1
Catalysis by Pincer Complexes: Synthesis of Esters, Amides, and Peptides

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1.1
Introduction and Background

Esters, amides, amines, acetals, and peptides are important industrial chemicals. Production of these chemicals is based on multistep processes using stoichiometric amounts of acid or base promoters and coupling reagents, and involves reactive intermediates derived from alcohols or acids (Scheme 1.1), which leads to very large amounts waste [1]. Controlling overoxidation of substrates in the synthetic methods of these products is a challenge, and hence stepwise syntheses are performed (see below) [2]. Thus, green processes that can circumvent stoichiometric reagents and the generation of reactive intermediates, such as acid chlorides, and directly deliver stable and useful industrial products, such as esters and amides, in an atom-economical, selective manner without producing waste are needed.

Pincer ligands, that is, tridentate ligands that enforce meridional geometry upon complexation to transition metals, result in pincer complexes which possess a unique balance of stability versus reactivity [3]. Transition-metal complexes of bulky, electron-rich ''pincer'' ligands have found important applications in synthesis, bond activation, and catalysis [4, 5]. Among these, pincer complexes of ^{i}Pr-PNP (2,6-bis-(di-*iso*-propylphosphinomethyl)pyridine), ^{t}Bu-PNP (2,6-bis-(di-*tert*-butylphosphinomethyl)pyridine), and PNN ((2-(di-*tert*-butylphosphinomethyl)-6-diethylaminomethyl)pyridine), PNN-BPy (6-di-*tert*-butylphosphinomethyl-2,2′-bipyridine) ligands exhibit diverse reactivity [6–8]. These bulky, electron-rich pincer ligands can stabilize coordinatively unsaturated complexes and participate in unusual bond activation and catalytic processes.

In most processes, homogeneously catalyzed by metal complexes, the ligands, while imparting critical properties on the metal center, do not participate directly in bond-making and -breaking processes with the substrates. In recent years, complexes in which the ligands actively cooperate with the metal center in bond-activation processes have been developed [9]. We have devised novel catalytic systems based on pincer complexes in which the pincer ligands cooperate with the metal center in a synergistic manner and their interplay facilitates the chemical processes. The pincer complexes are based on new pyridine- and acridine-type

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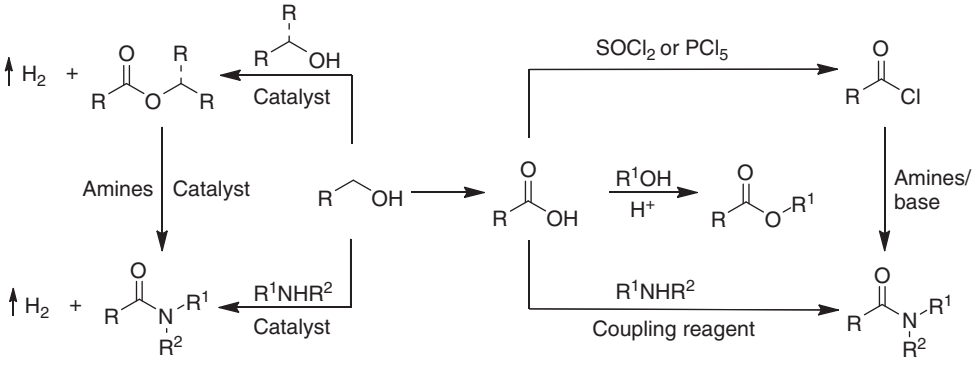
pincer ligands, which undergo bond-breaking and -making processes, involving aromatization–dearomatization of the pincer ligands [8]. Such cooperative pincer complexes catalyze several unique processes, as summarized in recent reviews [6–8, 10]. Here we concentrate on the selective synthesis of esters [11–13], amides [14, 15], acetals [16], amines [17], and imines [18], directly from alcohols. Using diols, polyesters were obtained [19]; diols and diamines provided polyamides [20, 21], and aminoalcohols resulted in formation of pyrazines and peptides [22]. Cooperative pincer complexes have also catalyzed the reverse reactions of esterification and amidation; thus, hydrogenation of esters [23, 24], formates, and carbonates [25] provides the corresponding alcohols, whereas amides give amines and alcohols [26] and urea provides methanol and amines [27]. Carbon dioxide also undergoes hydrogenation to formate salts [28] by pincer catalysts.



Scheme 1.1 Conventional versus catalytic synthesis of esters and amides.

Deprotonation of a pyridinylmethylenic proton of pyridine- and bipyridine-based pincer complexes can lead to dearomatization. The dearomatized complexes can then activate a chemical bond (H–Y, Y = H, OH, OR, NH_2, NR_2, C) by cooperation between the metal and the ligand, thereby regaining aromatization (Figure 1.1). The overall process does not involve a change in the metal's oxidation state [6–8]. In this chapter, we describe the novel, environmentally benign catalytic synthesis of esters, amides, and peptides that operate via this new metal–ligand cooperation based on aromatization–dearomatization processes.

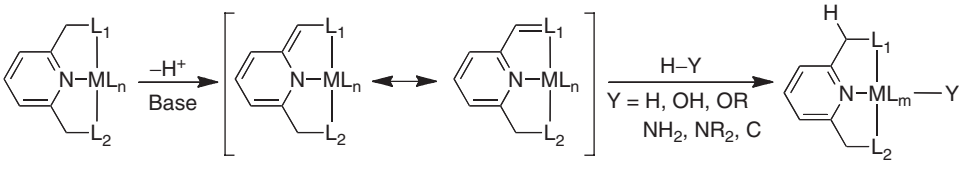
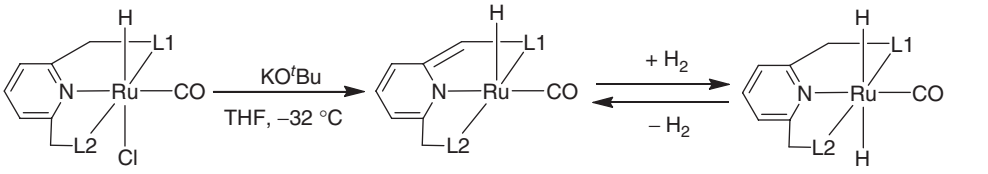


Figure 1.1 Metal–ligand cooperation based on aromatization–dearomatization.

1.2
Bond Activation by Metal–Ligand Cooperation

We have discovered a new mode of bond activation by metal–ligand cooperation based on aromatization–dearomatization of pyridine- and acridine-based heteroaromatic pincer complexes (Figure 1.1) [6–8, 29]. Recently, we have observed that bipyridine-derived PNN-Bipy ligands also exhibit similar metal–ligand cooperativity (Scheme 1.2) [13, 24–27]. Such reactivity, which is not possible with the corresponding aryl-based PCP pincer complexes, is made possible in pyridine-based pincer complexes by (i) the relatively low resonance energy of pyridine (28 kcal mol^{-1}; compared to benzene, 36 kcal mol^{-1}), (ii) the acidity of pyridinyl methylene protons in the pyridine-based pincer complexes, and (iii) stabilization of the dearomatized ligand by the metal center.



