Top Organomet Chem (2014) 48: 19–44
DOI: 10.1007/3418_2014_77

Published online: 22 March 2014

Hydrogenation of Polar Bonds Catalysed by Ruthenium-Pincer Complexes

Ekambaram Balaraman and David Milstein

Abstract Catalytic hydrogenation of polar bonds using molecular hydrogen is an important, atom-economical synthetic reaction. Classical reduction methods of polar bond often require reactive metal-hydride reagents in stoichiometric amount and produce copious waste. Hydrogenation of carbonyl compounds in particular provides 'green' approaches to synthetically important building blocks, such as alcohols and amines. We have designed and synthesized several ruthenium-based pincer catalysts for unprecedented hydrogenation reactions including: (1) amides to alcohols and amines, (2) biomass-derived di-esters to 1,2-diols and (3) CO_2 and CO derivatives to methanol. These atom-economical reactions operate under neutral, homogeneous conditions, at mild temperatures, mild hydrogen pressures, and can operate in absence of solvent with no generation of waste. The postulated mechanisms involve metal–ligand cooperation (MLC) by aromatization–dearomatization of the heteroaromatic pincer core.

Keywords Amides · Carbon dioxide · Esters · Hydrogen · Hydrogenation · Metal–ligand cooperation · Pincer complexes · Ruthenium

Contents

E. Balaraman (✉)
Catalysis Division, CSIR-National Chemical Laboratory, Dr. Homi Bhabha Road, Pashan, Pune 411008, India
e-mail: eb.raman@ncl.res.in

D. Milstein
Department of Organic Chemistry, Weizmann Institute of Science, Rehovot 76100, Israel
e-mail: david.milstein@weizmann.ac.il

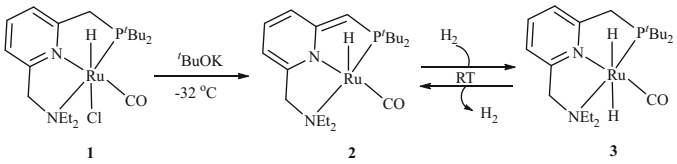
1 Introduction and Background

Design of new catalytic reactions for selective organic transformations is essential for the development of 'green' approaches to industrially important processes, which traditionally employ stoichiometric reagents and/or harsh conditions. Among organic transformations that are frequently used in industries, the reduction of compounds bearing polar carbonyl groups, such as esters and amides, is one of the most important reactions [1, 2]. Traditionally reduction of polar bonds is carried out by the use of toxic, reactive metal-hydride reagents in stoichiometric amounts, which produces copious waste and employs tedious procedures, making these methods problematic environmentally and economically [3–5].

In contrast, hydrogenation of polar bonds with gaseous hydrogen under mild conditions provides an atom-economical, environmentally benign and operationally simple synthetic process [6–10]. Noyori's well-defined catalysts for hydrogenation of carbonyl compounds gave a new dimension to the homogeneous hydrogenation catalysts [11–13]. On the other hand, the hydrogenation of uncreative carbonyl compounds, particularly carboxylic acid derivatives such as esters and amides, as well as carbonic acid derivatives such as dialkyl carbonates and carbamates, as well as urea derivatives, is still challenging.

In recent years, pincer ligands which bind to metal centres in a tri-dentate, meridional fashion have drawn much attention and serve as excellent ligands, due to stability and variability of the generated metal–ligand framework [14–17]. The donor/acceptor ability at both the central and adjacent side-arm positions of the pincer ligands can be controllable. And both the electronic and steric environment around the metal centre can also be tuneable.

We have developed several unique reactions catalysed by PNN and PNP Ru(II) pincer complexes based on pyridine, bipyridine and acridine backbones. These complexes show a new mode of metal–ligand cooperation (MLC) [18] based on ligand aromatization–dearomatization, which has led to a number of bond activation processes [19–22]. Deprotonation of a methylenic side-arm proton of pyridyl- and bypridyl-based pincer complexes leads to the corresponding dearomatized, coordinatively unsaturated 16 electron complexes. The dearomatized complex, which activates the dihydrogen by cooperation between the Ru-metal centre and the ligand, leads to *trans*-dihydride complex, thereby regaining aromatization (Scheme 1). This aromatization–dearomatization process is reversible and it can form the basis for efficient catalytic systems of both dehydrogenation of O–H



Scheme 1 Preparation of dearomatized PNN-Ru(II) complex and its reactivity towards H_2

bonds and selective hydrogenation of polar carbonyl compounds, including very challenging and less studied compounds. In this chapter we describe straightforward hydrogenation of various carbonyl compounds, in particular, carboxylic and carbonic acid derivatives catalysed by Ru(II)-pincer complexes. We have also reported Fe(II)-pincer catalysed hydrogenation of ketones and CO_2 under very mild conditions [23–25].

2 Synthesis of H-Ru(II)pincer Complexes and Activation of Dihydrogen via Metal–Ligand Cooperation Approach

Our approach towards activation of molecular hydrogen and hydrogenation reactions is based on the metal–ligand cooperation concept (MLC). In this section we describe the synthesis of Ru(II)-H pincer complexes prepared by our group and their activity towards activation of dihydrogen.

Dihydrogen addition to the bulky, electron-rich dearomatized pyridine-based Ru(II)PNN-complex **2** results in heterolytic dihydrogen cleavage (a hydride added to the metal centre and a 'proton' to the ligand), to form the coordinatively saturated, *trans*-dihydride complex **3** via MLC. It is important to note that the bond activation process does not involve a change in the formal oxidation state of the metal [26, 27]. Formation of *trans*-dihydride is a key step in the catalytic hydrogenation of polar bonds in our systems. The magnetically equivalent *trans*-dihydride resonates as a doublet at −4.08 ppm (J_{PH} = 17.1 Hz) in complex **3**. The complex slowly loses an H_2 molecule at room temperature to regenerate complex **2**. A single-crystal X-ray diffraction study of **3** (Fig. 1) reveals a distorted octahedral geometry around the ruthenium(II) centre, with the CO ligand coordinated *trans* to the pyridyl nitrogen atom.

Selected bond distances (Å): Ru1-N1 2.101 (3), Ru1-N2 2.251 (3), Ru1-P3 2.252 (1), Ru1-C1 1.821 (4), H1A-Ru1 1.71(4) Å, (H1B-Ru1 was not refined).

Selected bond angles (deg.): N1-Ru1-C1 175.0 (2), N1-Ru1-P3 82.6 (1), N1-Ru1-N2 78.0 (1), N2-Ru1-P3 160.6 (1), N2-Ru1-C1 104.8 (2), C1-Ru1-P3 94.6 (1).

The electron-rich bipyridine-based Ru(II)-PNN pincer complex **4** was synthesized by the reaction of the tridentate ligand, BPy-^{tBu}PNN (**5**) with [RuHCl(PPh_3)$_3$(CO)] in THF at 65°C (Scheme 2). The single-crystal X-ray structure of

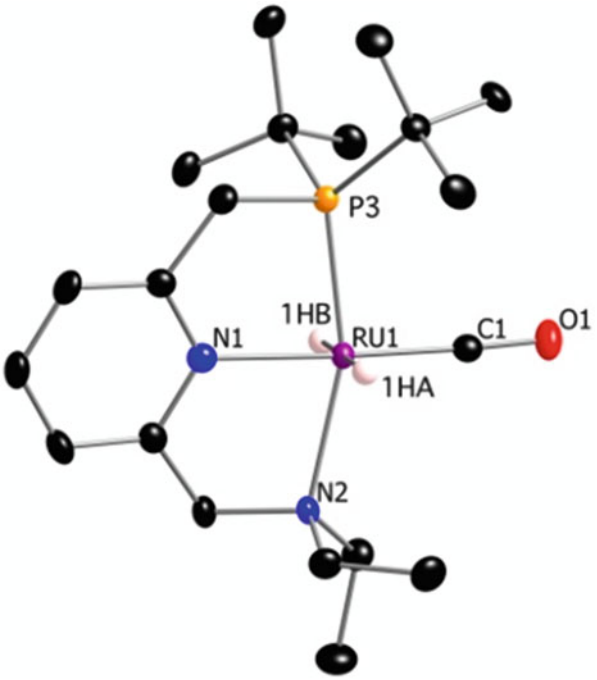
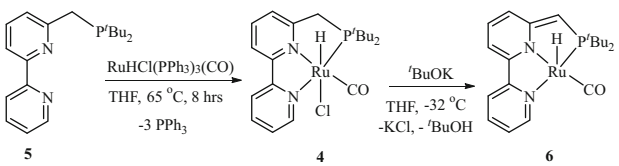


Fig. 1 X-ray structure of complex **3** (50% probability level). Hydrogen atoms (except hydrides) are omitted for clarity



Scheme 2 Synthesis of bipyridine-based H-Ru(II) Pincer complexes (**4** and **6**)

4 (Fig. 2) reveals a distorted octahedral geometry around the ruthenium centre, with the CO ligand coordinated *trans* to the central nitrogen atom of the pincer system, and the hydride *trans* to the chloride ligand [28]. Deprotonation of complex **4** with KO^{t}Bu at −32°C gave the dearomatized, coordinatively unsaturated complex **6** in good yield. The fully characterized **6** gives rise to doublet at −20.93 ppm ($^2J_{PH}$ = 25.0 Hz) in the ^{1}H NMR spectrum. The "arm" vinylic proton appears as singlet at 3.36 ppm and a doublet at 66.56 (J_{PC} = 48.8 Hz) in ^{13}C{^{1}H} NMR spectrum, indicating formation of an anionic PNN system.

