored by NMR spectroscopy at 70°C. The transesterification product was obtained as a corresponding product.



^{1}H NMR (C_6D_6): δ 8.21 (d, J(H-H) = 8.63 Hz, 1, 4-$H_2NC_6H_4C(O)OCH(CH_3)_2$), 6.24 (d, J(H-H) = 8.78 Hz, 1, 4-$H_2NC_6H_4C(O)OCH(CH_3)_2$), 5.32 (m, 1, 4-$H_2NC_6H_4C(O)OCH(CH_3)_2$), 3.11 (s, br, 2, 4-$H_2NC_6H_4C(O)OCH(CH_3)_2$), 1.24 (d, J(H-H) = 6.36 Hz, 6, 4-$H_2NC_6H_4C(O)OCH(CH_3)_2$). ^{1}H-^{13}C HSQC ($C_6D_6$): δ 165.9 (s, 4-$H_2NC_6H_4C(O)OCH(CH_3)_2$), 151.0 (s, 4-$H_2NC_6H_4C(O)OCH(CH_3)_2$), 132.1 (s, 4-

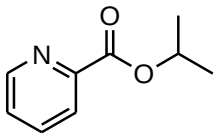
$H_2NC_6H_4C(O)OCH(CH_3)_2$), 120.2 (s, 4-$H_2NC_6H_4C(O)OCH(CH_3)_2$), 113.8 (s, 4-$H_2NC_6H_4C(O)OCH(CH_3)_2$), 67.6 (s, 4-$H_2NC_6H_4C(O)OCH(CH_3)_2$), 22.1 (s, 4-$H_2NC_6H_4C(O)OCH(CH_3)_2$). IR (neat): υ ($NH_2$) = 3426 cm^{-1}, υ (NH_2) = 3357 cm^{-1}, υ (C=O) = 1713 cm^{-1}.

Ethyl 4-dimethylaminobenzoate

To a solution of ethyl 4-dimethylaminobenzoate (19.3 mg, 0.05 mmol) and t-BuOK (0.56 mg, 0.005 mmol) in 2-propanol was added the Ru complex (5 mol %). The reaction was periodically monitored by NMR spectroscopy at 70°C. No further reaction was observed.

Ethyl 2-picolinate

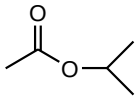
To a solution of ethyl 4-dimethylaminobenzoate (15.1 μL, 0.05 mmol) and t-BuOK (0.56 mg, 0.005 mmol) in 2-propanol was added the Ru complex (5 mol %). The reaction was periodically monitored by NMR spectroscopy at room temperature. The transesterification product was obtained as a corresponding product.



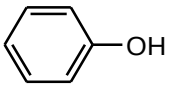
^{1}H NMR (C_6D_6): δ 8.51 (d, J(H-H) = 4.10 Hz, 1, $C_5H_4NC(O)OCH(CH_3)_2$), 8.07 (d, J(H-H) = 7.68 Hz, 1, $C_5H_4NC(O)OCH(CH_3)_2$), 7.03 (td, 1, $C_5H_4NC(O)OCH(CH_3)_2$), 6.68 (m, 2, $C_5H_4NC(O)OCH(CH_3)_2$), 5.31 (m, 1, $C_5H_4NC(O)OCH(CH_3)_2$), 1.25 (d, J(H-H) = 6.20 Hz, 6, $C_5H_4NC(O)OCH(CH_3)_2$). ^{1}H-^{13}C HSQC (C_6D_6): δ 164.8 (s, $C_5H_4NC(O)OCH(CH_3)_2$), 149.5 (s, $C_5H_4NC(O)OCH(CH_3)_2$), 148.9 (s, $C_5H_4NC(O)OCH(CH_3)_2$), 136.3 (s, $C_5H_4NC(O)OCH(CH_3)_2$), 125.4 (s, $C_5H_4NC(O)OCH(CH_3)_2$), 124.2 (s, $C_5H_4NC(O)OCH(CH_3)_2$), 68.1 (s, 148.9 (s, $C_5H_4NC(O)OCH(CH_3)_2$), 21.7 (s, $C_5H_4NC(O)OCH(CH_3)_2$). IR (neat): υ (C=O) = 1720 cm^{-1}.

Phenyl acetate

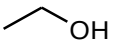
To a solution of phenyl acetate (13.6 μL, 0.1 mmol) and t-BuOK (1.12 mg, 0.01 mmol) in 2-propanol was added the Ru complex (5 mol %). The reaction was periodically monitored by NMR spectroscopy at room temperature. The product of transesterification was obtained first, then the reduction product was obtained in 14 % yield.



^{1}H NMR ($CH_3CH(OH)CH_3$): δ 5.27 (sept, J(H-H) = 6.25 Hz, 1, $CH_3COOC\mathit{H}(CH_3)_2$), 2.29 (s, 3, $C\mathit{H}_3COOCH(CH_3)_2$), 1.58 (d, J(H-H) = 6.23 Hz, 6, $CH_3COOCH(C\mathit{H}_3)_2$). ^{1}H-^{13}C HSQC ($CH_3CH(OH)CH_3$): δ 67.7 (s, $CH_3COO\mathit{C}H(CH_3)_2$), 20.8 (s, $\mathit{C}H_3COOCH(CH_3)_2$), 20.1 (s, $CH_3COOCH(\mathit{C}H_3)_2$).



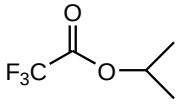
^{1}H NMR ($CH_3CH(OH)CH_3$): δ 7.41 (t, J(H-H) = 7.73 Hz, 2, *Ph*OH), 7.13 (d, J(H-H) = 8.16 Hz, 2, *Ph*OH), 7.04 (t, J(H-H) = 7.31 Hz, 1, *Ph*OH). ^{1}H-^{13}C HSQC ($CH_3CH(OH)CH_3$): δ 129.2 (s, *Ph*OH), 118.8 (s, *Ph*OH), 116.0 (s, *Ph*OH).



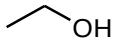
^{1}H NMR ($CH_3CH(OH)CH_3$): δ 3.94 (q, J(H-H) = 7.01 Hz, 2, $CH_3C\mathit{H}_2OH$).

Ethyl trifluoroacetate

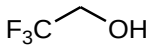
To a solution of ethyl trifluoroacetate (14.2 μL, 0.1 mmol) and t-BuOK (1.12 mg, 0.01 mmol) in 2-propanol was added the Ru complex (5 mol %). The reaction was periodically monitored by NMR spectroscopy at room temperature. The product of transesterification was obtained in a short time, then the reduction product was obtained in 56 % yield.



^{1}H NMR ($CH_3CH(OH)CH_3$): δ 5.53 (sept, J(H-H) = 6.14 Hz, 1, $CF_3COOC\mathit{H}(CH_3)_2$), 1.69 (d, J(H-H) = 6.24 Hz, 6, $CF_3COOCH(C\mathit{H}_3)_2$). ^{1}H-^{13}C HSQC ($CH_3CH(OH)CH_3$): δ 72.8 (s, $CF_3COO\mathit{C}H(CH_3)_2$), 21.1 (s, $CF_3COOCH(\mathit{C}H_3)_2$). ^{19}F NMR ($CH_3CH(OH)CH_3$): δ -76.07 (s, $C\mathit{F}_3COOCH(CH_3)_2$).



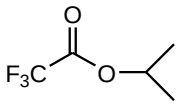
^{1}H NMR ($CH_3CH(OH)CH_3$): δ 3.94 (q, J(H-H) = 7.13 Hz, 2, $CH_3C\mathit{H}_2OH$).



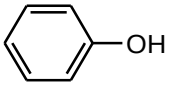
^{1}H NMR ($CH_3CH(OH)CH_3$): δ 6.82 (s, br, 1, $CF_3CH_2O\mathit{H}$), 4.14 (q, J(H-H) = 9.03 Hz, 2, $CF_3C\mathit{H}_2OH$). ^{13}C NMR ($CH_3CH(OH)CH_3$): δ 60.0 (q, $CF_3\mathit{C}H_2OH$). ^{19}F NMR ($CH_3CH(OH)CH_3$): δ -77.22 (t, J(H-F) = 9.32 Hz, $C\mathit{F}_3CH_2OH$).

Phenyl trifluoroacetate

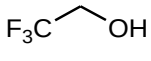
To a solution of Phenyl trifluoroacetate (19.0 μL, 0.1 mmol) and t-BuOK (1.12 mg, 0.01 mmol) in 2-propanol was added the Ru complex (5 mol %). The reaction was periodically monitored by NMR spectroscopy at room temperature.



^{1}H NMR ($CH_3CH(OH)CH_3$): δ 5.47 (sept, J(H-H) = 6.23 Hz, 1, $CF_3COOC\mathit{H}(CH_3)_2$), 1.64 (d, J(H-H) = 6.31 Hz, 6, $CF_3COOCH(C\mathit{H}_3)_2$). ^{1}H-^{13}C HSQC ($CH_3CH(OH)CH_3$): δ 73.2 (s, $CF_3COO\mathit{C}H(CH_3)_2$), 21.2 (s, $CF_3COOCH(\mathit{C}H_3)_2$). ^{19}F NMR ($CH_3CH(OH)CH_3$): δ -76.08 (s, $C\mathit{F}_3COOCH(CH_3)_2$).



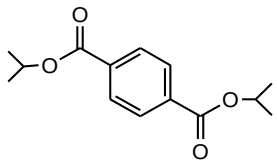
^{1}H NMR ($CH_3CH(OH)CH_3$): δ 7.41 (t, J(H-H) = 7.56 Hz, 2, *Ph*OH), 7.13 (d, J(H-H) = 7.89 Hz, 2, *Ph*OH), 7.04 (t, J(H-H) = 7.23 Hz, 1, *Ph*OH). ^{1}H-^{13}C HSQC ($CH_3CH(OH)CH_3$): δ 129.2 (s, *Ph*OH), 119.2 (s, *Ph*OH), 115.8 (s, *Ph*OH).