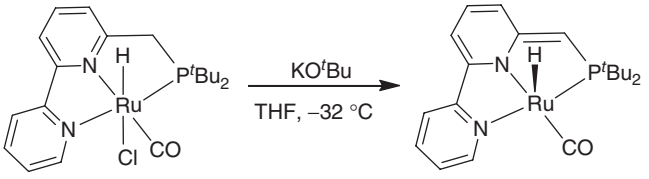
1: L1, L2 = P^{i}Pr$_2$
4: L1, L2 = P^{t}Bu$_2$,
7: L1 = P^{t}Bu$_2$, L2 = NEt$_2$

2: L1, L2 = P^{i}Pr$_2$
5: L1, L2 = P^{t}Bu$_2$,
8: L1 = P^{t}Bu$_2$, L$_2$ = NEt$_2$

3: L1, L2 = P^{i}Pr$_2$
6: L1, L2 = P^{t}Bu$_2$,
9: L1 = P^{t}Bu$_2$, L2 = NEt$_2$

Scheme 1.2 Preparation of dearomatized pyridine-based PNP and PNN pincer complexes and their reversible reaction with H_2.

For example, the pyridine-based pincer complexes **1**, **4**, **7**, and **10** undergo smooth deprotonation to provide complexes **2**, **5**, **8**, and **11** (Schemes 1.2 and 1.3). NMR studies of **2**, **5**, **8**, and **11** indicate dearomatization, as the pyridine protons are shifted to lower frequency (olefinic region). Moreover, the structure of complex **2** is unequivocally corroborated by single-crystal X-ray diffraction studies [23]. Importantly, the dearomatized complexes of **2**, **5**, and **8** activate dihydrogen by cooperation between the ruthenium center and the deprotonated phosphine arm, resulting in aromatization to quantitatively yield the ruthenium *trans*-dihydride complexes of **3**, **6**, and **9**, respectively (Schemes 1.2). The magnetically equivalent

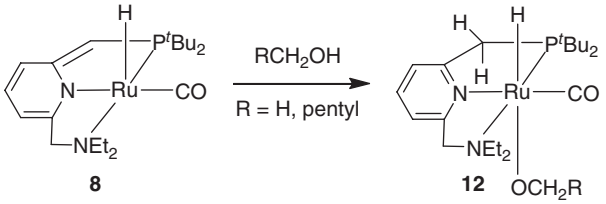


10 **11**

Scheme 1.3 Preparation of dearomatized bipyridine-derived PNN pincer complex **11**.

trans-dihydrides resonate as triplets in complexes **3** and **6** at −4.96 ppm ($^2J_{PH} = 20.0$ Hz) and −4.90 ppm ($^2J_{PH} = 17.0$ Hz), respectively, whereas they display doublets at −4.06 ppm ($^2J_{PH} = 17.0$ Hz) for complexes **9**. The *trans*-dihydride complexes **3**, **6**, and **9** slowly lose H_2 at room temperature to regenerate complexes **2**, **5**, and **8**, respectively.

In addition to the activation of dihydrogen [29d, 30], the dearomatized pyridine-derived pincer complexes also activate O–H bonds of alcohols [11–18, 31] and water [29e, 32], N–H bonds of amines and ammonia [29f,h], sp^3 C–H [29c] and sp^2 C–H bonds [29a,g], and carbon dioxide [33]. Among these various bond-activation reactions, of particular interest here is the O–H bond activation of alcohols, as complex **8** reacts with alcohols to provide the aromatic coordinatively saturated hydrido-alkoxy complexes **12** (Scheme 1.4), indicating the possibility of catalytic transformations based on dehydrogenation of alcohols.



Scheme 1.4 O–H activation by the dearomatized PNN pincer complex **8**.

Such dearomatization and aromatization of these electron-rich ligand systems in cooperation with metal centers present new opportunities for homogeneous catalysis.

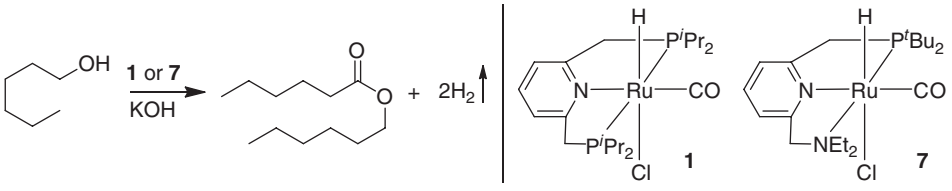
1.3 Synthesis of Esters

Esterification is an important reaction in organic synthesis. It has an assortment of applications in the production of synthetic intermediates, biologically active natural products, fragrances, polymers, polyesters, plasticizers, fatty acids, paints, and pharmaceuticals. Environmentally benign esterification methods catalyzed by pincer complexes that operate via metal–ligand cooperation are described in this section.

1.3.1 Synthesis of Esters from Primary Alcohols

When primary alcohols were heated with a catalytic amount of complex **1**, in the presence of a catalytic amount of base, an unusual dehydrogenative coupling to form esters with evolution of H_2 was observed [11]. Thus, refluxing a hexanol (bp 157 °C) solution containing complex **1** and KOH (0.1 mol% each) under argon in

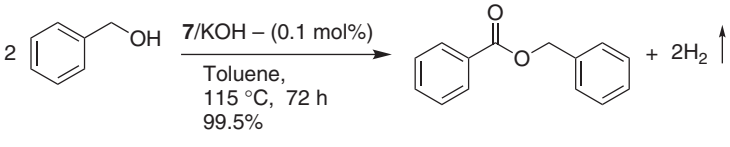
Table 1.1 Catalytic conversion of alcohols to esters by PNP (**1**) and PNN (**7**) complexes in the presence of catalytic base.



Catalyst	Solvent	Time	Temperature (°C)	Yield (%)	TON
1/KOH (0.1 mol%)	—	24	157	67	670
7/KOH (0.1 mol%)	Toluene	24	115	95	950

an open system for 24 h resulted in formation of hexyl hexanoate in 67% yield. The PNN complex **7**, which possesses a hemilabile amine "arm," was a significantly better catalyst (still in the presence of an equivalent of base) than the corresponding PNP complex **1**, leading to 95% (950 turnovers) hexyl-hexanoate after 24 h at 115 °C (Table 1.1) [11].