Selected bond distances (Å): Ru1–N1 2.124(2), Ru1–N2 2.086(2), Ru1–P1 2.2859(7), Ru1–C20 1.861(3).

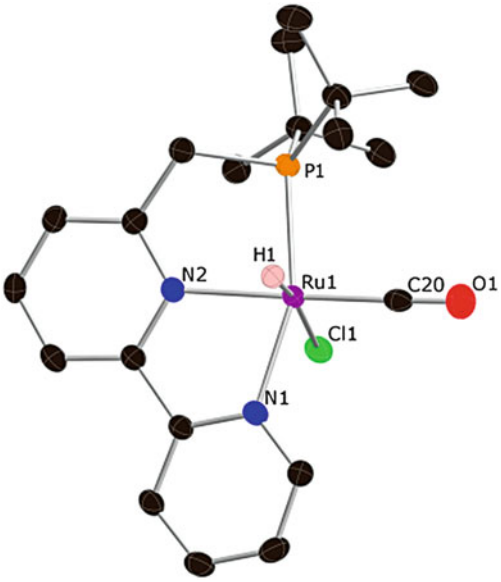
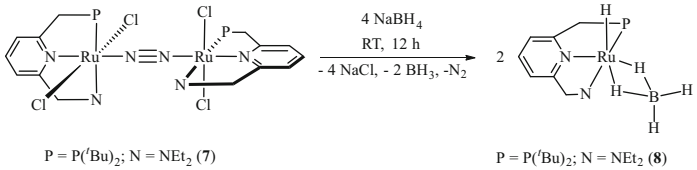


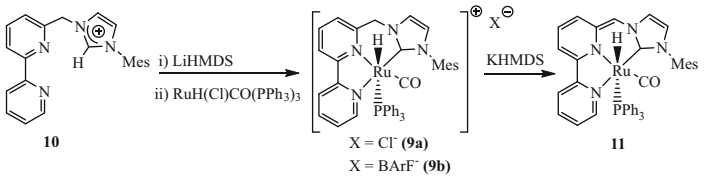
Fig. 2 X-ray structure of complex **4** (50% probability level). Hydrogen atoms (except hydride) are omitted for clarity



Scheme 3 Synthesis of ruthenium(II) hydrido borohydride complex **8**

Selected angles (deg): N2–Ru1–C20 173.34(10), N2–Ru1–H1 86.4(9), Cl1–Ru1–H1 170.4(9), N1–Ru1–P1 159.65(6).

In analogy to the *trans*-dihydride complex **3**, the Ru(II) hydridoborohydride complex **8** was prepared from the N_2-bridged binuclear complex $[(RuCl_2(^t$Bu-PNN$))_2](\eta^2$-$N_2)$ **7** [29]. Treatment of **7** with an excess (5 equiv.) of $NaBH_4$ in 2-propanol for 12 h resulted in the formation of complex **8** in excellent yield (Scheme 3). The hydride ligand of complex **8** gives rise to a doublet at −16.24 ppm with $J_{PH} = 28.0$ Hz in the ^{1}H NMR spectrum. The IR spectrum of **8** exhibits two strong bands in the terminal B-H region at 2,378 and 2,311 cm^{-1} and two bands in the bridging Ru-H-B region at 2,096 and 1,956 cm^{-1}, consistent with



Scheme 4 Synthesis of NHC-based H-Ru(II)-pincer complexes

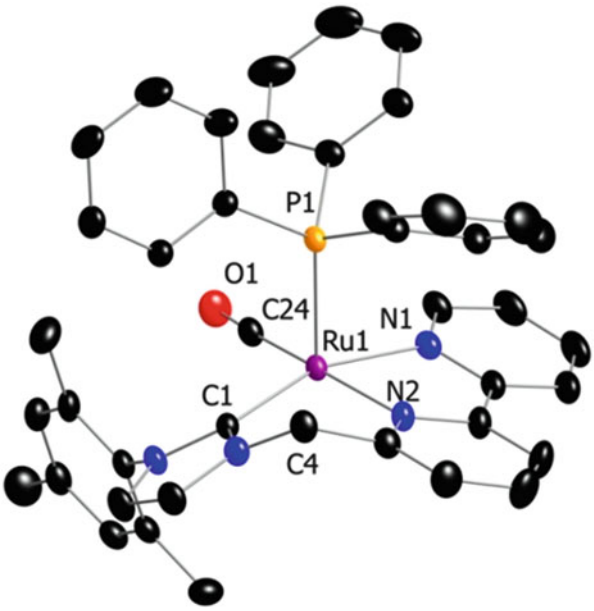


Fig. 3 ORTEP plot of complex **9b**. Hydrogen atoms and counter anion are omitted for clarity. Ellipsoids are drawn at 50% probability level

the bidentate η^2-BH_4 bonding mode. Complex **8** showed an interesting fluxional behaviour of the BH_4^- ligand [30].

The NHC analogue (**9a**) of the bipyridine-based Ru(II)-PNN pincer complex **4** was prepared by treatment of the in situ generated free NHC ligand (**10**) with $RuH(Cl)CO(PPh_3)_3$ (Scheme 4) [31]. Complex **9a** gives rise to a doublet at −7.96 ppm (J_{PH} = 106 Hz) in the ^{1}H NMR for the hydride ligand. The counter anion was exchanged with $BArF^-$ (tetrakis[(3,5-trifluoromethyl)phenylborate) and crystals of **9b** suitable for X-ray diffraction were grown from a pentane-ether solution. The X-ray structure of **9b** (Fig. 3) exhibits the CO ligand *trans* to the central nitrogen atom of the pincer system and the location of the hydride is *trans* to the phosphine. Deprotonation of complex **9a** with KHMDS in benzene or toluene resulted in formation of the dearomatized complex **11** as the only product. The hydride ligand of complex **11** resonates a doublet at −7.13 ppm (J_{PH} = 142.0 Hz)

in the ^{1}H NMR spectrum. The "arm" vinylic proton appears as a singlet at 5.87 ppm and the corresponding carbon exhibits a singlet at 89.7 ppm in the $^{13}C\{^{1}H\}$ NMR spectrum. Complexes (**2**, **6**, **8** and **11**) were used as catalysts for hydrogenation of carboxylic acid derivatives under neutral, homogeneous conditions and the results are discussed in the following sections.

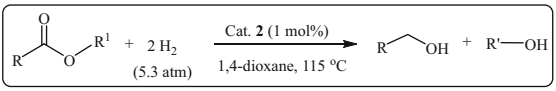
3 Catalytic Hydrogenation of Carbonyl Groups

Catalytic hydrogenation of carbonyl (C=O) groups using molecular hydrogen is a fundamentally important transformation and remains a challenging task in the context of hydrogen storage and sustainable chemistry. The order of susceptibility to nucleophilic attack by the hydride at the carbonyl carbon generally corresponds to the *hydridophilicity* of this carbon [32]. The lower *hydridophilicity* as a result of resonance effects involving alkoxy or amido group makes hydrogenation of carboxylic acid derivatives, in particular, esters, amides, and even more so, carbonic acid derivatives, such as organic carbonates, carbamates and urea derivatives, very difficult and less explored. The general trend in the ease of hydrogenation of polar carbonyl groups is $RC(O)H > RC(O)R' > > RC(O)OR' > RC(O)NR_2' >> > ROC(O)OR' > ROC(O)NR_2' > R_2NC(O)N_2R'$ [33, 34].