^{1}H NMR ($CH_3CH(OH)CH_3$): δ 6.82 (s, br, 1, $CF_3CH_2O\mathit{H}$), 4.12 (q, J(H-H) = 9.38 Hz, 2, $CF_3C\mathit{H}_2OH$). ^{19}F{^{1}H} NMR ($CH_3CH(OH)CH_3$): δ -77.19 (s, $C\mathit{F}_3CH_2OH$). ^{1}H-^{13}C HSQC ($CH_3CH(OH)CH_3$): δ 60.0 (q, $CF_3\mathit{C}H_2OH$). ^{19}F NMR ($CH_3CH(OH)CH_3$): δ -77.19 (t, J(H-F) = 9.54 Hz, $C\mathit{F}_3CH_2OH$).

Dimethyl terephthalate

To a solution of dimethyl terephthalate (19.4 mg, 0.1 mmol) and t-BuOK (1.12 mg, 0.01 mmol) in 2-propanol was added the Ru complex (5 mol %). The reaction was periodically monitored by NMR spectroscopy at room temperature.



^{1}H NMR ($CH_3CH(OH)CH_3$): δ 8.36 (s, 4, $C_6\mathit{H}_4(COOCH(CH_3)_2)_2$), 5.53 (sept, J(H-H) = 6.16 Hz, 2, $C_6H_4(COOC\mathit{H}(CH_3)_2)_2$), 1.67 (d, J(H-H) = 6.19 Hz, 12, $C_6H_4(COOCH(C\mathit{H}_3)_2)_2$). ^{1}H-^{13}C HSQC ($CH_3CH(OH)CH_3$): δ 129.3 (s, $\mathit{C}_6H_4(COOCH(CH_3)_2)_2$), 21.8 (s, $Ph(COOCH(\mathit{C}H_3)_2)_2$).

<u>CH_3OH</u>

^{1}H NMR ($CH_3CH(OH)CH_3$): δ 3.62 (s, 6, $2C\mathit{H}_3OH$). ^{1}H-^{13}C HSQC ($CH_3CH(OH)CH_3$): δ 48.7 (s, $\mathit{C}H_3OH$).

V.4.5. Synthesis of a possible intermediate

$Cp(PPr^i_3)Ru(CH_3CN)(H)$

To a solution of $[Cp(PPr^i_3)Ru(CH_3CN)_2]BF_4$ (20 mg, 0.04 mmol) and t-BuOK (4.5 mg, 0.04 mmol) in PhCl-d_5 was added 2-propanol (2.4 μL, 0.04mmol) at -30°C. The reaction was monitored by NMR spectroscopy at -30 to -20°C. Decomposition of the hydride complex was observed at room temperature.

^{1}H NMR (C_6D_5Cl): δ 4.34 (s, 5, Cp), 2.02 (s, 3, C*H*$_3$CN), 1.68 (s, br, 3, C*H*$(CH_3)_2$), 1.06 (s, br, 9, CH(C*H*$_3)_2$), 0.97 (s, br, 9, CH(C*H*$_3)_2$), -10.80 (d, J(H-P) = 40.18 Hz, 1, Ru-*H*). ^{31}P{^{1}H} NMR (C_6D_5Cl): δ 86.2 (s). ^{1}H-^{13}C HSQC (C_6D_5Cl): δ 168.1 (s, CH_3*C*N), 72.3 (s, Cp), 26.7 (s, *C*H$(CH_3)_2$), 21.2 (s, *C*H_3CN), The peaks of CH(*C*$H_3)_2$ overlap with the ones of the phosphine ligand and t-BuOH.

V.4.6. Transfer hydrogenation with ammonium formate

Benzonitrile

To a solution of benzonitrile (5.2 μL, 0.05 mmol) and ammonium formate (12.4 mg, 0.2 mmol) in CH_3OH was added the Ru complex (5 mol %). The reaction was periodically monitored by NMR spectroscopy at 60°C. The amine was obtained as a corresponding product.

$PhCH_2NH_2$

^{1}H NMR ($CDCl_3$): δ 7.31 (m, 5, *Ph*CH_2), 3.85 (s, 2, PhC*H*$_2NH_3$). ^{1}H-^{13}C HSQC ($CDCl_3$): δ 129.0 (s, *Ph*CH_2), 51.7(s, Ph*C*H_2).

Isolation

After reaction is finished, CH_3OH is removed and the brown oil is extracted with Et_2O. The solution of 1M KOH/H_2O is added to cleave the N-C bond of the possible by-product, $PhCH_2NHCOOH$ and stirred for 2 hours. Then the amine is protonated by

adding 2 M HCl to the Et_2O solution. Beige powder is obtained after removing Et_2O. (90mg, 63% yield)

$PhCH_2NH_3^+Cl^-$

^{1}H NMR ($CDCl_3$): δ 10.32 (s, br, 1, $PhCH_2NH_3$), 7.52 (m, 2, *Ph*CH_2), 7.38 (m, 3, *Ph*CH_2), 3.89 (s, 2, $PhCH_2NH_3$), 1.58 (s, 2, $PhCH_2NH_3$). ^{1}H-^{13}C HSQC ($CDCl_3$): δ 130.6 (s, *Ph*CH_2), 129.3 (s, *Ph*CH_2), 48.4 (s, $PhCH_2$).

4-methoxybenzonitrile

To a solution of 4-methoxybenzonitrile (6.7 mg, 0.05 mmol) and ammonium formate (12.4 mg, 0.2 mmol) in CH_3OH was added the Ru complex (5 mol %). The reaction was periodically monitored by NMR spectroscopy at 60°C. The amine was obtained as a corresponding product.

Isolation

After reaction is finished, CH_3OH is removed and the orange oil is extracted with Et_2O. The amine is protonated by adding 2 M HCl and dark yellow powder is obtained after removing Et_2O. (55 mg 32% yield)

$4\text{-}CH_3OC_6H_4CH_2NH_3^+Cl^-$

^{1}H NMR (D_2O): δ 7.28 (m, 2, $C_6H_4CH_2$), 6.93 (d, J(H-H) = 8.86 Hz, 2, $C_6H_4CH_2$), 4.08 (s, 1, $C_6H_4CH_2$), 4.02 (s, 1, $C_6H_4CH_2$), 3.75 (s, 3, $CH_3OC_6H_4$). ^{1}H-^{13}C HSQC (D_2O): δ 131.3 (s, $C_6H_4CH_2$), 114.7 (s, $C_6H_4CH_2$), 55.3 (s, $CH_3OC_6H_4$), 49.8 (s, $C_6H_4CH_2$).

4-aminobenzonitrile

To a solution of 4-aminobenzonitrile (5.9 mg, 0.05 mmol) and ammonium formate (12.4 mg, 0.2 mmol) in CH_3OH was added the Ru complex (5 mol %). The reaction was periodically monitored by NMR spectroscopy at 60°C. The amine was obtained as a corresponding product.

4-$H_2NC_6H_4CH_2NH_2$

^{1}H NMR (CH_2CH_2): δ 6.88 (m, 2, $C_6H_4CH_2NH_2$), 6.44 (d, J(H-H) = 8.00 Hz, 2, $C_6H_4CH_2NH_2$), 3.23 (s, 2, $C_6H_4CH_2NH_2$), 0.72 (s, br, 4, 4-$H_2NC_6H_4CH_2NH_2$).

Ethyl 4-cyanobenzoate

To a solution of ethyl 4-cyanobenzoate (8.8 mg, 0.05 mmol) and ammonium formate (12.4 mg, 0.2 mmol) in CH_3OH was added the Ru complex (5 mol %). The reaction was periodically monitored by NMR spectroscopy at 60°C. The amine was obtained as a corresponding product.

Isolation

After reaction is finished, CH_3OH is removed and the yellow oil is extracted with Et_2O. The amine is protonated by adding 2 M HCl and orange powder is obtained after removing Et_2O. (139mg 65% yield)

4-$CH_3CH_2OOCC_6H_4CH_2NH_3^+Cl^-$

^{1}H NMR (D_2O): δ 7.97 (d, J(H-H) = 8.36 Hz, 2, $C_6H_4CH_2$), 7.45 (d, J(H-H) = 8.26 Hz, 2, $C_6H_4CH_2$), 4.29 (q, 2, $CH_3CH_2OOCC_6H_4$), 4.16 (s, 2, $C_6H_4CH_2$), 1.28 (t, 3, $CH_3CH_2OOCC_6H_4$). ^{1}H-^{13}C HSQC (D_2O): δ 130.1 (s, $C_6H_4CH_2$), 129.1 (s, $C_6H_4CH_2$), 62.8 (s, $CH_3CH_2OOCC_6H_4$), 42.6 (s, $C_6H_4CH_2$), 13.3 (s, $CH_3CH_2OOCC_6H_4$).

V.5. Reduction of iminoyl chlorides to imines and aldehydes catalysed by Ru complex

V.5.1. The synthesis of ruthenium complex

Preparation of $[Cp(PPr^{i}_{3})Ru(CH_3CN)_2]PF_6$

To a yellow solution of $[CpRu(CH_3CN)_3]PF_6$ (0.50 g, 1.15 mmol) in CH_3CN (20 mL) was added PPr^{i}_{3} (0.22 mL, 1.15 mmol) *via* syringe. The resulting solution was stirred for 3 hours at ambient temperature. All volatiles were then removed under vacuum and the residue was washed with Et_2O (2*20 mL) and hexane (3*10 mL). The yellow solid was dried under vacuum. Yield 0.570 g (90%).

V.5.2. The synthesis of secondary amides and iminoyl chlorides

$PhCONHCH_2Ph$

To a solution of benzyl amine (20 mmol, 2.2 mL) in CH_2Cl_2 (30 mL) was added benzoyl chloride (20 mmol, 2.8 mL) and the reaction mixture was stirred overnight at ambient temperature. The mixture was then filtered and the solvent of filtrate was removed in vacuum. The product was washed with hexane (10 mL). Compound *N*-benzylbenzamide was obtained as a white powder after removal of hexane in vacuum. Yield 3.70 g (88%).