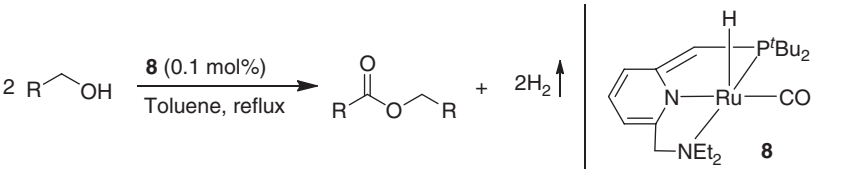
Good turnover numbers (TONs) and yields of esters were obtained with various alcohols at 115 °C. Reaction follow-up with benzyl alcohol indicated that 91% benzyl benzoate was formed already after 6 h, with turnover frequency (TOF) reaching 333 h^{-1} at the level of 50% benzyl benzoate. Formation of the ester became very slow after 6 h, perhaps because of retardation of the reaction by the high ester concentration. However, almost quantitative formation of benzyl benzoate was obtained (Scheme 1.5).



Scheme 1.5 Catalytic conversion of benzyl alcohol to benzyl benzoate by PNN complex **7**.

Further improvement in the reaction was possible by exclusion of the need for base. Thus, reaction of complex **7** with KO^{t}Bu resulted in the formation of the coordinatively unsaturated, 16e$^-$ Ru(II) neutral complex **8**. Indeed, **8** is an excellent catalyst for the dehydrogenative coupling of alcohols to esters and the reaction proceeds with liberation of H_2 under neutral conditions [11]. Table 1.2 provides a few examples. GC analysis of the reaction mixtures indicated that aldehydes were formed only in trace amounts. This catalytic reaction provided a new "green" pathway for the synthesis of esters directly from alcohols. Considerably less efficient methods had been reported previously for this transformation [34].

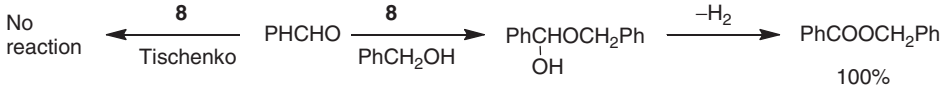
Table 1.2 Examples of dehydrogenative coupling of alcohols to form esters and dihydrogen catalyzed by dearomatized Ru PNN complex **8**.



Entry	R	Ester	Time (h)	Ester (%)
1[a]	Propyl	Butyl butyrate	5	90
2	Pentyl	Hexyl hexanoate	6	99
3	Ph	Benzyl benzoate	4	92

Conditions: 0.01 mmol catalyst **8**, 10 mmol alcohol, and toluene (2 ml) were refluxed (115 °C) under Ar flow.
[a]Neat reaction, heated at 117 °C.

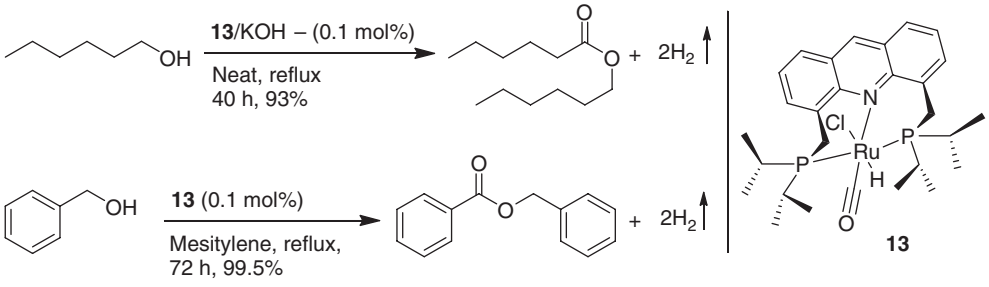
There are two potential pathways by which an ester can be formed, both involving an intermediate aldehyde, namely a Tischenko-type condensation [35] or hemiacetal formation followed by its dehydrogenation [34]. Our results establish that the second pathway is operative, at least in the case of benzyl alcohol [11]. Thus, employing benzaldehyde (in absence of alcohol) did not yield any ester. On the other hand, reaction of benzaldehyde with 1 equivalent of benzyl alcohol led to quantitative formation of benzyl benzoate (Scheme 1.6).



Scheme 1.6 Formation of ester via hemiacetal intermediary.

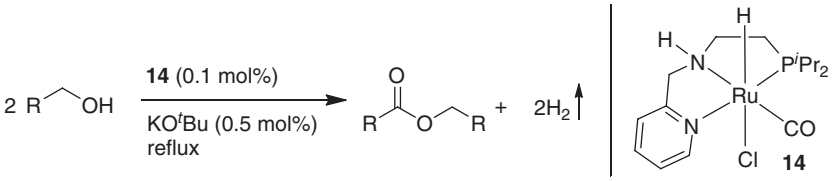
Using the acridine-derived PNP pincer complex **13**, primary alcohols can be directly transformed into acetals under neutral conditions [16, 36]. When the reactions were carried out in the presence of 1 equivalent of base (relative to complex **13**, 0.1 mol%), the corresponding esters were obtained in very good yields (Scheme 1.7). Mechanistic studies revealed that a β-hydrogen is essential for the acetal formation; thus, alcohols such as benzyl alcohol provided benzyl benzoate in 99.5% yield, rather than acetal, even under neutral conditions [16].

Recently, Gusev and coworkers [37] reported the PNN ruthenium pincer complex **14** with an aliphatic backbone, which displayed impressive catalytic activity in the presence of a base (KO^{t}Bu, 0.5 mol%) for the conversion of simple alcohols such as ethanol and propanol. Although the reactions worked at temperatures below 100 °C, good conversions required heating at higher temperatures (Table 1.3,



Scheme 1.7 Esterification of primary alcohols by acridine PNP ruthenium pincer complex **13**.

Table 1.3 Dehydrogenative coupling of alcohols to form esters and dihydrogen catalyzed by the Ru PNN complex **14**.



Entry	R	*T* (°C)	Time (h)	Conversion (%)
1	Me	78	7.5	30
2	Et	96	8	73
3	Pr	118	3	78
4	*i*-Amyl	131	2.5	92
5	Hexyl	158	1	86

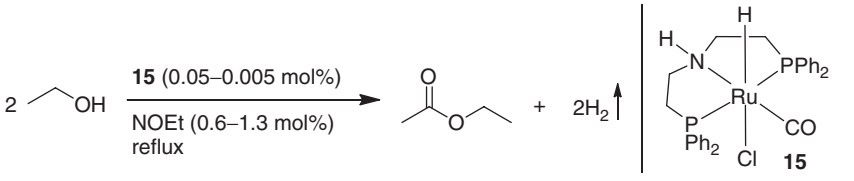
entries 4–5). An analogous dehalogenated osmium-based dimeric pincer complex was also reported to have comparable activity to that of complex **14**.