3.1 Efficient Hydrogenation Esters and Related Compounds

3.1.1 Hydrogenation of Non-activated Esters to the Corresponding Alcohols

While there are many examples of Ru-catalysed hydrogenations of ketones and aldehydes [7, 11], and recently Fe-catalysed hydrogenation of ketones was also reported [35–39], including our system based on pincer-iron complexes [24, 25], catalytic hydrogenation of esters, particularly non-activated ones, under mild conditions is a challenging task [6, 7, 9, 10, 40, 41]. In pioneering work by Elsevier et al. various aromatic and aliphatic esters were hydrogenated in fluorinated solvent using in situ prepared ruthenium complexes bearing P,P,P ligands at high pressure of dihydrogen under basic conditions [42]. In 2006, we originally reported hydrogenation of non-activated esters to corresponding alcohols under mild, neutral conditions, catalysed by well-defined Ru(II) pincer complex **2** under low hydrogen pressure (5.3 atm) [27]. The reaction is general, both aliphatic and aromatic esters were hydrogenated to corresponding alcohols under very mild conditions without the use of any additives (Fig. 4). The reaction provides an environmentally benign protocol for the synthesis of alcohols from esters, without the need of traditionally used classical approaches (reduction of esters using toxic, reactive aluminium hydrides and the Bouveault–Blanc reduction of esters with alkali metals in ethanol).



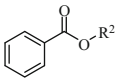
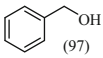
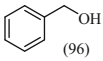
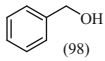
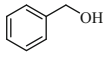
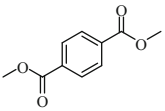
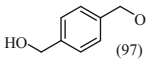
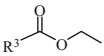
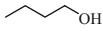
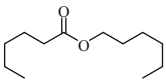
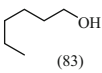
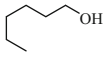
Entry	Ester		Time (hrs)	Conv. (%)	Yield (%)	
					RCH_2OH	R'-OH
1		$R^2 = -CH_3$	4	100	 (97)	CH_3OH (100)
		$R^2 = -CH_2CH_3$	4	99	 (96)	CH_3CH_2OH (99)
		$R^2 = -CH_2Ph$	7	99	 (98)	
2			5	100	 (97)	2 CH_3OH (100)
3		$R^3 = -CH_2CH_2CH_3$	4	100	 (98)	CH_3CH_2OH (99)
		$R^3 = -CH_3$	12	86	CH_3CH_2OH (86)	CH_3CH_2OH
4			5	83	 (83)	

Fig. 4 Hydrogenation of esters to alcohols catalysed by Ru(II)PNN pincer complex (**2**)

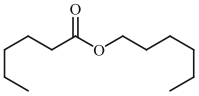
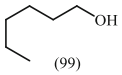
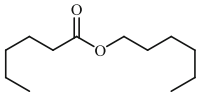
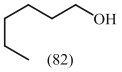
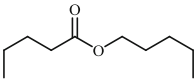
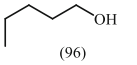
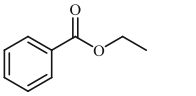
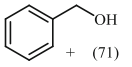
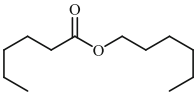
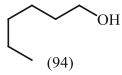
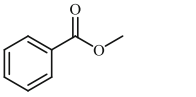
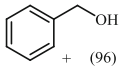
The conventional reduction methods encounter very serious drawbacks such as the use of hazardous reagents, challenging work-up procedures, safety, and crucially, generation of large amounts of waste [3, 43].

Typical Hydrogenation Procedure:

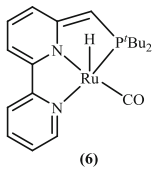
A 90 mL Fischer–Porter tube was charged under nitrogen with the catalyst **2** (0.02 mmol), an ester (2 mmol) and 1,4-dioxane (2 mL) followed by filled with H_2 (5.3 atm). The solution was heated at 115°C (actual solution temperature) with stirring for the specified period. After cooling to room temperature, excess H_2 was vented carefully and the product yields were determined by GC.

Other catalysts (in Sect. 2) prepared in our laboratory were also employed for the hydrogenation of non-activated esters under mild conditions [30, 44]. The results are summarized in Fig. 5. Notably, higher turnover numbers (up to 3,284 TON) were obtained using complex **6** as a catalyst at 50 atm of dihydrogen for the hydrogenation of hexyl hexanoate (Fig. 5, entry 2).

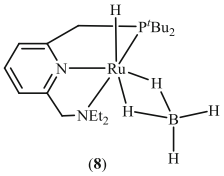
Subsequent to our original work, several reports on hydrogenation of esters to alcohols catalysed by various Ru(II) pincer complexes appeared (Scheme 5)

Entry	Ester	Catalyst	Reaction condition	Conv. (%)	Yield (%)	TON
1		**6**	**6** (0.01 mmol), ester (20 mmol), PH_2 = 50 atm, THF (5 mL), Temp. = 110 °C, t = 16 hrs	100	 (99)	2000
2		**6**	**6** (0.005 mmol), ester (20 mmol), PH_2 = 50 atm, THF (5 mL), Temp. = 110 °C, t = 16 hrs	82	 (82)	3284
3		**9a**	**9a** + ^{t}BuOK (each 0.01 mmol), ester (1 mmol), PH_2 = 5.4 atm, Toluene (2 mL), Temp. = 135 °C, t = 2 hrs	96	 (96)	96
4		**9a**	**9a** + ^{t}BuOK (each 0.025 mmol), ester (1 mmol), PH_2 = 5.4 atm, Toluene (2 mL), Temp. = 135 °C, t = 2 hrs	72	 + (71) CH_3CH_2OH (69)	2840
5		**8**	**8** (0.01 mmol), ester (2 mmol), PH_2 = 10 atm, THF (2 mL), Temp. = 110 °C, t = 12 hrs	94	 (94)	188
6		**8**	**8** (0.01 mmol), ester (2 mmol), PH_2 = 10 atm, THF (2 mL), Temp. = 110 °C, t = 12 hrs	97	 + (96) CH_3OH (93)	194

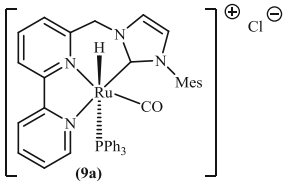
Catalysts:



(6)



(8)



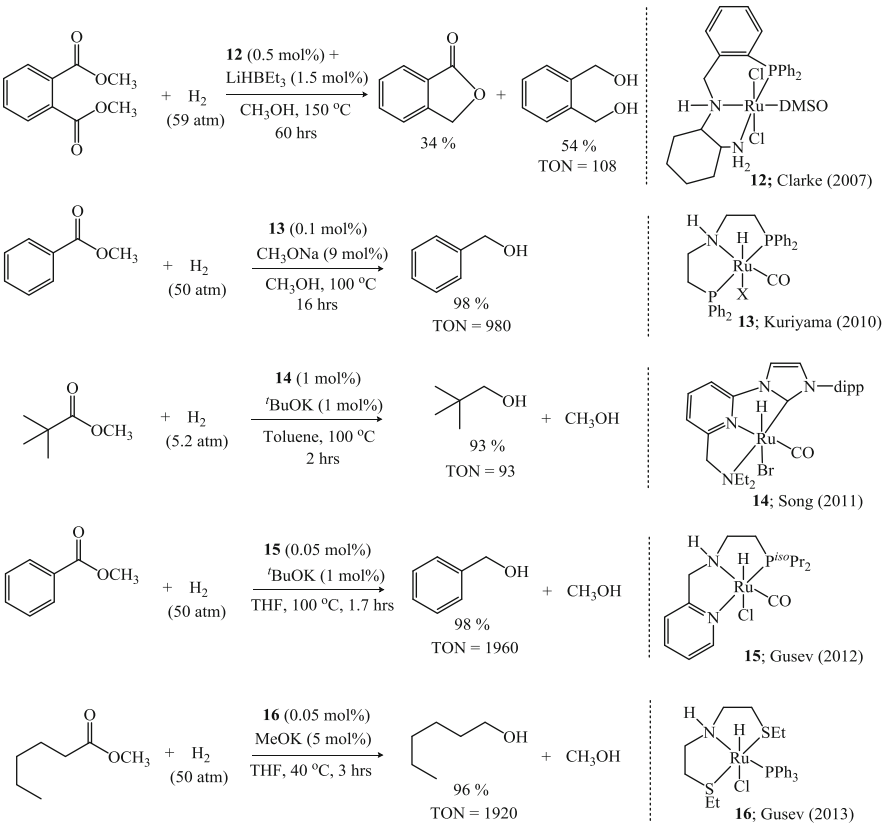
(9a)

Fig. 5 Catalytic hydrogenation of non-activated esters to alcohols

[45–51]. Very recently, Ikariya et al. reported the selective hydrogenation of α-fluorinated esters to fluorinated alcohols and fluoralhemiacetal intermediates catalysed by commercially available complex **13** under mild, homogeneous conditions [52]. For a recent review on hydrogenation of polar bonds, including esters, see [10].

3.1.2 Complete Hydrogenation of Biomass-Derived Di-esters to 1,2-diols

A selective, complete hydrogenation of cyclic di-esters, in particular the biomass-derived glycolide and lactide to the corresponding 1,2-diols was accomplished



Scheme 5 Ru(II) pincer complexes for homogeneous hydrogenation of esters to alcohols

using bipyridine-based pincer complexes (**6** and **11**) [53]. This method offers an environmentally benign approach to the indirect transformation of biomass to important synthetic building blocks, ethylene glycol and propylene glycol. Significantly, no racemization took place when a chiral di-ester (L-lactide) was used (Fig. 6).