^{1}H NMR (Acetone-d_6): δ 8.23 (s, br, 1, PhCON*H*), 7.95 (d, J(H-H) = 6.97 Hz, 2, *Ph*), 7.46 (m, 3, *Ph*), 7.32 (m, 3, *Ph*), 7.24 (m, 1, *Ph*), 4.61 (d, J(H-H) = 5.97 Hz, 2, NHC*H*$_2$Ph).

$PhCCl{=}NCH_2Ph$

To a solution of *N*-benzylbenzamide in CH_2Cl_2 (15 mL) was added 1.1 eq. of distilled $SOCl_2$ and the reaction mixture was stirred for overnight at 70°C. Solvent was then

removed in vacuum and the product was distilled under vacuum. Compound PhCCl=NCH$_2$Ph was obtained as orange-yellow oil. Yield 1.35 g (63 %).

^{1}H NMR (CH_2Cl_2): δ 7.10-7.91 (m, 10, *Ph*CCl=NCH$_2$*Ph*), 4.76 (s, 2, PhCCl=NC*H*$_2$Ph)

4-$CH_3OC_6H_4CONHCH_2Ph$

To a solution of benzyl amine (5 mmol, 0.84 mL) in CH_2Cl_2 (30 mL) was added 4-methoxybenzoyl chloride (5 mmol, 0.85 mL) and the reaction mixture was stirred overnight at ambient temperature. The mixture was then filtered and the solvent of filtrate was removed in vacuum. The product was washed with hexane (10 mL). Compound *N*-benzyl-4-methoxybenzamide was obtained as a white powder after removal of hexane in vacuum. Yield 0.97 g (85%).

^{1}H NMR (CH_2Cl_2): δ 7.92 (m, 1, *Ph*), 7.59 (d, J(H-H) = 7.94 Hz, 2, *Ph*), 7.20 (m, 3, *Ph*), 6.77 (m, 3, *Ph*), 6.33 (s, br, 1, C_6H_4CON*H*), 4.44 (d, J(H-H) = 5.81 Hz, 2, NHC*H*$_2$Ph), 3.69 (s, 3, C*H*$_3OC_6H_4$).

4-$CH_3OC_6H_4CCl=NCH_2Ph$

To a solution of *N*-benzyl-4-methoxybenzamide in CH_2Cl_2 (15 mL) was added 1.1 eq. of distilled $SOCl_2$ and the reaction mixture was stirred for overnight at 70°C. Solvent was then removed in vacuum and the product was distilled under vacuum. Compound 4-$CH_3OC_6H_4CCl=NCH_2Ph$ was obtained as yellow oil. Yield 0.60 g (64 %).

^{1}H NMR (CH_2Cl_2): δ 7.93 (d, J(H-H) = 8.88 Hz, 2, 4-CH_3OC_6*H*$_4$CCl=NCH$_2$Ph), 7.29 (d, J(H-H) = 7.73 Hz, 2, 4-$CH_3OC_6H_4CCl=NCH_2$*Ph(o)*), 7.19 (t, 2, 4-$CH_3OC_6H_4CCl=NCH_2$*Ph(m)*), 7.11 (t, 1, 4-$CH_3OC_6H_4CCl=NCH_2$*Ph(p)*), 6.79 (d, J(H-H) = 8.88 Hz, 2, 4-CH_3OC_6*H*$_4$CCl=NCH$_2$Ph), 4.78 (s, 2, 4-$CH_3OC_6H_4CCl=NC$*H*$_2$Ph), 3.71 (s, 3, 4-C*H*$_3OC_6H_4CCl=NCH_2$Ph).

t-BuCONHCH$_2$Ph

To a solution of benzyl amine (5 mmol, 0.84 mL) in CH_2Cl_2 (30 mL) was added trimethylacetyl chloride (5 mmol, 0.60 mL) and the reaction mixture was stirred overnight at ambient temperature. The mixture was then filtered and the solvent of filtrate was removed in vacuum. The product was washed with hexane (10 mL). Compound t-BuCCONHCH$_2$Ph was obtained as a white powder after removal of hexane in vacuum. Yield 0.60 g (70%).

^{1}H NMR (CH_2Cl_2): δ 7.18 (m, 2, *Ph*), 7.11 (m, 3, *Ph*), 5.88 (s, br, 1, CON*H*), 4.24 (d, J(H-H) = 5.83 Hz, 2, NHC*H*$_2$Ph), 1305 (s, 9, (C*H*$_3$)$_3$COPh).

t-BuCCl=NCH$_2$Ph

To a solution of t-BuCCONHCH$_2$Ph in CH_2Cl_2 (15 mL) was added 1.1 eq. of distilled $SOCl_2$ and the reaction mixture was stirred for overnight at 70°C. Solvent was then removed in vacuum and the product was distilled under vacuum. Compound t-BuCCl=NCH$_2$Ph was obtained as white oil. Yield 1.20 g (60 %).

^{1}H NMR (CH_2Cl_2): δ 7.18 (m, 4, t-BuCCl=NCH$_2$*Ph*), 7.09 (m, 1, t-BuCCl=NCH$_2$*Ph(p)*), 4.55 (s, 2, t-BuCCl=NC*H*$_2$Ph), 1.17 (s, 9, *t-Bu*CCl=NCH$_2$Ph).

CH$_3$CH$_2$CONHPh

To a solution of aniline (7.5 mmol, 0.70 mL) in CH_2Cl_2 (30 mL) was added propionyl chloride (7.5 mmol, 0.70 mL) and the reaction mixture was stirred overnight at ambient temperature. The mixture was then filtered and the solvent of the filtrate was removed in vacuum. The product was washed with hexane (10 mL). Compound *N*-phenylpropionamide was obtained as a light yellow powder after removal of hexane in vacuum. Yield 0.60 g (47%).

^{1}H NMR (CH_2Cl_2): δ 7.35 (d, J(H-H) = 7.91 Hz, 2, *Ph*), 7.26 (s, br, 1, CON*H*), 7.15 (t, J(H-H) = 8.27 Hz, 2, *Ph*), 6.94 (t, J(H-H) = 7.55 Hz, 1, *Ph*), 2.19 (q, J(H-H) = 7.41 Hz, 2, CH_3CH_2CO), 1.05 (t, J(H-H) = 7.41 Hz, 3, CH_3CH_2CO).

$CH_3CH_2CCl=NPh$

To a solution of $CH_3CH_2CONHPh$ in CH_2Cl_2 was added 1 eq. of PCl_5 and the reaction mixture was stirred for 1 h at room temperature. Solvent was then removed in vacuum and compound $CH_3CH_2CCl=NPh$ was obtained as clear oil.

^{1}H NMR (CH_2Cl_2): δ 7.18 (t, 2, $CH_3CH_2CCl=NPh(m)$), 6.98 (t, 1, $CH_3CH_2CCl=NPh(p)$), 6.70 (t, 2, $CH_3CH_2CCl=NPh(o)$), 2.61 (q, 2, $CH_3CH_2CCl=NPh$), 1.13 (t, 3, $CH_3CH_2CCl=NPh$).

$CH_3CH_2CONHC_6H_4COCH_3$

To a solution of 3-aminoacetophenone (7.5 mmol, 1.01 mg) in CH_2Cl_2 (30 mL) was added propionyl chloride (7.5 mmol, 0.70 mL) and the reaction mixture was stirred overnight at ambient temperature. The mixture was then filtered and the solvent of filtrate was removed in vacuum. The product was washed with hexane (10 mL). Compound *N*-(3-acetylphenyl)propionamide was obtained as a light yellow powder after removal of hexane in vacuum. Yield 0.69 g (48%).

^{1}H NMR (CH_2Cl_2): δ 7.91 (s, 1, *Ph*), 7.71(d, J(H-H) = 7.90 Hz, 1, *Ph*), 7.58 (s, br, 1, CON*H*), 7.50(d, J(H-H) = 7.62 Hz, 1, *Ph*), 7.27 (t, J(H-H) = 7.90 Hz, 1, *Ph*), 2.42 (s, 3, $COCH_3$), 2.24 (q, J(H-H) = 7.39 Hz, 2, CH_3CH_2CO), 1.06 (t, J(H-H) = 7.39 Hz, 3, CH_3CH_2CO).

$CH_3CH_2CCl=NC_6H_4COCH_3$

To a solution of $CH_3CH_2CONHC_6H_4COCH_3$ in CH_2Cl_2 was added 1 eq. of PCl_5 and the reaction mixture was stirred for 1 h at room temperature. Solvent was then

removed in vacuum and compound $CH_3CH_2CCl{=}NC_6H_4COCH_3$ was obtained as clear oil.

^{1}H NMR (CH_2Cl_2): δ 7.58 (d, J(H-H) = 8.10 Hz, 1, CH3$CH_2CCl{=}N$*Ph*$COCH_3$), 7.29 (t, 1, $CH_3CH_2CCl{=}N$*Ph*$COCH_3$), 7.28 (s, 1, $CH_3CH_2CCl{=}N$*Ph*$COCH_3$), 6.91 (d, J(H-H) = 8.10 Hz, 1, $CH_3CH_2CCl{=}N$*Ph*$COCH_3$), 2.64 (q, 2, CH_3C*H*$_2CCl{=}NPhCOCH_3$), 2.43 (s, 3, $CH_3CH_2CCl{=}NPhCOC$*H*$_3$), 1.15 (t, 1, C*H*$_3CH_2CCl{=}NPhCOCH_3$).

$CH_3CH_2CONHC_6H_4COOCH_2CH_3$

To a solution of ethyl-4-aminobenzoate (7.5 mmol, 1.24 mg) in CH_2Cl_2 (30 mL) was added propionyl chloride (7.5 mmol, 0.70 mL) and the reaction mixture was stirred overnight at ambient temperature. The mixture was then filtered and the solvent of filtrate was removed in vacuum. The product was washed with hexane (10 mL). Compound ethyl 4-propionamidobenzoate was obtained as a white powder after removal of hexane in vacuum. Yield 0.74 g (45%).