Though in moderate yield, the reported conversion of ethanol to ethyl acetate by complex **14** and a related osmium dimer complex [37] by Gusev generated interest in the catalytic synthesis of ethyl acetate from ethanol because it is a widely used fine chemical. Very recently, Beller *et al.* [38] screened the catalytic activity of various known pincer complexes for this transformation and found that Takasago's complex **15**, known as *Ru-MACHO catalyst*, is very efficient and the reaction in the presence of a base resulted in very good TON (Table 1.4).

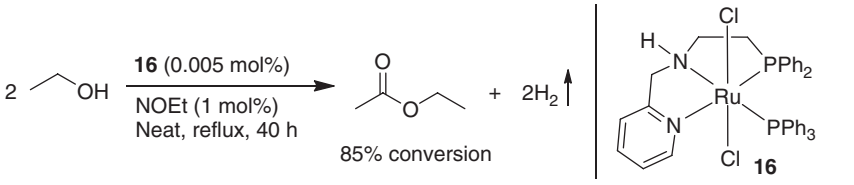
Simultaneously, Spasyuk and Gusev [39] also reported a similar finding; among the various screened pincer complexes, complex **16** showed impressive reactivity with 85% conversion of ethanol (Scheme 1.8).

In addition to these transformations by well-defined pincer complexes, the complexes assembled *in situ* from the metal precursor [Ru(COD)(methylallyl)$_2$] (COD, cyclooctadiene) and PNP or PNN pincer ligands (used for complexes

Table 1.4 Synthesis of ethyl acetate from ethanol by Ru-MACHO catalyst.



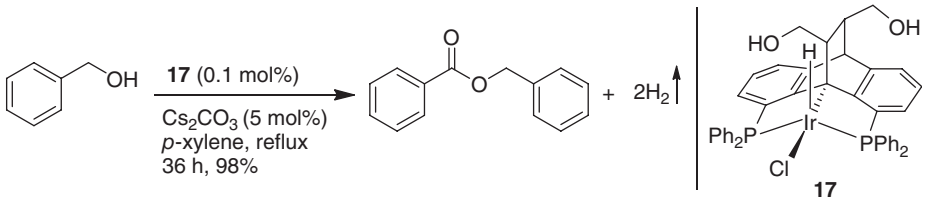
Entry	15 (mol%)	NaOEt (mol%)	Time (h)	*T* (°C)	Yield (%)	TON
1	0.05	1.3	6	90	81	1 620
2	0.05	1.3	24	70	70	1 400
3	0.005	0.6	46	90	77	15 400



Scheme 1.8 Synthesis of ethyl acetate from ethanol by the PNN ruthenium pincer complex **16**.

4 and **7**, respectively) also catalyzed the dehydrogenative coupling of alcohol into esters successfully [40]. The catalytically active complex (which could be complex **8**, the CO ligand generated from intermediate aldehyde) displayed similar reactivity as that of complex **8**. PNP and PNN ruthenium(II) hydrido borohydride complexes [(PNX)RuH(BH_4), X = P, N] [41] and PNS ruthenium complexes [(PNS^{tBu})RuHCl(CO)] [42], analogs to complex **7**, also show catalytic reactivity for the esterification of alcohols.

In 2011, Gelman and coworkers [43] reported a $PC_{sp}{}^3P$ iridium pincer complex (**17**), which exhibited efficient catalytic activity for the conversion of benzyl alcohol to benzyl benzoate (Scheme 1.9) and was suggested to operate via a novel metal–ligand cooperation mode. Both electron-withdrawing and electron-donating substituents



Scheme 1.9 Acceptor-less dehydrogenative coupling of benzyl alcohols to form esters and dihydrogen catalyzed by the Ir(III) $PC_{sp}{}^3P$ complex **17**.

on the aromatic ring are tolerated, and the corresponding esters were obtained in good yields (88–97%).

1.3.2
Synthesis of Cross-Esters from Primary and Secondary Alcohols

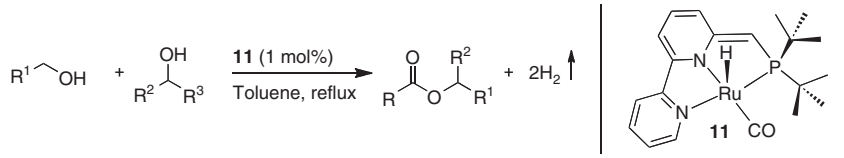
When a toluene solution of complex **11** (1 mol%) was refluxed with equimolar amounts of 1-hexanol and cyclohexanol, cyclohexyl hexanoate was obtained in 79% yield, together with 16% hexyl hexanoate, resulting from self-coupling of 1-hexanol, and 12% of cyclohexanone by dehydrogenation of cyclohexanol [13]. Despite the use of equimolar amounts of primary and secondary alcohols, the formation of the ester cyclohexyl hexanoate as the major product from dehydrogenative cross-esterification is noteworthy. The yield of the cross-esterification products significantly improved when an excess of secondary alcohols was used in the reaction. Thus, in a similar reaction, refluxing a toluene solution containing cyclohexanol and 1-hexanol in a molar ratio of 2.5/1 with complex **11** (1 mol%), cyclohexyl hexanoate was obtained in 93% yield (based on 1-hexanol). Cyclohexanone (34%) was also formed, and the products were isolated by column chromatography. The synthetic potential and substrate scope of this selective dehydrogenative cross-esterification process were demonstrated [13] with various cyclic and acyclic secondary alcohols and other primary alcohols, and the results are summarized in Table 1.5.

1.3.3
Synthesis of Esters by Acylation of Secondary Alcohols Using Esters

The transesterification reaction is a useful transformation that converts esters to other esters upon reaction with alcohols, as a result of exchange of alkoxy groups, avoiding the use of air- and moisture-sensitive reagents, such as acid chlorides. Further, ester-to-ester transformation is particularly useful when the carboxylic acid and their activated derivatives are not readily available [44]. In general, transesterification of secondary alcohols is slower than that of primary alcohols. The reaction is not atom-economical, as it produces, in addition to the desired ester, an equivalent of alcohol. Circumventing this undesired path, we have devised a novel method for transesterification in which dihydrogen is formed as the only byproduct, rather than alcohols, upon reaction of symmetrical esters with secondary alcohols.

Thus, refluxing a benzene solution of complex **8** (1 mol%), ethyl acetate (5 mmol) and cyclohexanol (15 mmol) under an argon atmosphere for 28 h resulted in complete consumption of ethyl acetate [12]. Cyclohexyl acetate was the only product formed (95%, Table 1.6) as observed by GC analysis and further confirmed by characterization of the isolated product. Similarly, refluxing a toluene solution containing 1 equivalent of an ester, such as hexyl hexanoate, pentyl pentanoate, and butyl butyrate, and 3 equivalent of various secondary alcohols in the presence of 1 mol% of complex **8** resulted in cross-esters in very good yields (Table 1.6). Somewhat lower yields of products were obtained when only 2 equivalent of secondary alcohols was used.