Hydrogenation Procedure:

Catalyst (0.2–1 mol%), di-esters, H_2 and dry THF (3–5 mL) were heated in a Fischer–Porter tube or a high-pressure reactor at 110°C (oil bath temperature) and the yields of 1,2-diols were analysed by GC. In the case of complex **9a**, 1 equiv. (relative to Ru) of KO^{t}Bu was used for the in-situ generation of the dearomatized catalyst.

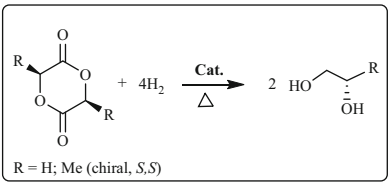


Fig. 6 Hydrogenation of cyclic di-esters to 1,2-diols

Entry	Cat.	Ester R	$P(H_2)$ atm	Yield	TON
1	**6**	R = H	10	93	93
2	**6**	R = H	50	85	425
3	**9a**	R = H	50	58	290
4	**6**	R = Me (chiral, *S,S*)	10	82	82
5	**6**	R = Me (chiral, *S,S*)	50	91	455
6	**9a**	R = Me (chiral, *S,S*)	50	67	335

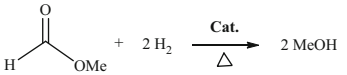
3.1.3 Straightforward Hydrogenation of Organic Formates to Methanol

The selective hydrogenation of methyl formate to methanol, catalysed by the Ru(II)-PNN complexes **2–3** and **6**, proceeds efficiently under mild, neutral conditions using low hydrogen pressure, and low temperature, without generation of any waste or by-products and in high turnover numbers was reported by us [54]. The reaction proceeds very well also under neat conditions without using any solvents, representing an ultimate "green" hydrogenation reaction (Fig. 7). The reaction is general and other alkyl formate esters are also hydrogenated efficiently leading to methanol and the corresponding alcohols (ethyl formate to methanol and ethanol and butylformate to methanol and *n*-butanol, respectively) in excellent yields without formation of CO [55–57].

Reaction Conditions:

Catalyst, methyl formate, H_2 and dry THF (3–5 mL) were heated in a Fischer–Porter tube or a high-pressure reactor at specified temperature and the yields of methanol were quantified on GC.

A possible mechanism for general ester hydrogenation to alcohols is depicted in Fig. 8. Initially, reaction of coordinatively unsaturated dearomatized complex **2** with H_2 leads to the fully characterized *trans*-dihydride (**3**) via metal–ligand cooperation (MLC). Decoordination of the hemilabile amine 'arm' can provide a site for ester to coordinate with ruthenium centre, and forming intermediate **A**. Hydride transfer to the ester carbonyl gives hemiacetoxy intermediate **B**. Subsequent coordination of amine arm followed by dearomatization of the pincer core regenerate the original complex **2** with elimination of a hemiacetal, which is in



Entry	Cat.	Solvent	Temp. (°C)	PH_2 (atm)	Time (hrs)	Conv. (%)	Yield (%)	TON
1	**2**	THF	110	10	48	78	77	1155
2	**3**	THF	110	10	48	84	81	1215
3	**6**	THF	110	10	48	96	96	1440
4	**6**	THF	110	50	14	94	94	4700
5	**6**	Neat	80	10	8	~99	98	980

Fig. 7 Hydrogenation of methyl formate to methanol

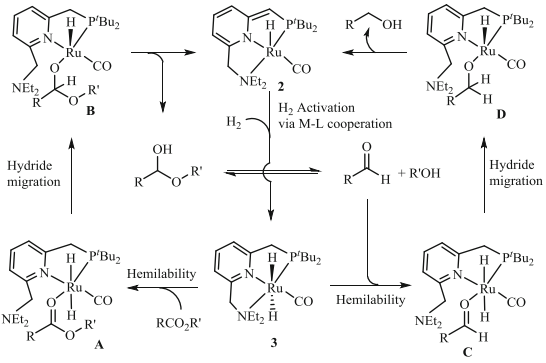
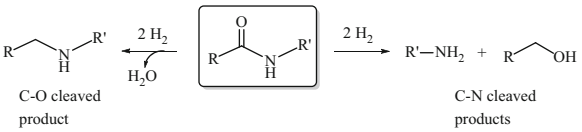


Fig. 8 Proposed catalytic cycle for the hydrogenation of esters to alcohols by complex **2**

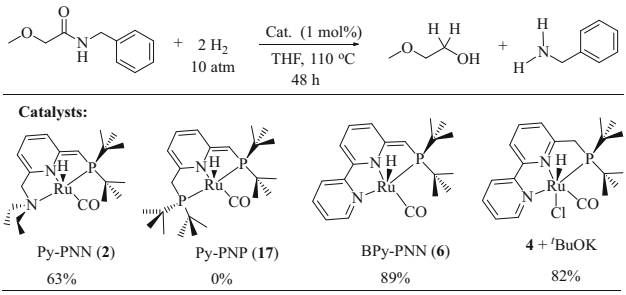
equilibrium with the aldehyde. In general, aldehydes are more susceptible to undergo hydrogenation much faster than esters and thus following the similar catalytic cycle (involving the intermediates **C** and **D**) to lead to the corresponding alcohol. The direct attack of the *trans*-dihydride on the ester carbonyl group, without prior coordination, is also possible. Based on DFT calculations, Hasanayn and his co-workers reported a metathesis-type mechanism [58], in which a hydride transfer from Ru-H to esters can directly lead to aldehyde and Ru-alkoxide in the hydrogenation of esters catalysed complex **2**. This approach can give a new dimension to an active catalyst design for future directions.

3.2 Selective Hydrogenation of Amides to Alcohols and Amines

Among the carboxylic acid derivatives amides, bearing a less electrophilic (hydridophilic) carbonyl group, are the most challenging substrates to hydrogenate



Scheme 6 Possible pathways for the hydrogenation of amides



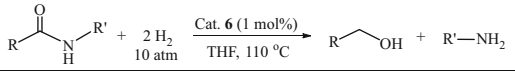
Scheme 7 Hydrogenation of amides using various pincer catalysts

[59, 60]. Possible pathways for the hydrogenation of amides are shown in Scheme 6. A few cases of reductive cleavage of the C=O bond with the formation of a secondary amine were reported [61–65].

The (unprecedented at the time) selective hydrogenation of amides (both aliphatic and aromatic) to the corresponding alcohols and amines in excellent yields, involving C–N bond cleavage was selectively catalysed by **2** and **6** under mild hydrogen pressure and temperature [28], the expected products of C–O cleavage not being formed. Initial screening (Scheme 7; Fig. 9) showed that the bipyridyl-based Ru(II)-pincer complex (**6**) was a more effective catalyst than the pyridyl-based PNN-Ru(II) pincer complex (**2**). Later, other reports on the hydrogenation of amides to alcohols and amines were reported [34, 66–68].

Like in the case of **2**, the bipyridine-based Ru(II)-PNN pincer complex **6** plausibly displays a novel type of metal–ligand cooperative activity through aromatization–dearomatization processes. Recently, a DFT calculation on classical C–O cleavage *vs* our newly reported C–N bond breaking in the amide hydrogenation reaction was reported by Cantillo [69].

In continuation of our research on design of novel catalysts for selective organic transformations, we have synthesized more flexible, expanded PNN-type pincer ruthenium complexes (**18**–**20**). However, only modest catalytic activity and selectivity was observed with these bridged-bipyridine-based PNN-Ru(II) complexes in amide hydrogenation (25–65% yields) and other reactions [70]. This is likely a result of cyclometalation of the active species **21** and **22**, which is detrimental to the catalysis (Scheme 8; Fig. 10). The low stability of the expected dearomatized complex (**20a**) formed by deprotonation of **20** was also detrimental to catalysis.