^{1}H NMR (CH_2Cl_2): δ 7.81 (d, J(H-H) = 8.79 Hz, 2, C$_6$*H*$_4$), 7.45 (d, J(H-H) = 8.79 Hz, 2, C$_6$*H*$_4$), 7.34 (s, br, 1, CON*H*), 4.16 (q, J(H-H) = 6.75 Hz, 2, COOC*H*$_2CH_3$), 2.23 (q, J(H-H) = 7.39 Hz, 2, CH_3C*H*$_2$CO), 1.21 (t, J(H-H) = 7.01 Hz, 3, $COOCH_2C$*H*$_3$), 1.05 (t, J(H-H) = 7.66 Hz, 3, C*H*$_3CH_2$CO).

$CH_3CH_2CCl{=}NC_6H_4COOCH_2CH_3$

To a solution of $CH_3CH_2CONHC_6H_4COOCH_2CH_3$ in CH_2Cl_2 was added 1 eq. of PCl_5 and the reaction mixture was stirred for 1 h at room temperature. Solvent was then removed in vacuum and compound $CH_3CH_2CCl{=}NC_6H_4COOCH_2CH_3$ was obtained as pale yellow oil.

^{1}H NMR (CH_2Cl_2): δ 7.86 (d, J(H-H) = 8.78 Hz, 2, NC_6*H*$_4COOCH_2CH_3$), 6.74 (d, J(H-H) = 8.01 Hz, 2, NC_6*H*$_4COOCH_2CH_3$), 4.15 (q, 2, NC_6H_4COOC*H*$_2CH_3$), 2.64 (q, 2, CH_3C*H*$_2CCl{=}N$), 1.20 (t, 3, $NC_6H_4COOCH_2C$*H*$_3$), 1.14 (t, 3, C*H*$_3CH_2CCl{=}N$).

***N*-benzylthiophene-2-carboxamide**

To a solution of benzyl amine (5 mmol, 0.84 mL) in CH_2Cl_2 (30 mL) was added thiophene-2-carbonyl chloride (5 mmol, 0.73 mL) and the reaction mixture was stirred overnight at ambient temperature. The mixture was then filtered and the solvent of filtrate was removed in vacuum. The product was washed with hexane (10 mL). Compound *N*-benzylthiophene-2-carboxamide was obtained as a white powder after removal of hexane in vacuum. Yield 0.70 g (69%).

^{1}H NMR (CH_2Cl_2): δ 7.34 (m, 2, C_4H_3S and *Ph*), 7.19 (m, 4, *Ph*), 7.13 (m, 1, C_4H_3S), 6.93 (t, J(H-H) = 4.35 Hz, 1, C_4H_3S), 6.33 (s, br, 1, CON*H*), 4.42 (d, J(H-H) = 5.87 Hz, 2, CH_2Ph).

***N*-benzylthiophene-2-carbiminoyl chloride**

To a solution of *N*-benzylthiophene-2-carboxamide in CH_2Cl_2 was added 1 eq. of PCl_5 and the reaction mixture was stirred for 1 h at room temperature. Solvent was then removed in vacuum and compound *N*-benzylthiophene-2-carbiminoyl chloride was obtained.

^{1}H NMR (CH_2Cl_2): δ 7.57 (d, J(H-H) = 3.88 Hz, 1, C_4H_3SCCl), 7.35 (m, 1, C_4H_3SCCl), 7.12 (m, 5, $C_4H_3SCCl=NCH_2Ph$), 6.93 (t, 1, C_4H_3SCCl), 4.72 (s, 2, $C_4H_3SCCl=NCH_2Ph$).

***N*-benzylfuran-2-carboxamide**

To a solution of benzyl amine (5 mmol, 0.84 mL) in CH_2Cl_2 (30 mL) was added 2-furoyl chloride (5 mmol, 0.65 mL) and the reaction mixture was stirred overnight at ambient temperature. The mixture was then filtered and the solvent of filtrate was removed in vacuum. The product was washed with hexane (10 mL). Compound *N*-benzylfuran-2-carboxamide was obtained as a white powder after removal of hexane in vacuum. Yield 0.64 g (68%).

^{1}H NMR (CH_2Cl_2): δ 7.30 (d, J(H-H) = 1.02 Hz, 1, C_4H_3O), 7.19 (m, 5, *Ph*), 6.93 (d, J(H-H) = 3.37 Hz, 1, C_4H_3O), 6.60 (s, br, 1, CONH), 6.36 (m, 1, C_4H_3O), 4.41 (d, J(H-H) = 5.99 Hz, 2, CH_2Ph).

***N*-benzylfuran-2-carbiminoyl chloride**

To a solution of *N*-benzylfuran-2-carboxamide in CH_2Cl_2 was added 1 eq. of PCl_5 and the reaction mixture was stirred for 1 h at room temperature. Solvent was then removed in vacuum and compound *N*-benzylthiophene-2-carbiminoyl chloride was obtained.

^{1}H NMR (CH_2Cl_2): δ 7.45 (m, 1, C_4H_3OCCl), 7.12 (m, 5, $C_4H_3OCCl=NCH_2Ph$), 7.00 (d, J(H-H) = 3.49 Hz, 1, C_4H_3OCCl), 6.39 (dd, J(H-H) = 3.85 and 1.99 Hz, 1, C_4H_3OCCl), 4.74 (s, 2, $C_4H_3OCCl=NCH_2Ph$).

***N*-benzylnicotinamide**

To a solution of benzyl amine (5 mmol, 0.84 mL) in CH_2Cl_2 (30 mL) was added nicotinoyl chloride (5 mmol, 0.89 mg) and Et_3N (10 mmol, 1.02 mL). The reaction mixture was stirred overnight at ambient temperature. The mixture was then filtered and the solvent of filtrate was removed in vacuum. The crude product was extracted with Et_2O (2*20 mL). Compound *N*-benzylnicotinamide was obtained as a white powder after removal of Et_2O in vacuum. Yield 0.60 g (57%).

^{1}H NMR (CH_2Cl_2): δ 11.84 (s, br, 1, CONH), 8.89 (d, J(H-H) = 1.83 Hz, 1, C_5H_4N), 8.52 (dd, J(H-H) = 1.47 and 4.72 Hz, 1, C_5H_4N), 8.00 (dt, J(H-H) = 2.15 and 7.72 Hz, 1, C_5H_4N),7.21 (m, 5, *Ph*), 7.11 (m, 1, C_5H_4N), 4.45 (d, J(H-H) = 5.90 Hz, 2, CH_2Ph).

***N*-benzylnicotiniminoyl chloride**

To a solution of *N*-benzylnicotinamide in CH_2Cl_2 was added 1 eq. of PCl_5 and the reaction mixture was stirred for 1 h at room temperature. Solvent was then removed in vacuum and compound *N*-benzylnicotiniminoyl chloride was obtained.

^{1}H NMR (CH_2Cl_2): δ 9.11 (s, br, 1, $C_5H(2)_4NCCl$), 8.57 (d, J(H-H) = 4.10 Hz, 1, $C_5H(6)_4NCCl$), 8.37 (d, J(H-H) = 8.20 Hz, 1, $C_5H(4)_4NCCl$), 7.41 (dd, J(H-H) = 7.70 and 2.21 Hz, 1, $C_5H(5)_4NCCl$), 7.19 (m, 4, $CCl=NCH_2Ph$), 7.12 (t, 1, $CCl=NCH_2Ph$), 4.80 (s, 2, $CCl=NCH_2Ph$).

$PhCH=CHCONHCH_2Ph$

To a solution of benzyl amine (5 mmol, 0.84 mL) in CH_2Cl_2 (30 mL) was added cinnamoyl chloride (5 mmol, 0.83 mg) and the reaction mixture was stirred overnight at ambient temperature. The mixture was then filtered and the solvent of filtrate was removed in vacuum. The product was washed with hexane (10 mL). Compound *N*-benzylfuran-2-carboxamide was obtained as a white powder after removal of hexane in vacuum. Yield 0.90 g (81%).

^{1}H NMR (CH_2Cl_2): δ 7.43 (d, J(H-H) = 15.08 Hz, 1, PhC*H*=CH), 7.35 (m, 3, *Ph*), 7.17 (m, 7, *Ph*), 6.29 (d, J(H-H) = 15.64 Hz, 1, PhCH=C*H*), 5.99 (s, br, 1, CON*H*), 4.36 (d, J(H-H) = 5.84 Hz, 2, CH_2Ph).

$PhCH=CHCCl=NCH_2Ph$

To a solution of $PhCH=CHCONHCH_2Ph$ in CH_2Cl_2 was added 1 eq. of PCl_5 and the reaction mixture was stirred for 1 h at room temperature. Solvent was then removed in vacuum and compound $PhCH=CHCCl=NCH_2Ph$ was obtained.

^{1}H NMR (CH_2Cl_2): δ 7.59 (q, 2, PhC*H*=C*H*CCl), 7.19 (m, 10, *Ph*CH=CHCCl=NCH_2*Ph*), 4.83 (s, 2, PhCH=CHCCl=NCH_2Ph).

$CH_3CH_2CONHC_6H_4CN$

To a solution of 4-aminobenzonitrile (7.5 mmol, 0.89 mg) in CH_2Cl_2 (30 mL) was added propionyl chloride (7.5 mmol, 0.70 mL) and the reaction mixture was stirred overnight at ambient temperature. The mixture was then filtered and the solvent of filtrate was removed in vacuum. The product was washed with hexane (10 mL).

Compound *N*-(4-cyanophenyl)propionamide was obtained as a white powder after removal of hexane in vacuum. Yield 0.49 g (38%).