Table 1.5 Dehydrogenative cross-coupling of primary and secondary alcohols catalyzed by **11**.[a]



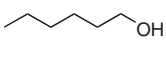
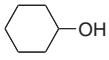
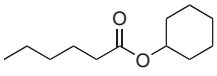
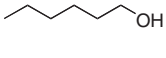
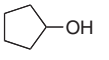
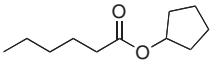
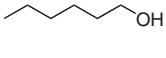
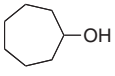
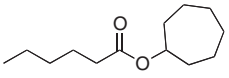
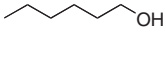
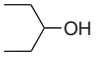
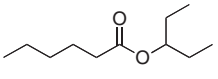
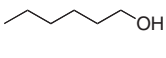
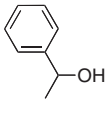
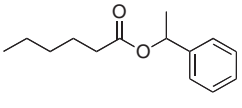
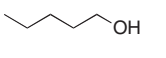
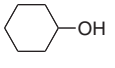
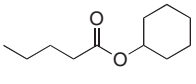
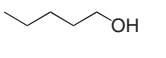
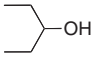
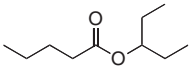
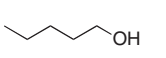
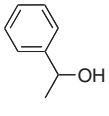
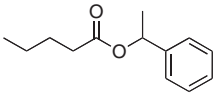
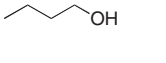
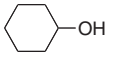
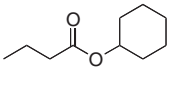
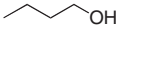
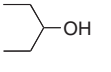
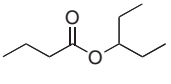
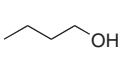
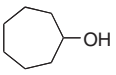
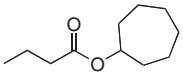
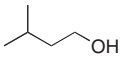
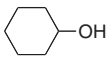
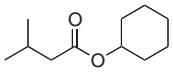
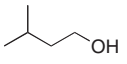
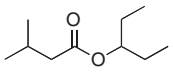
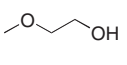
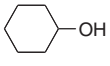
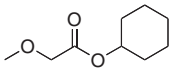
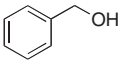
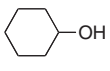
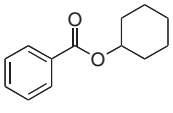
Entry	1° alcohol	2° alcohol	Cross ester	Time (h)	Yield (%)
1				24	93
2				26	63
3				26	90
4				26	93
5				26	58
6				25	95
7				24	96
8				38	46
9				25	95
10				26	93

Table 1.5 (*Continued*)

Entry	1° alcohol	2° alcohol	Cross ester	Time (h)	Yield (%)
11				26	70
12				25	99
13				25	95
14				24	98
15				24	91

[a]Complex **11** (0.03 mmol), primary alcohol (3 mmol), secondary alcohol (7.5 mmol), and toluene (2 ml) were refluxed under argon. Yields of products were determined by GC using *m*-xylene as an internal standard.

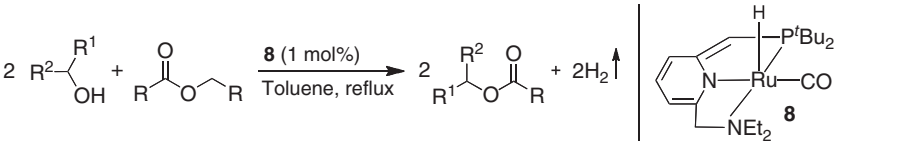
When the unsymmetrical ester ethyl butyrate was reacted with 3-pentanol in the presence of **8** (1 mol%) under refluxing toluene, 75% conversion of ethyl butyrate took place to yield 73% of 3-pentyl butyrate (entry 14, Table 1.6). 3-Pentyl acetate, which was expected to be formed from the ethanol intermediate, was observed only in trace amounts, perhaps as a result of the loss of ethanol under reflux conditions. Likewise, the reaction of methyl hexanoate with cyclohexanol results in 42% conversion with the formation of 42% cyclohexyl hexanoate (entry 15).

Dehydrogenation of the secondary alcohol to the corresponding ketone is a slower reaction than the dehydrogenative coupling of the primary alcohol to ester, and thus most of the secondary alcohol reacts with the ester, although some ketone formation is observed as excess of alcohol is used. When symmetrical esters are used, both acyl and alkoxy parts of the substrate ester are incorporated into the product ester with liberation of hydrogen, providing an atom-economical and environmentally benign method for the transesterification reactions [12].

1.3.4
Synthesis of Polyesters from Diols

Polyesters are generally synthesized by a step-growth polycondensation reaction or through chain-growth ring-opening polymerization. However, achieving high molecular weights by the known methods for the synthesis of polyesters is

Table 1.6 Acylation of secondary alcohols catalyzed by the complex **8**.[a]



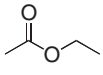
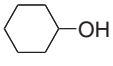
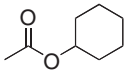
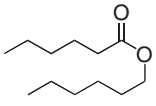
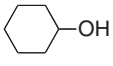
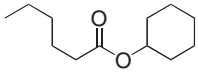
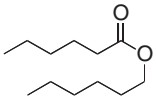
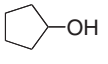
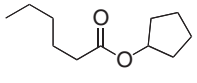
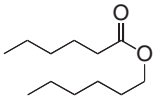
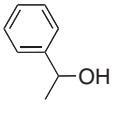
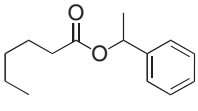
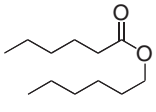
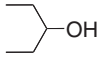
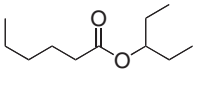
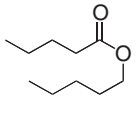
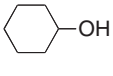
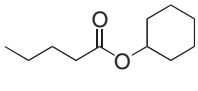
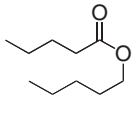
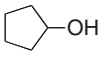
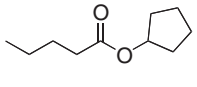
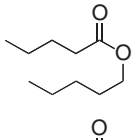
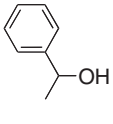
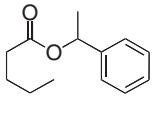
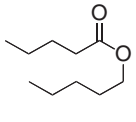
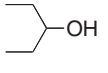
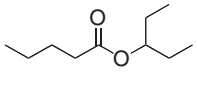
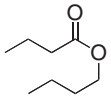
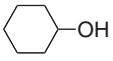
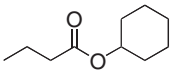
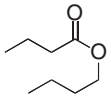
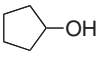
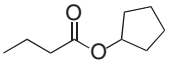
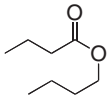
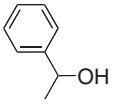
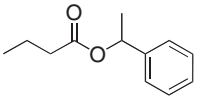
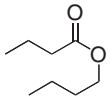
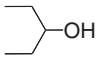
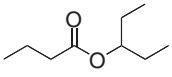
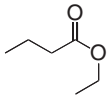
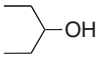
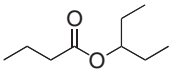
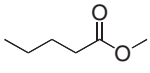
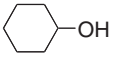
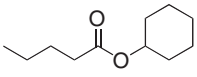
Entry	Ester	Alcohol	Cross-esters	Time	Conversion	Yield (%)
1[b]				28	100	95
2				26	96	95
3				26	71	70
4				36	50	49
5				26	91	90
6				36	93	93
7				36	87	85
8				18	51	49
9				26	91	90