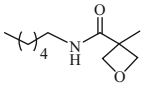
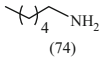
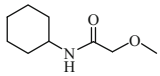
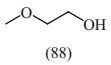
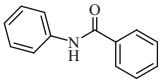
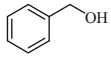
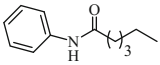
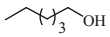
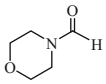
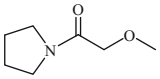
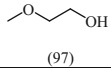
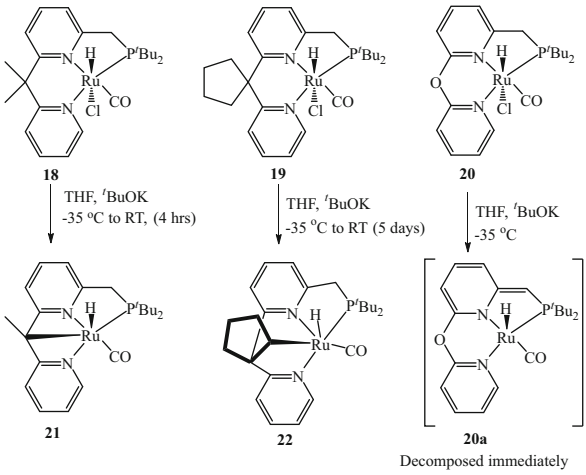
Entry	Amide	Products (yield [%]) Alcohol	Amine
1		 (74)	 (74)
2		 (88)	 (87)
3		 (92)	 (91)
4		 (92)	 (92)
5		EtOH (97)	 (98)
6		MeOH (97)	 (98)
7		 (97)	 (97)

Fig. 9 Selective hydrogenation of amides to the corresponding alcohols and amines catalysed by complex **6**



Scheme 8 Cyclometalated Ru(II)-pincer complexes

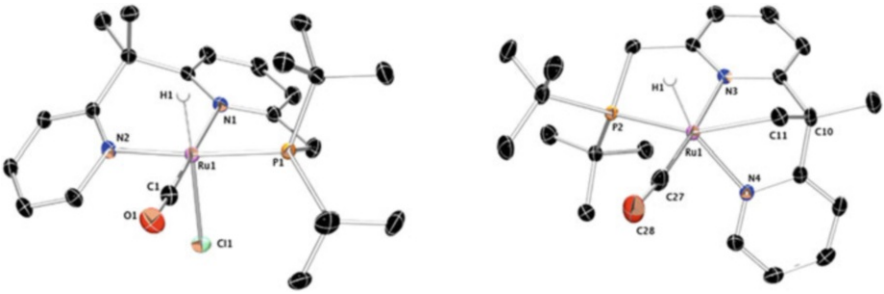


Fig. 10 ORTEP drawing at 50% of probability of Ru(II) complexes **18** and **21.** Hydrogen atoms (except hydride) are omitted for clarity

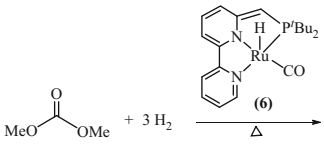
3.3 Hydrogenation of CO_2 Derivatives to Methanol

3.3.1 Selective Hydrogenation of Organic Carbonates (e.g., DMC) to Methanol

In continuation of our research aimed at sustainable catalytic hydrogenation of various demanding substrates, we reported yet another unprecedented hydrogenation of extremely challenging polar carbonyl compounds, including organic carbonates, carbamates and urea derivatives selectively to methanol, which can serve as an efficient energy storage chemical and a convenient fuel-substitute in the foreseeable future. Catalytic hydrogenation of these important families of compounds under very mild operational conditions is of significant interest, since these compounds can be produced from CO_2 and CO, and their selective hydrogenation would ultimately represent an indirect approach to transformation of C1 sources (CO_2 and CO) to fuel, which is of intense current interest with regard to "methanol economy" [71–74].

The simplest organic carbonate, dimethyl carbonate (DMC), serves as a stable and 'green' solvent [75], and is even used as an inert solvent for hydrogenation reactions under extremely harsh conditions with regard to temperature and pressure. In industry, DMC is produced from CO or CO_2 either by oxidative carbonylation of methanol or by straightforward synthesis from CO_2 and methanol, respectively [76–79]. The hydrogenation of DMC to methanol under mild conditions (either by heterogeneous or homogeneous) has not previously been achieved, prior to our report [54].

Dimethyl carbonate was quantitatively hydrogenated into methanol under mild, neutral conditions, catalysed by the Ru(II)-pincer complexes **2–3** and **6** under low hydrogen pressure and relatively low temperature with high TON (up to 4,400 after 14 h). Moreover, the hydrogenation of dimethyl carbonate proceeds smoothly under *solvent free* conditions in case of catalyst **2** and TON more than 990 were achieved after 8 h.



Entry	Solvent	PH_2 (atm)	Time (hrs)	Conv. (%)	Yield (%)	TON
1	THF	10	48	96	96	960
2	THF	50	14	89	88	4400
3	Neat	10	2	89	89	890
4	Neat	10	8	>99	>99	>990

Fig. 11 Hydrogenation of dimethyl carbonate to methanol catalysed by BPy-PNN Ru(II) (**6**)

The attractive characteristics of DMC hydrogenation to methanol, namely solvent free, waste-free, atom-economical, mild pressure and temperature, high turnover numbers (TON), and high selectivity, represent an ultimate green process and make this catalytic transformation an attractive technology for methanol synthesis [80–82]. Some representative examples catalysed by complex **6** are presented in Fig. 11 (vide supra).

Based on model stoichiometric experiments and known metal–ligand cooperation by aromatization–dearomatization of the pincer complex **2**, a mechanism for the selective hydrogenation of dimethyl carbonate to methanol is proposed (Fig. 12). A possible catalytic cycle is as follows: (1) formation of the *trans*-dihydride complex **3** via metal–ligand cooperation (MLC), (2) hydride transfer from the *trans*-dihydride complex to dimethyl carbonate may lead to intermediate **A** which forms methanol by deprotonation of the pincer ligand, generating the methyl formato-dearomatized complex **B**, (3) hydrogen addition and hydride transfer to the coordinated formato moiety forming intermediate **C**, followed by proton abstraction from the pincer ligand leads to methanol and the formaldehyde complex **D**. Addition of hydrogen to form complex **23**, followed by methanol elimination regenerated the dearomatized complex **2** and completes the catalytic cycle.

Recently, density functional computation on hydrogenation of dimethyl carbonate to methanol, catalysed by Ru(II)-PNN catalyst **2** supported a stepwise hydrogenation mechanism (Fig. 13) [83, 84]. A hydride/methoxide metathesis-based mechanism was suggested by DFT [85].

Ding and co-workers demonstrated the hydrogenation of cyclic carbonates selectively to methanol and corresponding diols [86] in good yields catalysed by complex **13** using 0.05 mol% and catalytic amount of base under 50 atm of hydrogen pressure and at 140°C (Scheme 9).

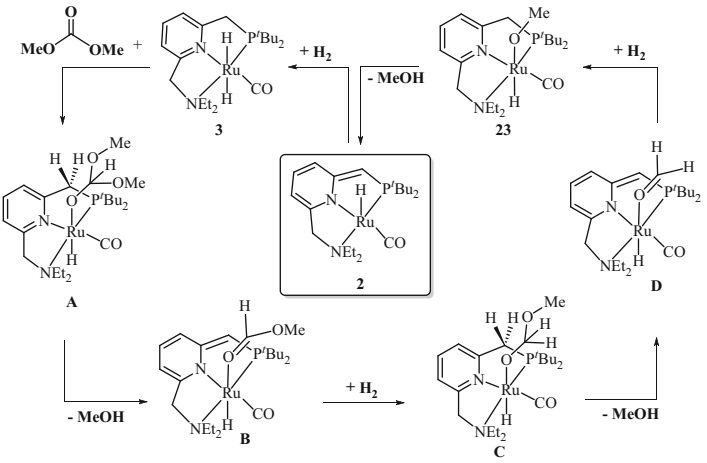


Fig. 12 Postulated mechanism for the selective hydrogenation of DMC to methanol catalysed by **2**

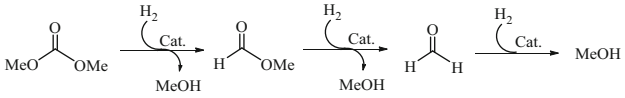
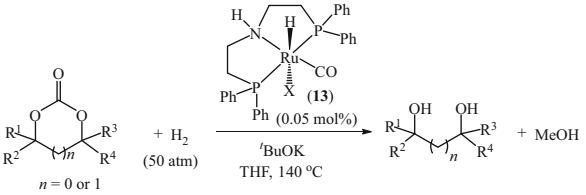


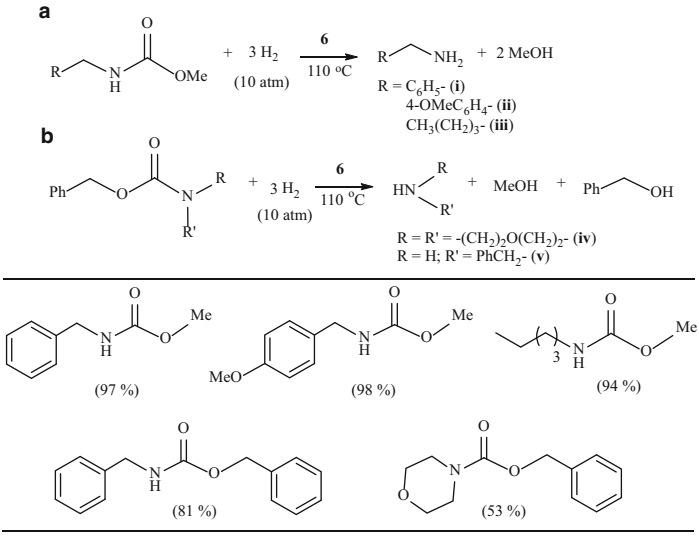
Fig. 13 Catalytic stepwise hydrogenation of DMC to methanol