^{1}H NMR (CH_2Cl_2): δ 7.51 (d, J(H-H) = 8.81 Hz, 2, C_6H_4), 7.44 (d, J(H-H) = 8.81 Hz, 2, C_6H_4), 7.38 (s, br, 1, CONH), 2.24 (q, J(H-H) = 7.61 Hz, 2, CH_3CH_2CO), 1.05 (t, J(H-H) = 7.14 Hz, 3, CH_3CH_2CO).

$CH_3CH_2CCl=NC_6H_4CN$

To a solution of $CH_3CH_2CONHC_6H_4CN$ in CH_2Cl_2 was added 1 eq. of PCl_5 and the reaction mixture was stirred for 1 h at room temperature. Solvent was then removed in vacuum and compound $CH_3CH_2CCl=NC_6H_4CN$ was obtained.

^{1}H NMR (CH_2Cl_2): δ 7.50 (d, J(H-H) = 8.64 Hz, 2, NC_6H_4CN), 6.78 (d, J(H-H) = 8.38 Hz, 2, NC_6H_4CN), 2.64 (q, 2, CH_3CH_2CCl), 1.14 (t, 3, CH_3CH_2CCl).

$PhCH_2NHCOC_6H_4CN$

To a solution of 4-cyanobenzoic acid (10 mmol, 1.66 g) in CH_2Cl_2 (50 mL) was added benzyl amine (10 mmol, 1.07 mL). The reaction mixture was stirred overnight at ambient temperature. The mixture was then filtered and the solvent of filtrate was removed in vacuum. Compound $PhCH_2NHCOC_6H_4CN$ was obtained as a white powder. Yield 1.6 g (68%).

^{1}H NMR (CH_2Cl_2): δ 7.71 (d, J(H-H) = 8.45 Hz, 2, C_6H_4), 7.56 (d, J(H-H) = 8.20 Hz, 2, C_6H_4), 7.19 (m, 5, *Ph*), 6.50 (s, br, 1, CONH), 4.45 (d, J(H-H) = 5.75 Hz, 2, $PhCH_2NH$).

$PhCH_2N=CClC_6H_4CN$

To a solution of $PhCH_2NHCOC_6H_4CN$ in CH_2Cl_2 (50 mL) was added 1 eq. of PCl_5 and the reaction mixture was stirred for 1 h at room temperature. Solvent was then removed in vacuum and compound $PhCH_2N=CClC_6H_4CN$ was obtained as pale pink oil. Yield 1.3 g (75%).

^{1}H NMR (CH_2Cl_2): δ 7.57 (d, J(H-H) = 8.52 Hz, 2, *Ph*CH_2N), 7.13 (d, J(H-H) = 8.68 Hz, 2, *Ph*CH_2N), 6.76 (m, 4, N=CClC$_6$*H*$_4$CN), 6.68 (m, 1, *Ph*CH_2N), 4.35 (s, 2, NC*H*$_2$Ph).

$C_6H_{11}NHCOC_6H_4CN$

To a solution of 4-cyanobenzoic acid (10 mmol, 1.66 g) in CH_2Cl_2 (50 mL) was added cyclohexyl amine (11 mmol, 1.09 mL) and Et_3N (22 mmol, 2.2 mL).The reaction mixture was stirred overnight at ambient temperature. The mixture was then filtered and the solvent of filtrate was removed in vacuum. Then the solid was extracted with Et_2O. Compound $C_6H_{11}NHCOC_6H_4CN$ was obtained as a white powder after removal of Et_2O in vacuum. Yield 0.46 g (20%).

^{1}H NMR (CH_2Cl_2): δ 7.67 (d, J(H-H) = 7.99 Hz, 2, C$_6$*H*$_4$), 7.57 (d, J(H-H) = 7.49 Hz, 2, C$_6$*H*$_4$), 5.97 (s, br, 1, CON*H*), 3.77 (m, 1, C$_6$H$_{10}$*H*NHCO), 1.84 (d, J(H-H) = 11.27 Hz, 2, C$_6$*H*$_{10}$), 1.60 (m, 2, C$_6$*H*$_{10}$), 1.49 (m, 1, C$_6$*H*$_{10}$), 1.26 (m, 2, C$_6$*H*$_{10}$), 1.09 (m, 3, C$_6$*H*$_{10}$).

$C_6H_{11}N=CClC_6H_4CN$

To a solution of $C_6H_{11}NHCOC_6H_4CN$ in CH_2Cl_2 (50 mL) was added 1 eq. of PCl_5 and the reaction mixture was stirred for 1 h at room temperature. Solvent was then removed in vacuum and compound $C_6H_{11}N=CClC_6H_4CN$ was obtained as pale yellow powder. Yield 0.41 g (88%).

^{1}H NMR (CH_2Cl_2): δ 7.96 (d, J(H-H) = 8.85 Hz, 2, NCC$_6$*H*$_4$CCl), 7.56 (d, J(H-H) = 8.85 Hz, 2, NCC$_6$*H*$_4$CCl), 3.73 (tt, 1, CCl=NC*H*), 1.15 (m, 10, CCl=NCHC$_5$*H*$_{10}$).

$CH_3CH_2CONHC_6H_4NO_2$

To a solution of 4-nitroaniline (7.5 mmol, 1.04 mg) in CH_2Cl_2 (30 mL) was added propionyl chloride (7.5 mmol, 0.70 mL) and the reaction mixture was stirred overnight at ambient temperature. The mixture was then filtered and the solvent of

filtrate was removed in vacuum. The product was washed with hexane (10 mL). Compound *N*-(4-nitrophenyl)propionamide was obtained as a white powder after removal of hexane in vacuum. Yield 0.38 g (26%).

^{1}H NMR (CH_2Cl_2): δ 8.02 (d, J(H-H) = 9.07 Hz, 2, C_6H_4), 7.56 (d, J(H-H) = 8.89 Hz, 2, C_6H_4), 7.37 (s, br, 1, CONH), 2.27 (q, J(H-H) = 7.78 Hz, 2, CH_3CH_2CO), 1.07 (t, J(H-H) = 7.55 Hz, 3, CH_3CH_2CO).

$CH_3CH_2CCl=NC_6H_4NO_2$

To a solution of $CH_3CH_2CONHC_6H_4NO_2$ in CH_2Cl_2 was added 1 eq. of PCl_5 and the reaction mixture was stirred for 1 h at room temperature. Solvent was then removed in vacuum and compound $CH_3CH_2CCl=NC_6H_4NO_2$ was obtained.

^{1}H NMR (CH_2Cl_2): δ 8.06 (d, J(H-H) = 8.85 Hz, 2, $NC_6H_4NO_2$), 6.82 (d, J(H-H) = 8.85 Hz, 2, $NC_6H_4NO_2$), 2.66 (q, 2, CH_3CH_2CCl), 1.15 (t, 3, CH_3CH_2CCl).

$PhCONHC_6H_4COCH_3$

To a solution of 1-(3-aminophenyl)ethanone (15 mmol, 2.03 g) in CH_2Cl_2 (30 mL) was added benzoyl chloride (15 mmol, 2.11 mL) and the reaction mixture was stirred overnight at ambient temperature. The mixture was then filtered and the solvent of filtrate was removed in vacuum. The product was washed with hexane (10 mL). Compound $PhCONHC_6H_4COCH_3$ was obtained as a white powder after removal of hexane in vacuum. Yield 1.96 g (55%).

^{1}H NMR (CH_2Cl_2): δ 8.01 (s, 1, $NHC_6H_4COCH_3$), 7.93 (s, br, 1, CONH), 7.82 (dd, J(H-H) = 1.32 and 8.11 Hz, 1, $NHC_6H_4COCH_3$), 7.72 (m, 2, $NHC_6H_4COCH_3$), 7.56 (d, J(H-H) = 7.72 Hz, 1, *Ph*CONH), 7.36 (m, 4, *Ph*CONH), 2.43 (s, 3, $PhCOCH_3$).

$PhCCl=NC_6H_4COCH_3$

To a solution of $PhCONHC_6H_4COCH_3$ in CH_2Cl_2 (15 mL) was added 1.1 eq. of distilled $SOCl_2$ and the reaction mixture was stirred for overnight at 70°C. Solvent

was then removed in vacuum and the product was distilled under vacuum. Compound $PhCCl{=}NC_6H_4COCH_3$ was obtained as orange-yellow oil. Yield 1.60 g (42 %).

^{1}H NMR (CH_2Cl_2): δ 7.96 (d, J(H-H) = 9.07 Hz, 2, *Ph(o)*CCl=N), 7.58 (d, J(H-H) = 7.83 Hz, 1, $NC_6\mathit{H}_4COCH_3$), 7.28 (m, 5, *Ph(m, p)*CCl=$NC_6\mathit{H}_4COCH_3$), 7.00 (d, J(H-H) = 7.41 Hz, 1, $NC_6\mathit{H}_4COCH_3$), 2.40 (s, 3, $NC_6H_4COC\mathit{H}_3$).

$PhCONHC_6H_4COOCH_2CH_3$

To a solution of ethyl-4-aminobenzoate (15 mmol, 2.43 g) in CH_2Cl_2 (30 mL) was added benzoyl chloride (15 mmol, 2.11 mL) and the reaction mixture was stirred overnight at ambient temperature. The mixture was then filtered and the solvent of filtrate was removed in vacuum. The product was washed with hexane (10 mL). Compound $PhCONHC_6H_4COOCH_2CH_3$ was obtained as a white powder after removal of hexane in vacuum. Yield 2.21 g (55%).

^{1}H NMR (CH_2Cl_2): δ 7.89 (s, br, 1, CON*H*), 7.87 (d, J(H-H) = 8.53 Hz, $NHC_6\mathit{H}_4CO$), 7.70 (d, J(H-H) = 7.17Hz, 2, *Ph*CONH), 7.58 (d, J(H-H) = 8.53 Hz, $NHC_6\mathit{H}_4CO$), 7.38 (m, 3, *Ph*CONH), 4.17 (q, J(H-H) = 7.26 Hz, 2, $C_6H_4COOC\mathit{H}_2CH_3$), 1.22 (t, J(H-H) = 7.26 Hz, 3, $C_6H_4COOCH_2C\mathit{H}_3$).