Table 1.6 (*Continued*)

Entry	Ester	Alcohol	Cross-esters	Time	Conversion	Yield (%)
10				34	93	92
11				28	75	74
12				36	41	39
13				18	77	76
14[c]				20	75	73
15				17	42	42

[a] Complex **8** (0.05 mmol), ester (5 mmol), and toluene (3 ml) were refluxed under argon. Conversion and yields are based on GC analysis using internal standard.
[b] Benzene was used as solvent.
[c] *m*-Xylene was used as solvent.

challenging [45]. Further, the byproducts (H_2O, CH_3OH, HCl, salts) that are produced during a polycondensation can be challenging to remove from a viscous polymer solution, resulting in low conversion and poor polymer properties. By using complex **8** as a catalyst, Robertson [19] achieved the synthesis of high molecular weight polyesters from diols in a remarkable process that used complex **8** as a catalyst. Concomitantly generated dihydrogen was efficiently removed by performing the polymerization reaction under reduced pressure, leading to the formation of high molecular weight polyesters.

Complex **8** (0.2 mol%), generated *in situ* by deprotonation of complex **7** (Scheme 1.2), catalyzed polymerization of diols (higher than pentanediol) by heating under vacuum. Comparison of the molecular weight versus reaction time for the polymerization of 1,10-decanediol under vacuum versus nitrogen purge (Figure 1.2) revealed that polymer growth occurred faster and reached a higher molecular weight when the reaction was performed under reduced pressure.

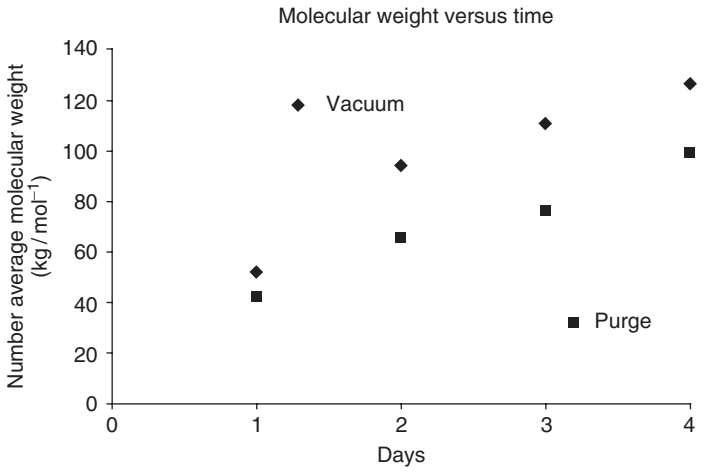


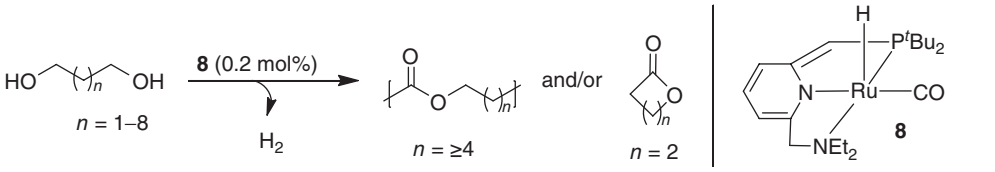
Figure 1.2 Plot of M_n versus reaction time for the polymerization of 1,10-decanediol under vacuum compared to using a nitrogen purge. (Reproduced with permission. Copyright © 2012 Wiley-VCH [19].)

Molecular weights higher than 125 000 g mol^{-1} were attained. Considering the reaction conditions, which involve vacuum and rapidly lose solvent and become highly viscous with the reaction's progress, achieving such high molecular weights is noteworthy. The better performance under vacuum is attributed to the efficient removal of the hydrogen byproduct (which in turn helps to drive the equilibrium toward further polymerization) from the highly viscous molten polymer solution.

Diols such as 1,10-decanediol, 1,9-nonanediol, 1,8-octanediol, 1,6-hexanediol, and 1,5-pentanediol were polymerized using a catalyst loading of 0.2 mol% of complex **8** under vacuum. Table 1.7 summarizes the yields and some properties of the polymers. Polymerization of 1,10-decanediol leads to a polymer with M_n approaching 140 000 g mol^{-1} and a degree of polymerization over 800 (entry 1). The molecular weights of the polymers and the degree of polymerization decrease as the molecular weight and length of the monomer decrease, which may be due to the viscosity differences of the molten polymer. The dehydrogenation of 1,5-pentanediol resulted in the predominant formation of thermodynamically stable and kinetically favored six-membered δ-valerolactone and 29% of polyester (entry 6). The reaction of 1,4-butanediol with complex **8** provided γ-butyrolactone exclusively.

In general, a range of esters is accessible directly from alcohols by dehydrogenative coupling and also from esters via transesterification catalyzed by ruthenium pincer complexes. The dearomatized complex **8** efficiently catalyzes the formation of polyesters from diols under vacuum. Although low catalyst loading and nonpurified monomeric diols were used, high degrees of polymerizations were achieved. These reactions take place with the liberation of dihydrogen (the only byproduct) under mild and neutral conditions, thus providing highly atom-economical processes for the formation esters and polyesters.

Table 1.7 Polymerization of linear aliphatic diols catalyzed by the complex **8** under vacuum and nitrogen purge.[a]



Entry	*n* (diol)	M_n (kg mol^{-1})[b]	M_w/M_n[b]	Degree of polymerization	T_m (°C)[c]	Yield (%)
1	8	138	2.7	811	51	78
2	7	91.8	3.1	587	42	85
3	6	76.6	2.3	538	40	95
4[d]	4	55.5	2.0	486	13	70
5[e]	4	29.4	1.6	258	14	97
6	3	57.7	2.9	576	−2	29[f]
7	2	—	—	—	—	90[g]

Taken from Robertson *et al.* [19].
[a] Complex **8** (0.2 mol%) and monomeric diol were heated at 150 °C with a 3 h purge and 5 day vacuum.
[b] Determined by gel permeation chromatography (GPC) using polystyrene standard.
[c] Determined by differential scanning calorimetry (DSC).
[d] Nitrogen purge instead of vacuum.
[e] 5 h nitrogen purge prior to vacuum to promote oligomerization and minimize loss of monomer.
[f] Isolated yield of polymer. Remaining volatiles in vacuum trap were solvent and lactone.
[g] Yield of lactone.