Scheme 9 Hydrogenation of cyclic carbonates to methanol and diols [86]

3.3.2 Catalytic Hydrogenation of Carbamates by BPy-PNN Ru(II) Pincer Complex (6)

We have reported the first example of catalytic hydrogenation of carbamates to selectively form methanol and the corresponding amines and alcohols, without cleavage of the arylalkyl-O bond under mild hydrogen pressure and neutral conditions, with no generation of waste, using catalyst **6** (Scheme 10, yields are based on methanol) [54]. The reaction proceeds well with 1 mol% of complex **6**. In contrast to the well-known hydrogenation of benzyl carbamates by heterogeneous catalysts (e.g. Pd/C), in which the carbonyl group is not reduced, forming CO_2, amine and

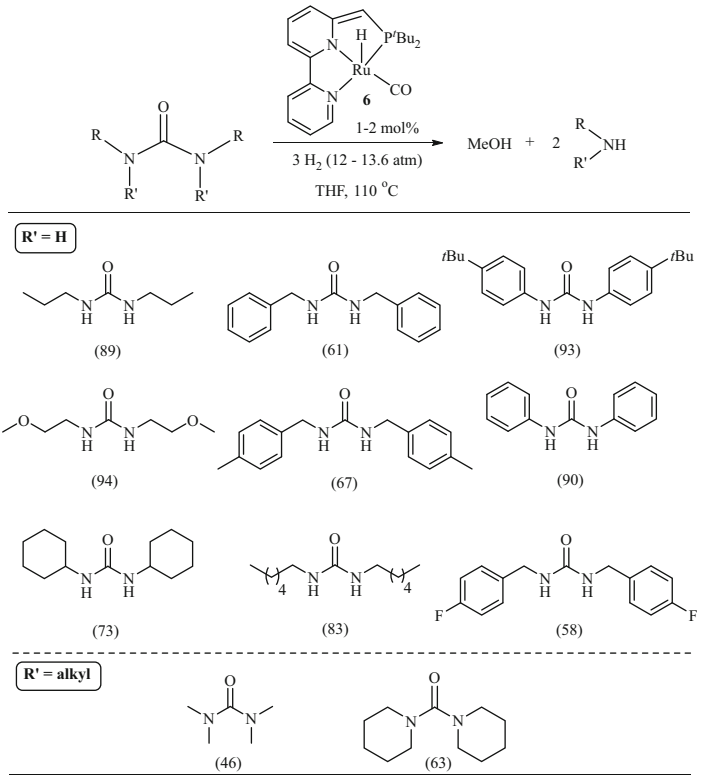


Scheme 10 Catalytic hydrogenation of (**a**) methyl and (**b**) benzyl carbonates to methanol

hydrocarbon, with no methanol formation [87], the Ru(II) pincer complex **6** catalyses hydrogenation of the carbonyl group, forming methanol, together with the corresponding alcohols and amines. Notably, carbamates are derivatives of CO_2 and synthetic methods for their formation are well established [78, 88, 89].

3.3.3 Hydrogenation of Urea Derivatives to Methanol and Amines

Among carbonyl compounds, hydrogenation of urea derivatives is the most challenging due to the low electrophilicity of the carbonyl group as a result of the resonance effect. Notably, alkyl urea compounds have been used as solvents in catalytic hydrogenation reactions of other compounds and as 'green' solvents in metal-mediated organic transformations [90, 91]. Unprecedented hydrogenation of urea derivatives was achieved with complex **6** as catalyst. In this process, cleavage of two strong C–N bonds takes place, using various alkyl- and aryl- urea derivatives, selectively producing methanol and the respective amines in high yield under mild reaction conditions, namely 110°C and 13.6 atm H_2 pressure [92]. Traces of formamides were observed in several cases, confirming the stepwise hydrogenation mechanism (urea to formamide to methanol) like in the case of dimethyl carbonate hydrogenation (Scheme 11; GC yields are based on methanol). Since alkyl- and aryl-urea derivatives are readily obtained from CO_2 and amines [93], their hydrogenation offers an environmentally benign, mild, atom-economical approach to the indirect transformation of CO_2 to methanol [81].

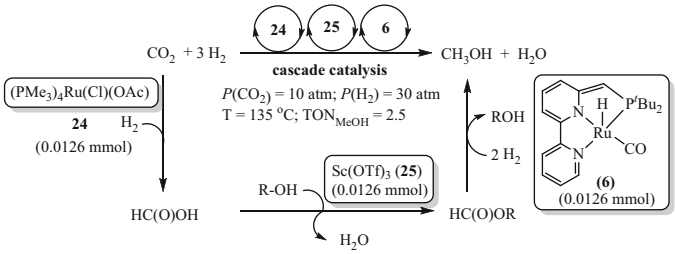


Scheme 11 Unprecedented hydrogenation of urea derivatives to methanol and amines catalysed by **6**

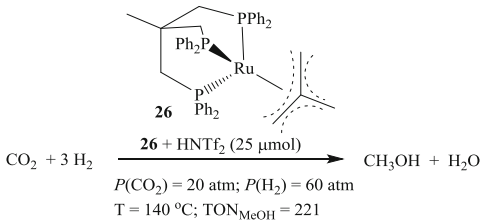
4 Direct Hydrogenation of CO_2

Sanford et al. recently demonstrated "cascade catalysis" aimed at the direct hydrogenation of CO_2 to methanol by using a $(PMe_3)_4Ru(Cl)(CO)$ **24/** $Sc(OTf)_3$ **25/** (BPy-PNN^-)RuH(CO) **6** homogeneous catalyst combination to effect the stepwise (CO_2 to $HC(O)OCH_3$ [via HC(O)OH] to CH_3OH) hydrogenation with low TON (2.5) [94]. The cascade direct hydrogenation of CO_2 to methanol involves three steps, (1) conversion of CO_2 to formic acid affected by Jessop's catalyst (**24**), (2) Lewis-acid catalysed esterification of formic acid with methanol to provide methyl formate and (3) effective methyl formate hydrogenation by (BPy-PNN^-) RuH(CO) **6** to liberate 2 equiv. of CH_3OH (Scheme 12).

Direct hydrogenation of CO_2 to methanol was recently reported by Klankermayer and Leitner using a non-pincer catalytic system, comprised of a ruthenium(II)-complex [(triphos)Ru-(TMM)] **26** (TMM = trimethylenemethane), and an acid, achieving turnover numbers up to 221 [95]. Catalytic *N*-methylation of secondary and primary aromatic amines using CO_2 as C1 source and molecular



Scheme 12 Triple catalyst cascade hydrogenation of CO_2 to methanol [94]



Scheme 13 Ru(II) catalysed direct hydrogenation of CO_2 to methanol [95]

hydrogen directly as reducing agent was also reported by Klankermayer and Leitner using the Ru(II)-complex **26** and an acid ($HNTf_2$) (Scheme 13) [96].

Sanford and co-workers subjected our catalyst (**2**) for highly efficient catalytic hydrogenation of CO_2 to formate salts [97] and displays similar activity to known Nozaki's Ir(III) pincer catalyst **27** (TON = 3,500,000 and TOF = 150,000 h^{-1} for CO_2 to HC(O)OK) [98, 99]. Heating a diglyme solution of complex **2**, base (K_2CO_3), carbon dioxide, and hydrogen resulted in the formation of potassium formate with excellent TON of 23,000 and TOF of up to 2,200 h^{-1}. The postulated mechanism for the hydrogenation of CO_2 by **2** is shown in Fig. 14. Hydrogenation of carbon dioxide catalysed by ruthenium(II)-PNP pincer (**17**) was reported by Pidko et al. indicating that CO_2 binding to the deprotonated pincer arm inhibits the reaction, whereas faddition of water restores reactivity [100].

Efficient hydrogenation of CO_2 using an iron-based catalyst is an important goal. Beller and co-workers reported hydrogenation of bicarbonates and carbon dioxide to formates and formamides catalysed by well-defined Fe(II) complexes [101, 102]. Thus, heating a methanol solution of $Fe(BF_4)_2.6H_2O$ and the ligand **28** (in situ generated complex **29**), $HNMe_2$ (80 mmol), carbon dioxide (30 atm), and hydrogen (30 atm) resulted in the formation of DMF (74%) and formic acid (7.7%) with TON of 5,104 (Scheme 14).