$PhCCl{=}NC_6H_4COOCH_2CH_3$

To a solution of $PhCONHC_6H_4COOCH_2CH_3$ in CH_2Cl_2 was added 1 eq. of PCl_5 and the reaction mixture was stirred for 1 h at room temperature. Solvent was then removed in vacuum and compound $PhCCl{=}NC_6H_4COOCH_2CH_3$ was obtained.

^{1}H NMR (CH_2Cl_2): δ 7.98 (d, J(H-H) = 7.71 Hz, 2, *Ph(o)*CCl=N), 7.90 (d, J(H-H) = 8.69 Hz, 2, $NC_6\mathit{H}_4COOCH_2CH_3$), 7.40 (m, 1, *Ph(p)*CCl=N), 7.32 (m, 2, *Ph(m)*CCl=N), 6.86 (d, J(H-H) = 8.63 Hz, 2, $NC_6\mathit{H}_4COOCH_2CH_3$), 4.14 (q, 2, $NC_6H_4COOC\mathit{H}_2CH_3$), 1.18 (t, 3, $NC_6H_4COOCH_2C\mathit{H}_3$).

4-(Dimethylamino)-*N*-isopropyl benzamide

To a solution of 4-dimethylamino benzoyl chloride (10 mmol, 1.80 g) and Et_3N (10 mmol, 1.01 mL) in Et_2O (100 mL) was slowly added isopropyl amine (12 mmol, 0.7 mL). The reaction mixture was stirred overnight at ambient temperature. The solvent was removed in vacuum and the product was washed with hexane (30 mL). Compound 4-(dimethylamino)-*N*-isopropyl benzamide was obtained as a white powder after removal of hexane in vacuum. Yield 1.21 g (60%).

4-$(CH_3)_2NC_6H_4CCl$=NCH$(CH_3)_2$

To a solution of 4-(dimethylamino)-*N*-isopropyl benzamide in CH_2Cl_2 was added 1 eq. of PCl_5 and the reaction mixture was stirred for overnight at room temperature. Solvent was then removed in vacuum and compound 4-$(CH_3)_2NC_6H_4CCl$=NCH$(CH_3)_2$ was obtained as yellow powder. Yield 1.33g (98%).

^{1}H NMR (CH_2Cl_2): δ 8.12 (d, J(H-H) = 6.62 Hz, 2, 4-$(CH_3)_2C_6H_4$ *(3,5)*CCl), 7.19 (d, J(H-H) = 6.98 Hz, 2, 4-$(CH_3)_2C_6H_4$ *(2,6)*CCl), 4.20 (m, 1, Cl=NC*H*$(CH_3)_2$), 3.00 (s, 6, 4-(C*H*$_3)_2C_6H_4$CCl), 1.28-1.30 (d, J(H-H) = 3.69 Hz, 6, Cl=NCH(C*H*$_3)_2$).

3-(Trifluoromethyl)-*N*-isopropyl benzamide

To a solution of 3-trifluoromethyl benzoyl chloride (10 mmol, 2.0 mL) and Et_3N (10 mmol, 1.01 mL) in Et_2O (100 mL) was slowly added isopropyl amine (12 mmol, 0.7 mL). The reaction mixture was stirred overnight at ambient temperature. The solvent was removed in vacuum and the product was washed with hexane (30 mL). Compound 3-(trifluoromethyl)-*N*-isopropyl benzamide was obtained as a white powder after removal of hexane in vacuum. Yield 1.94 g (85%).

^{1}H NMR ($CDCl_3$): δ 8.01 (s, 1, $CF_3C_6H_4$), 7.94 (d, J(H-H) = 8.09 Hz, 1, $CF_3C_6H_4$), 7.75 (d, J(H-H) = 7.75 Hz, 1, $CF_3C_6H_4$), 7.56 (t, J(H-H) = 7.75 Hz, 1, $CF_3C_6H_4$), 5.97

(s, br, 1, CON*H*), 4.33 (sep, J(H-H) = 6.69 Hz, 1, C*H*(CH_3)$_2$), 1.29 (d, J(H-H) = 6.60 Hz, 6, CH(C*H*$_3$)$_2$).

3-$CF_3C_6H_4CCl=NCH(CH_3)_2$

A solution of 3-(trifluoromethyl)-*N*-isopropyl benzamide in distilled $SOCl_2$ was refluxed for 2 hours. Solvent was then removed in vacuum and the product was dried under vacuum. Compound 3-$CF_3C_6H_4CCl=NHCH(CH_3)_2$ was obtained as white oil. Yield 1.90 g (90%).

^{1}H NMR (CH_2Cl_2): δ 8.12 (s, 1, 3-$CF_3C_6H_4$*(2)*CCl), 8.03 (d, J(H-H) = 8.05 Hz, 1, 3-$CF_3C_6H_4$*(4)*CCl), 7.56 (d, J(H-H) = 7.71 Hz, 1, 3-$CF_3C_6H_4$*(6)*CCl), 7.43 (m, 1, 3-$CF_3C_6H_4$*(5)*CCl), 4.02 (m, 1, Cl=NC*H*(CH_3)$_3$), 1.12 (d, J(H-H) = 6.39 Hz, 6, Cl=NCH(C*H*$_3$)$_2$).

4-Chloro-*N*-isopropyl benzamide

To a solution of 4-chlorobenzoyl chloride (10 mmol, 1.75 mL) and Et_3N (10 mmol, 1.01 mL) in Et_2O (100 mL) was slowly added isopropyl amine (12 mmol, 0.7 mL). The reaction mixture was stirred overnight at ambient temperature. The solvent was removed in vacuum and the product was washed with hexane (30 mL). Compound 4-Chloro-*N*-isopropyl benzamide was obtained as a white powder after removal of hexane in vacuum. Yield 0.75 g (38%).

^{1}H NMR ($CDCl_3$): δ 7.69 (d, J(H-H) = 8.60 Hz, 2, ClC_6H_4), 7.40 (d, J(H-H) = 8.60 Hz, 2, ClC_6H_4), 5.87 (s, br, 1, CON*H*), 4.30 (sep, J(H-H) = 6.61 Hz, 1, C*H*(CH_3)$_2$), 1.27 (d, J(H-H) = 6.61 Hz, 6, CH(C*H*$_3$)$_2$).

4-$ClC_6H_4CCl=NCH(CH_3)_2$

To a solution of 4-Chloro-*N*-isopropyl benzamide in CH_2Cl_2 was added 1 eq. of PCl_5 and the reaction mixture was stirred for overnight at room temperature. Solvent was

then removed in vacuum and compound 4-$ClC_6H_4CCl{=}NCH(CH_3)_2$ was obtained as yellow oil. Yield 0.60g (79%).

^{1}H NMR (CH_2Cl_2): δ 7.77 (d, J(H-H) = 8.84 Hz, 2, 4-ClC_6H_4*(m)*CCl), 7.23 (d, J(H-H) = 8.47 Hz, 2, 4-ClC_6H_4*(o)*CCl), 3.98 (m, 1, Cl=NC*H*$(CH_3)_2$), 1.10 (d, J(H-H) = 6.08 Hz, 6, Cl=NCH(C*H*$_3)_2$).

4-$CH_3OOCC_6H_4CONHCH(CH_3)_2$

To a solution of methyl-4-(chlorocarbonyl)benzoate (7 mmol, 1.4 g) and Et_3N (8 mmol, 0.81 mL) in Et_2O (100 mL) was slowly added isopropyl amine (8 mmol, 0.48 mL). The reaction mixture was stirred overnight at ambient temperature. The solvent was removed in vacuum and the product was washed with hexane (30 mL). Compound 4-$CH_3OOCC_6H_4CONHCH(CH_3)_2$ was obtained as a pale yellow powder after removal of hexane in vacuum. Yield 1.2 g (77%).

^{1}H NMR (CH_2Cl_2): δ 7.92 (d, J(H-H) = 8.01 Hz, 2, $CH_3OC_6H_4$), 7.64 (d, J(H-H) = 8.45 Hz, 2, $CH_3OC_6H_4$), 5.87 (s, br, 1, CON*H*), 4.07 (sep, J(H-H) = 6.75 Hz, 1, C*H*$(CH_3)_2$), 3.77 (s, 3, C*H*$_3OC_6H_4$), 1.10 (d, J(H-H) = 6.62 Hz, 6, CH(C*H*$_3)_2$).

4-$CH_3OOCC_6H_4CCl{=}NCH(CH_3)_2$

To a solution of 4-$CH_3OOCC_6H_4CONHCH(CH_3)_2$ in CH_2Cl_2 was added 1 eq. of PCl_5 and the reaction mixture was stirred for overnight at room temperature. Solvent was then removed in vacuum and compound 4-$CH_3OOCC_6H_4CCl{=}NCH(CH_3)_2$ was obtained as light yellow powder. Yield 1.27g (98%).

^{1}H NMR (CH_2Cl_2): δ 7.94 (m, 4, 4-$CH_3OOCC_6H_4$CCl), 4.18 (m, 1, Cl=NC*H*$(CH_3)_2$), 3.78 (s, 3, 4-C*H*$_3OOCC_6H_4$CCl), 1.24 (d, J(H-H) = 6.26 Hz, 6, CNCH(C*H*$_3)_2$).

V.5.3. Reduction of iminoyl chlorides

Reduction of iminoyl chlorides to imines

$PhCH=NCH_2Ph$

In a representative procedure, to a solution of $HSiMe_2Ph$ (145.0 μL, 1.04 mmol) and $PhCCl=NCH_2Ph$ (150.0 mg, 0.69 mmol) in CD_2Cl_2 was added a solution of $[CpRu(PPr^i_3)(CH_3CN)_2]PF_6$ (20 mg, 0.034 mmol) and t-BuCN (15 μL, 0.17 mmol) in CD_2Cl_2. The reaction was periodically monitored by NMR spectroscopy. $PhCH=NCH_2Ph$ was obtained as a product.