1.4 Synthesis of Amides

Amide formation plays a very important role in chemical synthesis [1, 46]. Preparation of amides under neutral conditions and without generation of waste is a challenging goal [46–48]. Applying our pyridine-based ruthenium pincer complexes as catalysts, amides were synthesized directly from amines and alcohols or esters; polyamides were obtained from diols and diamines, as delineated in this section.

1.4.1 Synthesis of Amides from Alcohols and Amines

Direct catalytic conversion of alcohols and amines into amides and dihydrogen is a desirable method for the synthesis of amides. Using this environmentally benign reaction [14], an assortment of simple alcohols and amines were converted

into amides, with high atom economy. The liberated hydrogen gas shifts the equilibrium toward the completion of the reaction.

The reaction mixtures were refluxed under a flow of argon to facilitate the formation of product amides by hydrogen removal. When simple linear alcohols such as 1-hexanol and 1-pentanol were used, the corresponding amides were obtained in very good yields. 2-Methoxyethanol reacted with diverse amines to generate the amides in almost quantitative yields. When aniline was subjected to acylation with 1-pentanol, the amide was obtained in 58% yield. The lower reactivity of aniline may be attributed to its lower nucleophilicity as compared with that of alkylamines. The amidation reactions are sensitive to steric hindrance at the alcohol or the amine. Thus, when 2-methyl-1-butanol reacted with benzylamine, the corresponding amide was obtained in 70% yield, the rest of the alcohol being converted to the ester 2-methylbutyl-2-methylbutanoate. A similar pattern was also observed when 2-methylhexamine was reacted with 1-hexanol, leading to 72% yield of the corresponding amide (Table 1.8).

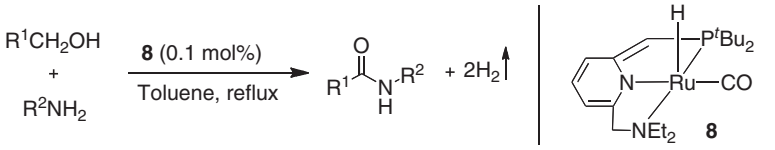
Amino alcohols also undergo amidation reactions. Gratifyingly, when chiral amino alcohols were used, the amide products were obtained with the retention of configuration. For example, reaction of (*S*)-2-amino-3-phenylpropan-1-ol, benzylamine, and 1 mol% of the complex **8** in toluene at reflux for 6 h led to (*S*)-2-amino-*N*-benzyl-3-phenylpropanamide in 58% yield after column chromatography (Scheme 1.10) [22]. The specific rotation of the product amide (+16.08) obtained from this catalysis reaction is essentially the same as reported [49]. The neutral reaction conditions likely help to prevent racemization.

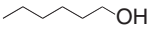
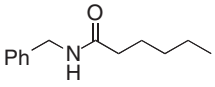
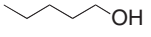
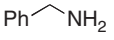
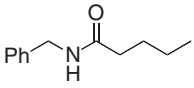
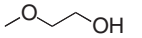
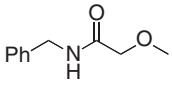
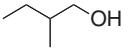
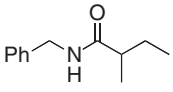
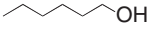
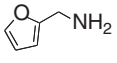
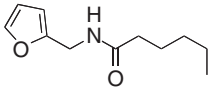
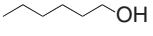
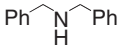
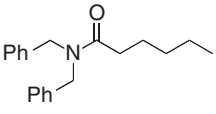
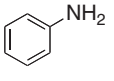
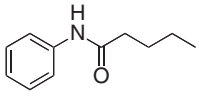
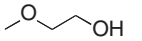
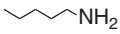
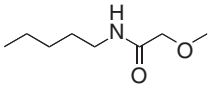
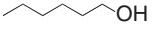
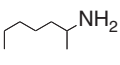
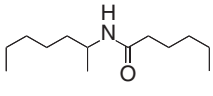
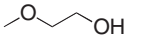
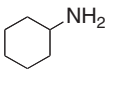
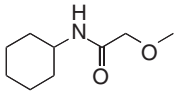
Secondary amines do not react under these conditions. Thus, heating dibenzylamine with 1-hexanol under the experimental conditions resulted in a quantitative yield of hexyl hexanoate (entry 6, Table 1.8). The scope of this method was extended to the bis-acylation processes with diamines. Upon refluxing a slight excess of a primary alcohol and catalyst **1** with diamines (500 equivalent relative to **1**) in toluene under argon, bis-amides were produced in high yields (Table 1.9). The high selectivity of the dehydrogenative amidation reaction to primary amine functionalities enabled the direct bis-acylation of diethylenetriamine with 1-hexanol to provide the bis-amide in 88% yield without the need to protect the secondary amine functionality [14].

This is a fundamentally new chemical transformation. The reaction mechanism likely involves metal–ligand cooperation that operates in complex **8**. The reaction plausibly proceeds via a hemiaminal intermediate (Scheme 1.11) formed by the nucleophilic attack of the amine on an intermediate aldehyde that is either coordinated to the metal or free in solution [7, 32, 50].

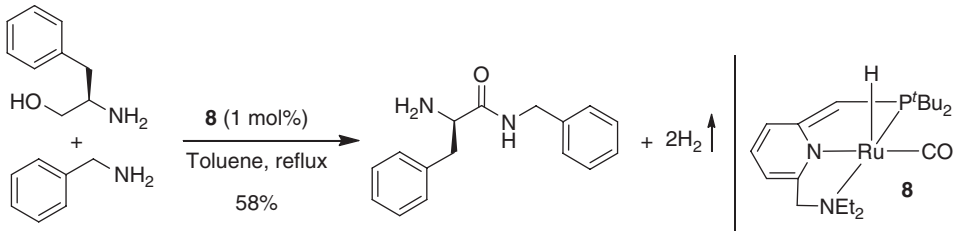
The discovery of the catalytic amide formation with liberation of dihydrogen provides the most atom-economical method to make amides directly from amines and alcohols; as such, it elicited much research interest in this direction and diverse catalytic systems were reported, although generally in significantly lower catalyst turnovers [51].