Recently, we reported an efficient hydrogenation of carbon dioxide and sodium bicarbonate to formate salt catalysed by the dihydride Fe(II)-pincer complex **30**. Carbon dioxide and sodium bicarbonate are economically hydrogenated in aqueous media at 80°C under remarkably low pressures (6–10 bar), with TON up to 788 (Scheme 15) [23].

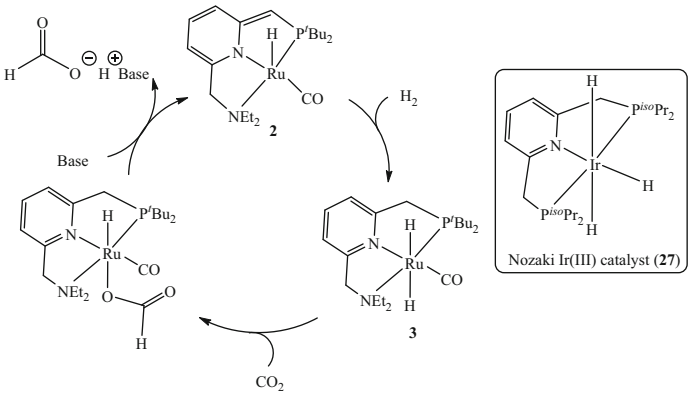
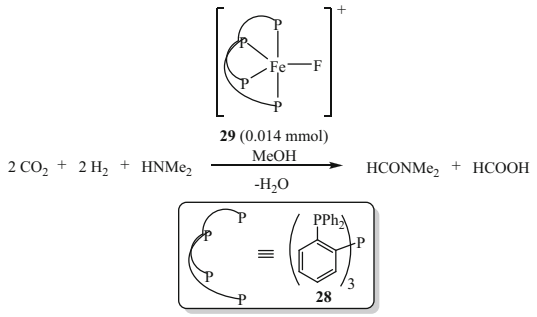
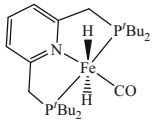


Fig. 14 Proposed catalytic cycle for the hydrogenation of CO_2 by **2**



$$2\,CO_2 + 2\,H_2 + HNMe_2 \xrightarrow[-H_2O]{\textbf{29}\ (0.014\ mmol),\ MeOH} HCONMe_2 + HCOOH$$

Scheme 14 Catalytic hydrogenation of CO_2 to formamide and formic acid by iron complex **29** (in situ generated)



$$\textbf{(a)}\quad CO_2 + H_2 + NaOH \xrightarrow[H_2O/THF\ (10:1)]{\textbf{30}\ (0.1\ mol\%)} HCOONa + H_2O$$

$$\textbf{(b)}\quad NaHCO_3 + H_2 \xrightarrow[H_2O/THF\ (10:1)]{\textbf{30}\ (0.1\ mol\%)} HCOONa + H_2O$$

Scheme 15 Iron pincer complex (**30**) catalysed hydrogenation of (**a**) CO_2 and (**b**) bicarbonate to formate salt

A possible catalytic cycle for the hydrogenation of CO_2 to formate catalysed by the iron pincer complex **30** is as follows (Fig. 15): (1) Formation of the hydrido-formato complex **31** by direct electrophilic attack of CO_2 on the *trans*-dihydride **30**,

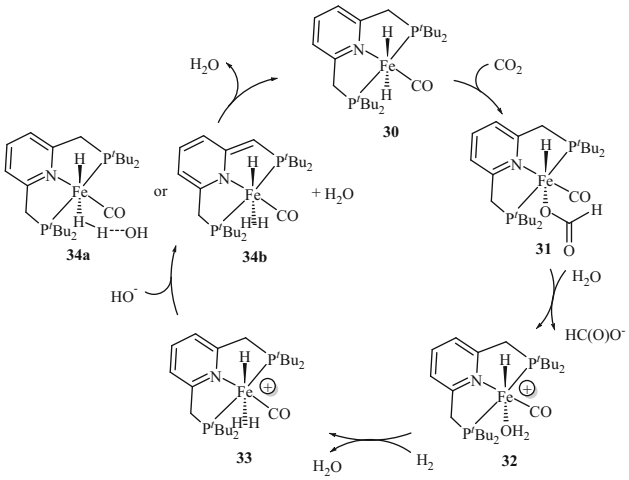


Fig. 15 Proposed mechanism for the hydrogenation of CO_2 to formate salt catalysed by the iron pincer complex **30**

(2) displacement of the formate ligand (as a formate salt) by a water molecule, forming complex **32**, (3) formation of the dihydrogen intermediate **33** under hydrogen pressure, followed by regeneration of the *trans*-dihydride **30** either by heterolytic cleavage of the coordinated H_2 by ^{-}OH (**34a**) or by dearomatization and subsequent proton migration (**34b**). Based on DFT calculations, similar catalytic cycles were postulated for iridium, cobalt and iron pincer complexes [103–105].

5 Conclusion

In this chapter, we have discussed hydrogenation of carbonyl compounds, in particular, esters, amides, and the CO_2-derived formates, carbonates, carbamates and ureas to fundamentally important building blocks, catalysed by pincer-based Ru(II) complexes. These efficient, atom-economical reactions operate under very mild low hydrogen pressure, produce no waste and provide alternative, environmentally benign approaches to traditional reduction methods, which often produce copious waste. The metal–ligand cooperation approach (MLC) significantly contributes to the reactivity and selectivity in the hydrogenation reactions. Still there is room to improve the catalytic reactivity and selectivity (e.g. in direct, efficient hydrogenation of CO_2 to methanol). The development of efficient catalysts based on iron pincer complexes is an important challenge; promising results in the hydrogenation of ketones and CO_2 were already obtained [23–25].

Acknowledgements Supported by the European Research Council (ERC) under the FP7 framework (No. 246837), Kimmel Center for Molecular Design and CSIR-NCL (start-up grant to E.B, MLP028726). D.M. is the Israel Matz Professorial Chair of Organic Chemistry.

References

1. Constable DJC, Dunn PJ, Hayler JD, Humphrey GR, Leazer HL, Linderman RJ Jr, Lorenz K, Manley J, Pearlman BA, Wells A, Zaks A, Zhang TY (2007) Green Chem 9:411
2. Aldridge S (2008) Pharm Technol Eur 20:15
3. Seyden-Penne J (1997) Reductions by alumino- and borohydrides in organic synthesis. Wiley, New York
4. Gribble GW (1998) Chem Soc Rev 27:395
5. Rothenberg G (2008) Catalysis: Concepts and Green Applications. Wiley-VCH, Weinheim
6. Clapham SE, Hadzovic A, Morris RH (2004) Coord Chem Rev 248:2201
7. Ito M, Ikariya T (2007) Chem Commun 5134
8. Kubas GJ (2007) Chem Rev 107:4152
9. Wylie WNO, Lough AJ, Morris RH (2010) Chem Commun 46:8240
10. Dub PA, Ikariya T (2012) ACS Catal 2:1718
11. Noyori R (2002) Angew Chem Int Ed 41:2008
12. Ohkuma T, Ooka H, Hashiguchi S, Ikariya T, Noyori R (1995) J Am Chem Soc 117:2675
13. Ohkuma T, Noyori R (2001) Angew Chem Int Ed 40:40
14. Albrecht M, Van Koten G (2001) Angew Chem Int Ed 40:3750
15. van der Boom ME, Milstein D (2003) Chem Rev 103:1759
16. Morales-Morales D, Jensen CM (eds) (2007) The chemistry of pincer compounds. Elsevier, Amsterdam
17. van Koten G, Milstein D (eds) (2013) Organometallic pincer chemistry. Springer-Verlag Berlin Heidelberg
18. Kanai M, Ikariya T, Ooi T, Ding K, Milstein D (2013) Recent topics in cooperative catalysis: asymmetric catalysis, polymerization, hydrogen activation, and water splitting. In: Ding K, Dai L-X (eds) Organic chemistry- breakthroughs and perspectives. Wiley-VCH, Weinheim, pp 385–412
19. Milstein D (2010) Top Catal 53:915
20. Gunanathan C, Milstein D (2011) Top Organomet Chem 37:55
21. Gunanathan C, Milstein D (2011) Acc Chem Res 44:588
22. Gunanathan C, Milstein D (2013) Science 341:249
23. Langer R, Diskin-Posner Y, Leitus G, Shimon LJW, Ben-David Y, Milstein D (2011) Angew Chem Int Ed 50:9948
24. Langer R, Leitus G, Ben-David Y, Milstein D (2011) Angew Chem Int Ed 50:2120
25. Langer R, Iron MA, Konstantinovski L, Diskin-Posner Y, Leitus G, Ben-David Y, Milstein D (2012) Chem Eur J 18:7196
26. Zhang J, Leitus G, Ben-David Y, Milstein D (2005) J Am Chem Soc 127:12429
27. Zhang J, Leitus G, Ben-David Y, Milstein D (2006) Angew Chem Int Ed 45:1113
28. Balaraman E, Gnanaprakasam B, Shimon LJW, Milstein D (2010) J Am Chem Soc 132:16756
29. Zhang J, Gandelman M, Shimon LJW, Milstein D (2007) J Chem Soc Dalton Trans 107
30. Zhang J, Balaraman E, Leitus G, Milstein D (2011) Organometallics 30:5716
31. Fogler E, Balaraman E, Ben-David Y, Leitus G, Shimon LJW, Milstein D (2011) Organometallics 30:3826
32. Carey FA, Sundberg RJ (2000) Advanced Organic Chemistry. Kluwer Academic/Plenum, New York
33. McAlees AJ, McCrindle R (1969) J Chem Soc 2425
34. Ito M, Ootsuka T, Watari R, Shiibashi A, Himizu A, Ikariya T (2011) J Am Chem Soc 133:4240
35. Casey CP, Guan H (2007) J Am Chem Soc 129:5816
36. Bullock RA (2007) Angew Chem Int Ed 46:7360
37. Morris RH (2009) Chem Soc Rev 38:2282
38. Bauer G, Kirchner KA (2011) Angew Chem Int Ed 50:5798