$PhCH=NCH_2Ph$

^1H NMR ($CDCl_3$): δ 8.44 (s, 1, PhC*H*=NCH_2Ph), 7.39 (m, 10, *Ph*CH=NCH*2Ph*), 4.88 (s, 2, PhCH=NC*H*$_2$Ph). ^1H-^{13}C HSQC (CD_2Cl_2): δ 162.1 (s, Ph*C*H=NCH_2Ph), 127.05, 130.82 (s, *Ph*CH=NCH*2Ph*), 65.4 (s, PhCH=N*C*H_2Ph).

t-$BuCH=NCH_2Ph$

^1H NMR ($CDCl_3$): δ 7.69 (s, 1, $(CH_3)_3C$*H*=NCH_2Ph), 7.26 (m, 5, $(CH_3)_3CH=NCH_2$*Ph*), 4.61 (s, 2, $(CH_3)_3CH=NC$*H*$_2$Ph), 1.15 (s, 1, $(C$*H*$_3)_3CH=NCH_2Ph$). ^1H-^{13}C HSQC (CD_2Cl_2): δ 173.5 (s, $(CH_3)_3$*C*H=NCH_2Ph), 126.8, 127.6, 128.4 (s, $(CH_3)_3CH=NCH_2$*Ph*), 64.5 (s, $(CH_3)_3CH=N$*C*H_2Ph), 27.0 (s, $(C$*H*$_3)_3CH=NCH_2Ph$).

4-$CH_3OC_6H_4CH=NCH_2Ph$

^1H NMR (CH_2Cl_2): δ 7.54 (d, J(H-H) = 8.83 Hz, 2, CH_3OC_6*H*$_4$), 7.06 (m, 2, CH_2*Ph*), 6.97 (m, 3, CH_2*Ph*), 6.67 (d, J(H-H) = 8.88 Hz, 2, CH_3OC_6*H*$_4$), 4.59 (s, 2, C*H*$_2$), 3.67 (s, 3, OC*H*$_3$).

$PhCH{=}NC_6H_4COCH_3$

^{1}H NMR ($CDCl_3$): δ 8.52 (s, 1, Ph*C**H***=$NC_6H_4COCH_3$), 7.27 (m, 4, ***Ph***$CH{=}NC_6$***H***$_4COCH_3$), 2.66 (s, 3, $PhCH{=}NC_6H_4COC$***H***$_3$). ^{1}H-^{13}C HSQC (CD_2Cl_2): δ 26.8 (s, $PhCH{=}NC_6H_4CO$***C***H_3), 161.4 (s, Ph***C***$H{=}NC_6H_4COCH_3$).

$CH_3CH_2CH{=}NC_6H_4COCH_3$

^{1}H NMR (CH_2Cl_2): δ 7.74 (t, 1, C***H***), 7.38 (m, 2, NC_6***H***$_4COCH_3$), 7.17 (m, 2, NC_6***H***$_4COCH_3$), 2.42 (s, 3, OC***H***$_3$), 2.22 (m, 2, CH_3C***H***$_2$), 1.02 (t, 3, C***H***$_3CH_2$).

$CH_3CH_2CH{=}NC_6H_4COOCH_2CH_3$

^{1}H NMR (CH_2Cl_2): δ 7.81 (d, J(H-H) = 9.11 Hz, 2, C_6***H***$_4$), 7.69 (t, 1, C***H***), 6.83 (d, J(H-H) = 9.11 Hz, 2, C_6***H***$_4$), 4.14 (m, 2, OC***H***$_2CH_3$), 2.27 (m, 2, CHC***H***$_2CH_3$), 1,21 (m, 3, OCH_2C***H***$_3$), 1.01 (t, 3, $CHCH_2C$***H***$_3$).

$CH_3CH_2CH{=}NPh$

^{1}H NMR (CH_2Cl_2): δ 7.69 (t, 1, C***H***), 7.38 (m, 2, N***Ph***), 6.98 (t, 1, N***Ph***), 6.82 (d, J(H-H) = 6.96 Hz, 2, N***Ph***), 2.25 (m, 2, CH_3C***H***$_2$), 1.01 (t, 3, C***H***$_3CH_2$).

3-$CF_3C_6H_4CH{=}NCH(CH_3)_2$

^{1}H NMR (CH_2Cl_2): δ 8.38 (s, 1, 3-$CF_3C_6H_4C$***H***$=$N), 8.07 (s, 1, 3-CF_3C_6***H***$_4$), 7.95 (d, J(H-H) = 7.53 Hz, 1, 3-CF_3C_6***H***$_4$), 7.72 (m, 1, 3-CF_3C_6***H***$_4$), 7.56 (m, 1, 3-CF_3C_6***H***$_4$), 3.61 (m, 1, CH_3C***H***CH_3), 1.30 (s, 3, CH_3CHC***H***$_3$), 1.28 (s, 3, C***H***$_3CHCH_3$).

4-$ClC_6H_4CH{=}NCH(CH_3)_2$

^{1}H NMR (CH_2Cl_2): δ 8.11 (s, 1, 4-ClC_6H_4C***H***$=$N), 7.51 (d, J(H-H) = 8.75 Hz, 2, 4-ClC_6***H***$_4$), 7.23 (d, J(H-H) = 8.23 Hz, 2, 4-ClC_6***H***$_4$), 3.38 (m, 1, CH_3C***H***CH_3), 1.09 (s, 3, CH_3CHC***H***$_3$), 1.07 (s, 3, C***H***$_3CHCH_3$).

Isolation of imines

PhCCl=NCH$_2$Ph

In a representative procedure, to a mixture solution of PhCH=NCH$_2$Ph and ClSiMe$_2$Ph in Hexane was added 1 eq. of 2 M HCl in Et$_2$O. The precipitate was then dissolved in Et$_2$O and 1.2 eq. of Et$_3$N was added. The solution was filtered and the filtrate was dried under vacuum. Compound PhCH=NCH$_2$Ph was obtained as yellow oil. Yield 0.42 g (43 %).

^{1}H NMR (CDCl$_3$): δ 8.44 (s, 1, PhC*H*=NCH$_2$Ph), 7.39 (m, 10, *Ph*CH=NCH*2Ph*), 4.88 (s, 2, PhCH=NC*H*$_2$Ph). ^{1}H-^{13}C HSQC (CD$_2$Cl$_2$): δ 162.1 (s, Ph*C*H=NCH$_2$Ph), 127.05-130.82 (s, *Ph*CH=NCH*2Ph*), 65.4 (s, PhCH=N*C*H$_2$Ph). IR (neat): υ (C=N) =1025 cm^{-1}.

t-BuCH=NCH$_2$Ph

To a mixture solution of (CH$_3$)$_3$CH=NCH$_2$Ph and ClSiMe$_2$Ph in Hexane was added 1 eq. of 2 M HCl in Et$_2$O. The precipitate was then dissolved in Et$_2$O and 2 eq. of Et$_3$N was added. The solution was filtered and the filtrate was dried under vacuum. Compound (CH$_3$)$_3$CH=NCH$_2$Ph was obtained as pale green oil. Yield 0.15 g (57 %).

^{1}H NMR (CDCl$_3$): δ 7.69 (s, 1, (CH$_3$)$_3$C*H*=NCH$_2$Ph), 7.26 (m, 5, (CH$_3$)$_3$CH=NCH$_2$*Ph*), 4.61 (s, 2, (CH$_3$)$_3$CH=NC*H*$_2$Ph), 1.15 (s, 1, (C*H*$_3$)$_3$CH=NCH$_2$Ph). ^{1}H-^{13}C HSQC (CD$_2$Cl$_2$): δ 64.5 (s, (CH$_3$)$_3$CH=NC*H*$_2$Ph), 27.0 (s, (*C*H$_3$)$_3$CH=NCH$_2$Ph), 173.5 (s, (CH$_3$)$_3$*C*H=NCH$_2$Ph), 128.4, 127.6, 126.8 (s, (CH$_3$)$_3$CH=NCH$_2$*Ph*), IR (neat): υ (C=N) =1029 cm^{-1}.

PhCH=NC$_6$H$_4$COCH$_3$

To a mixture solution of PhCH=NPhCOCH$_3$ and ClSiMe$_2$Ph in Hexane was added 1 eq. of 2 M HCl in Et$_2$O. The precipitate was then dissolved in Et$_2$O and 1.2 eq. of

Et_3N was added. The solution was filtered and the filtrate was dried under vacuum. Compound $PhCH{=}NPhCOCH_3$ was obtained as yellow oil. Yield 0.114 g (40 %).

^1H NMR ($CDCl_3$): δ 8.52 (s, 1, $PhC\mathit{H}{=}NC_6H_4COCH_3$), 7.27 (m, 4, $\mathit{Ph}CH{=}NC_6\mathit{H}_4COCH_3$), 2.66 (s, 3, $PhCH{=}NC_6H_4COC\mathit{H}_3$). ^1H-^{13}C HSQC (CD_2Cl_2): δ 26.8 (s, $PhCH{=}NC_6H_4CO\mathit{C}H_3$), 161.4 (s, $Ph\mathit{C}H{=}NC_6H_4COCH_3$), IR (neat): υ (C=N) =1074 cm^{-1}.

Reduction of iminoyl chlorides to aldehydes

3-$CF_3C_6H_4CCl{=}NCH(CH_3)_2$

After the reaction was completed, the catalyst was removed by extracting with hexane. Then the mixture of 3-$CF_3C_6H_4CH{=}NCH(CH_3)_2$ and $ClSiMe_2Ph$ was hydrolysed by adding 1M H_2O/HCl. The 3-$CF_3C_6H_4CHO$ and $PhMe_2SiOSiMe_2Ph$ were then extracted with CH_2Cl_2 and the solution was dried over $MgSO_4$. The 3-CF_3PhCHO was isolated by chromatography over silica using 15:1 hexane : ethyl acetate as eluent to afford the product as a white oil. (89 mg, 64% yield).

3-$CF_3C_6H_4CHO$

^1H NMR (CH_2Cl_2): δ 10.02 (s, 1, $C_6H_4C\mathit{H}O$), 8.10 (s, 1, $CF_3C_6\mathit{H}_4$(2)), 8.03 (d, J(H-H) = 8.15 Hz, 1, $CF_3C_6\mathit{H}_4$(4)), 7.84 (d, J(H-H) = 8.15 Hz, 1, $CF_3C_6\mathit{H}_4$(6)), 7.64 (t, 1, $CF_3C_6\mathit{H}_4$(5)). ^{19}F NMR ($CDCl_3$): δ -62.94 (s, 1, 3-$C\mathit{F}_3C_6H_4CHO$). ^1H-^{13}C HSQC ($CDCl_3$): δ 186.3 ($C_6H_4\mathit{C}HO$) 132.4 ($CF_3\mathit{C}_6H_4$(4)), 131.0 ($CF_3\mathit{C}_6H_4$(6)), 129.7 ($CF_3\mathit{C}_6H_4$(5)), 126.5 ($CF_3\mathit{C}_6H_4$(2)).

***N*-benzylthiophene-2-carbiminoyl chloride**

100% conversion was achieved in 4 h and a mixture of products was obtained. After the reaction was completed, the catalyst was removed by extracting with hexane. Then the mixture was hydrolysed by adding H_2O/HCl, extracted with CH_2Cl_2 and the

solution was dried over $MgSO_4$. The CH_2Cl_2 solution contains $PhMe_2SiOSiMe_2Ph$ but does not contain the corresponding aldehyde. The H_2O solution does not contain the aldehyde either.

4-$ClC_6H_4CCl=NCH(CH_3)_2$

After the reaction was completed, the catalyst was removed by extracting with hexane. Then the mixture of 4-$ClC_6H_4CH=NCH(CH_3)_2$ and $ClSiMe_2Ph$ was hydrolysed by adding 1M H_2O/HCl. The 4-ClC_6H_4CHO and $PhMe_2SiOSiMe_2Ph$ were then extracted with CH_2Cl_2 and the solution was dried over $MgSO_4$. The 4-ClC_6H_4CHO was isolated by chromatography over silica using 20:1 hexane : ethyl acetate as eluent to afford the product as a white solid. (71 mg, 51% yield).

4-ClC_6H_4CHO

^{1}H NMR (CH_2Cl_2): δ 9.86 (s, 1, C_6H_4CHO), 7.70 (d, J(H-H) = 8.35 Hz, 2, ClC_6H_4), 7.41 (d, J(H-H) = 8.35 Hz, 2, ClC_6H_4). ^{13}C NMR (CH_2Cl_2): δ 190.4 (C_6H_4CHO) 140.5 (4-ClC_6H_4*(4)*), 134.7 (4-ClC_6H_4*(1)*), 130.7 (4-ClC_6H_4*(3,5)*), 129.2 (4-ClC_6H_4*(2,6)*).

4-$(CH_3)_2NC_6H_4CCl=NCH(CH_3)_2$

100% conversion was achieved in 4 h and a mixture of products was obtained. After the reaction was completed, the catalyst was removed by extracting with hexane. Then the mixture was hydrolysed by adding H_2O/HCl, extracted with CH_2Cl_2 and the solution was dried over $MgSO_4$. The CH_2Cl_2 solution contains $PhMe_2SiOSiMe_2Ph$ but does not contain the corresponding aldehyde.

4-$CH_3OOCC_6H_4CCl=NCH(CH_3)_2$

After the reaction was completed, the catalyst was removed by extracting with hexane. Then the mixture of 4-$CH_3OOCC_6H_4CH=NCH(CH_3)_2$ and $ClSiMe_2Ph$ was hydrolysed by adding 1M H_2O/HCl. The 4-$CH_3OOCC_6H_4CHO$ and $PhMe_2SiOSiMe_2Ph$ were then extracted with CH_2Cl_2 and the solution was dried over

$MgSO_4$. The 4-$CH_3OOCC_6H_4CHO$ was isolated by chromatography over silica using 15:1 hexane : ethyl acetate as eluent to afford the product as a white powder. (75 mg, 46% yield).

4-$CH_3OOCC_6H_4CHO$

^{1}H NMR (CH_2Cl_2): δ 9.96 (s, 1, C_6H_4CHO), 8.05 (d, J(H-H) = 8.15 Hz, 2, 4-$CH_3OOCC_6H_4$), 7.81 (d, J(H-H) = 8.15 Hz, 2, 4-$CH_3OOCC_6H_4$), 3.81 (s, 3, 4-$CH_3OOCC_6H_4$). ^{1}H-^{13}C HSQC (CH_2Cl_2): δ 191.5 (C_6H_4CHO), 129.9 (4-$CH_3OOCC_6H_4$), 129.1 (4-$CH_3OOCC_6H_4$), 52.3 (4-$CH_3OOCC_6H_4$).

VI. Appendix

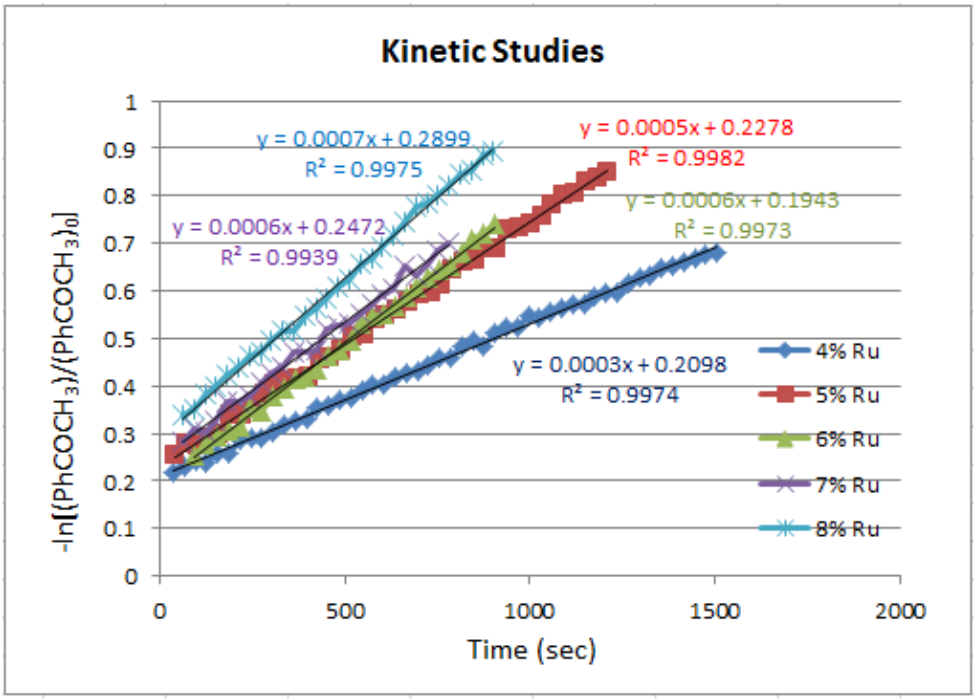


Figure 16. The dependence of –Ln(1-[substrate]/[substrate]$_0$) on time with 4 – 8 mol % **2**

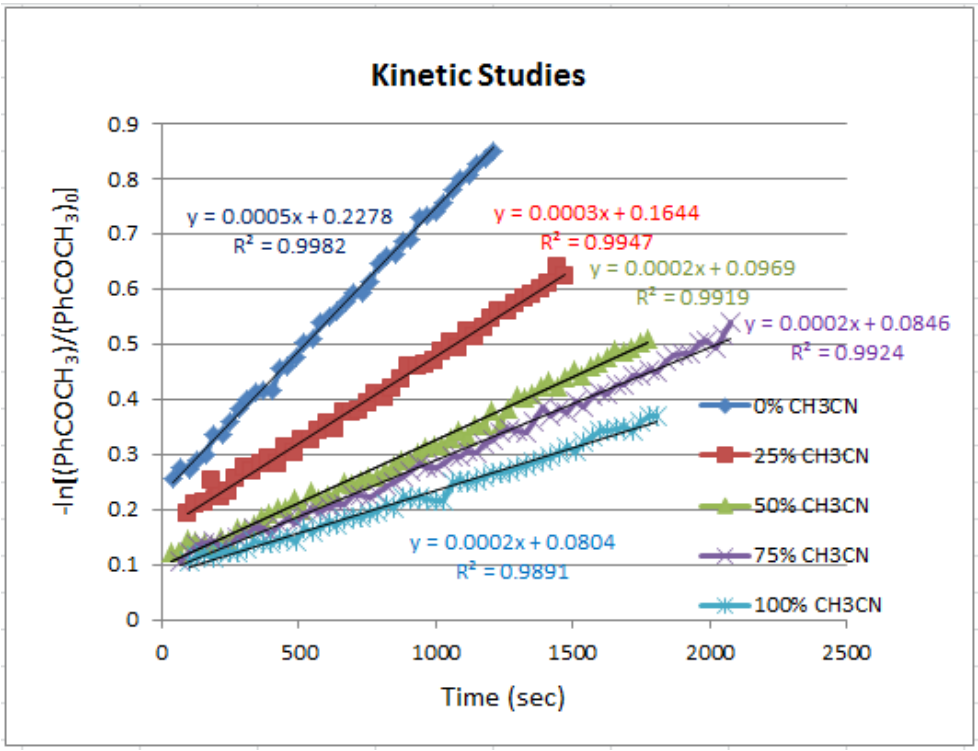


Figure 17. The dependence of –Ln(1-[substrate]/[substrate]$_0$) on time with 0 - 100 mol % CH_3CN

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