39. Junge K, Schröder K, Beller M (2011) Chem Commun 47:4849
40. Grey RA, Pez GP, Wallo A (1981) J Am Chem Soc 103:7536
41. Clarke ML (2012) Catal Sci Technol 2:2418
42. Teunissen HT, Elsevier CJ (1998) Chem Commun 1367
43. Vogt P, Bodnar B (2009) Spec Chem Mag 29/7:22
44. Milstein D, Balaraman E, Gunanathan C, Gnanaprakasam B, Zhang J (2012) WO 2012/052996A2
45. Clarke ML, Diaz-Valenzuela MB, Slawin AMZ (2007) Organometallics 26:16
46. Clarke ML, Roff GJ (2007) in Handbook of Homogeneous Hydrogenation 1:413; de Vries JG, Elsevier CJ (eds) Wiley, New York
47. Kuriyama W, Matsumoto T, Ino Y, Ogata O (2011) Takasago International Corporation, Japan WO2011048727A1
48. Kuriyama W, Matsumoto T, Ogata O, Ino Y, Aoki K, Tanaka S, Ishida K, Kobayashi T, Sayo N, Saito T (2012) Org Process Res Dev 16:166
49. Sun YS, Koehler C, Tan RY, Annibale VT, Song DT (2011) Chem Commun 47:8349
50. Spasyuk D, Smith S, Gusev DG (2012) Angew Chem Int Ed 51:2772
51. Spasyuk D, Smith S, Gusev DG (2013) Angew Chem Int Ed 52:2538
52. Otsuka T, Ishii A, Dub PA, Ikariya T (2013) J Am Chem Soc 135:9600
53. Balaraman E, Fogler E, Milstein D (2012) Chem Commun 48:1111
54. Balaraman E, Gunanathan C, Zhang J, Shimon LJW, Milstein D (2011) Nature Chem 3:609
55. Gormley RJ, Rao VUS, Soong Y (1992) Appl Catal A 87:81
56. Iwasa N, Terashita M, Arai M, Takezawa N (2001) React Kinet Catal Lett 74:93
57. Monti DM, Kohler MA, Wainwright MS, Trimm DL, Cant NW (1986) Appl Catal 22:123
58. Hasanayn F, Baroudi A (2013) Organometallics 32:2493
59. Robin MB, Bovey FA, Basch, H (1970) in The Chemistry of Amides (ed: Zabicky, J), Interscience, New York
60. Hartwig J (2010) Organotransition Metal Chemistry; University Science Books: Sausalito, CA
61. Nu´n˜ezMagro AA, Eastham GR, Cole-Hamilton DJ (2007) Chem Commun 3154
62. Beamson G, Papworth AJ, Philipps C, Smith AM, Whyman R (2010) Adv Synth Catal 352:869
63. Stein M, Breit B (2013) Angew Chem Int Ed 52:2231
64. Coetzee J, Deborah L. Dodds DL, Klankermayer J, Brosinski S, Leitner W, Slawin AMZ, Cole-Hamilton DJ (2013) Chem Eur J 19:11039
65. Coetzee J, Manyar HG, Hardacre C, Cole-Hamilton DJ (2013) ChemCatChem 5:2843
66. John JM, Bergens SH (2011) Angew Chem Int Ed 50:10377
67. John JM, Bergens SH (2012) Angew Chem Int Ed 51:2533
68. Miura T, Held IE, Oishi S, Naruto M, Saito S (2013) Tetrahedron Lett 54:2674
69. Cantillo D (2011) Eur J InorgChem3008
70. Barrios-Francisco R, Balaraman E, Diskin-Posner Y, Leitus G, Shimon LJW, Milstein D (2013) Organometallics 32:2973
71. Olah GA, Goeppert A, Prakash GKS (2006) Beyond Oil and Gas: The Methanol Economy. Wiley-VCH, Weinheim
72. Olah GA (2005) Angew Chem Int Ed 44:2636
73. Olah GA, Goeppert A, Prakash GKS (2009) J Org Chem 74:487
74. Cokoja M, Bruckmeier C, Rieger B, Herrmann WA, Kühn FE (2011) Angew Chem Int Ed 50:8510
75. Schaffner B, Schaffner F, Verevkin SP, Borner (2010) Chem Rev 110:4554
76. Delledonne D, Rivetti F, Romano U (1995) J Organomet Chem 448:C15
77. Delledonne D, Rivetti F, Romano U (2001) Appl Catal A 221:241
78. Sakakura T, Kohno K (2009) Chem Commun 45:1312
79. Sakakura T, Choi JC, Yasuda H (2007) Chem Rev 107:2365
80. Dixneuf PH (2011) Nature Chem 3:578

81. Choudhury J (2012) ChemCatChem 4:609
82. Li Y, Junge K, Beller M (2013) ChemCatChem 5:1072
83. Li H, Wen M, Wang Z-X (2012) Inorg Chem 51:5716
84. Yang X (2012) ACS Catal 2:964
85. Hasanayn F, Baroudi A, Bengali AA, Goldman AS (2013) Organometallics 32:6969
86. Han Z, Rong L, Wu J, Zhang L, Wang Z, Ding K (2012) Angew Chem Int Ed 51:13041
87. Kocienski PJ (2005) Protecting Groups, Thieme
88. Abla M, Choi JC, Sakakura T (2001) Chem Commun 37:2238
89. Abla M, Choi JC, Sakakura T (2004) Green Chem 6:524
90. Ohgomori Y, Mori S, Yoshida S, Watanabe Y (1987) J Mol Catl 40:223
91. Imperato G, Höger S, Lenoir D, König B (2006) Green Chem 8:1051
92. Balaraman E, Ben-David Y, Milstein D (2011) Angew Chem Int Ed 50:11702
93. Wu C, Cheng H, Liu R, Wang Q, Hao Y, Yu Y, Zhao F (2010) Green Chem 12:1811
94. Huff CA, Sanford MS (2011) J Am Chem Soc 133:18122
95. Wesselbaum S, vom Stein T, Klankermayer J, Leitner W (2012) Angew Chem Int Ed 51:7499
96. Beydoun K, vom Stein T, Klankermayer J, Leitner W (2013) Angew Chem Int Ed 52:9554
97. Huff CA, Sanford MS (2013) ACS Catal 3:2412
98. Tanaka R, Yamashita M, Nozaki K (2009) J Am Chem Soc 131:14168
99. Federsel C, Jackstell R, Beller M (2010) Angew Chem Int Ed 49:6254
100. Filonenko GA, Conley MP, Copéret C, Lutz M, Hensen EJM, Pidko EA (2013) ACS Catal 3:2522
101. Federsel C, Boddien A, Jackstell R, Jennerjahn R, Dyson PJ, Scopelliti R, Laurenczy G, Beller M (2010) Angew Chem Int Ed 49:9777
102. Ziebart C, Federsel C, Anbarasan P, Jackstell R, Baumann W, Spannenberg A, Beller M (2012) J Am Chem Soc 134:20701
103. Schmeier TJ, Dobereiner GE, Crabtree RH, Hazari N (2011) J Am Chem Soc 133:9274
104. Ahlquist MSG (2010) J Mol Catal A 324:3
105. Yang X (2011) ACS Catal 1:849

http://www.springer.com/978-3-319-08481-7

Ruthenium in Catalysis

Dixneuf, P.H.; Bruneau, C. (Eds.)
2014, VIII, 401 p. 511 illus., 27 illus. in color., Hardcover
ISBN: 978-3-319-08481-7