Table 1.8 Synthesis of amides directly from alcohols and amines.[a]



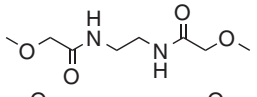
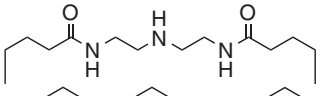
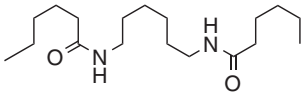
Entry	R^1CH_2OH	R^2NH_2	Time (h)	Amides	Yield (%)[b]
1			7		96
2			7		97
3			9		99
4			12		70[c]
5			8		78[c]
6			8		0[c]
7			8		58[c]
8			8		99
9			8		72[c]
10			8		99

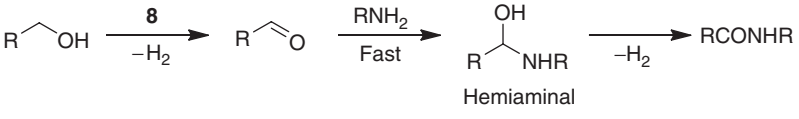
[a] Conditions: Catalyst **8** (0.01 mmol), alcohol (10 mmol), amine (10 mmol), and toluene (3 ml) were refluxed under argon flow.
[b] Isolated yields.
[c] The remaining alcohol was converted into the corresponding ester. In the reactions involving hexanol and pentanol, trace amounts of the corresponding secondary amines were detected (GC–MS).



Scheme 1.10 Synthesis of a chiral amide from amino alcohol and benzylamine.

Table 1.9 Dehydrogenative coupling of di- and tri-amines with alcohols to form bis-amides, catalyzed by complex **8**.

Entry	Diamine	Time (h)	Bis-amide	Yield (%)
1	Ethylenediamine	9		99
2	Diethylenetriamine	8		88
3	1,6-Diaminohexane	9		95

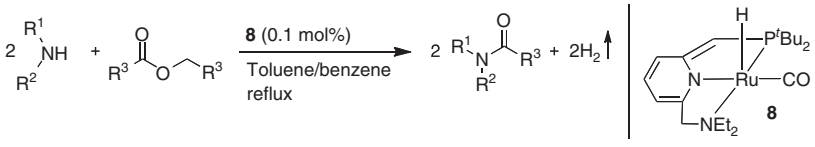


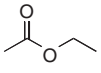
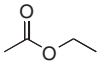
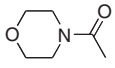
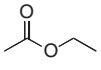
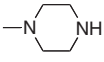
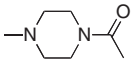
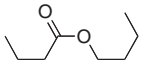
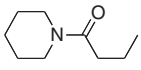
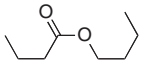
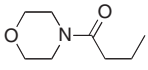
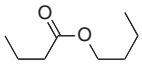
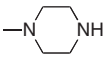
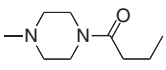
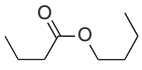
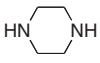
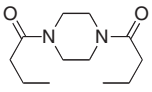
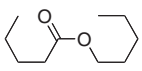
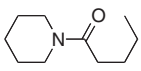
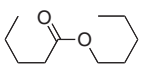
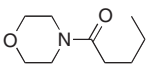
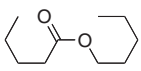
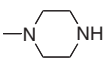
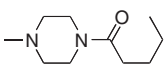
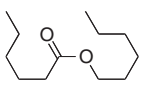
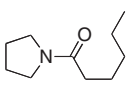
Scheme 1.11 Amide formation via hemiaminal intermediary.

1.4.2
Synthesis of Amides from Esters and Amines

Synthesis of amides from the coupling reactions of esters and amines is a potentially attractive method; however, stoichiometric amounts of promoters or metal mediators are normally required [52]. Complex **8** also catalyzes the amide synthesis from esters and amines and the reaction is general and efficient, and proceeds under neutral conditions, thus providing an environmentally benign method [15]. As demonstrated in the alcohol acylation process (Section 1.3.3, Table 1.6), when symmetrical esters are used, acylation of amines occurs by both acyl and alkoxo parts of the esters and they are incorporated in the products, and the only byproduct generated from this reaction is H_2.

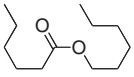
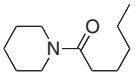
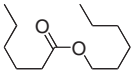
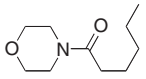
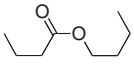
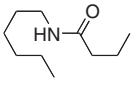
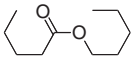
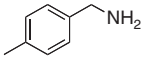
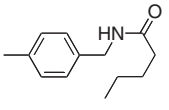
Table 1.10 Synthesis of amides from esters and amines catalyzed by complex **8**.[a]



Entry	Ester	Amine	Conversion of amine/time (% / h)	Amides	Isolated yields (%)
1[b]			100/26		99
2[b]			69/36		66
3[b]			54/24		52
4			100/19		94
5			100/21		95
6			100/24		94
7			100/36		56
8			100/19		96
9			100/26		92
10			100/24		94
11			100/18		97

(continued overleaf)

Table 1.10 (*Continued*)

Entry	Ester	Amine	Conversion. of amine/time (% / h)	Amides	Isolated yields (%)
12			100/26		94
13			100/18		93
14			100/24		97
15			100/18		98

[a] Complex **8** (0.01 mmol), ester (5 mmol), amine (10 mmol), and toluene/benzene (3 ml) were refluxed at an oil bath temperature of 135 °C in a Schlenk tube. Conversion of amine was analyzed by GC using *m*-xylene as an internal standard.
[b] Benzene was used as a solvent.

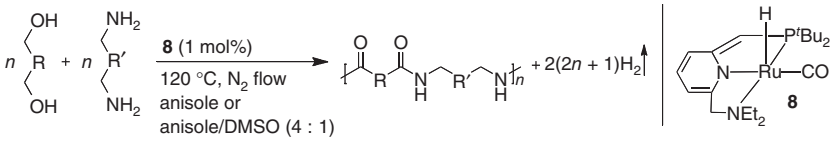
When a benzene solution of complex **8** (0.1 mol%) containing pyrrolidine and ethyl acetate was refluxed under an argon atmosphere, quantitative conversion of pyrrolidine was observed by GC after 28 h, and *N*-acetylpyrrolidine was isolated in 98% yield (Table 1.10, entry 1). The same results were obtained when the reaction was carried out in refluxing toluene. The scope of the ester amidation reaction was explored with various esters and amines, and the results are summarized in Table 1.10.

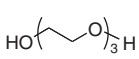
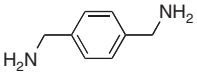
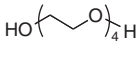
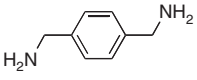
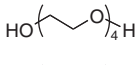
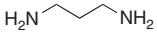
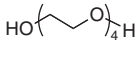
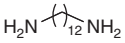
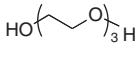
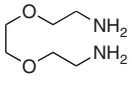
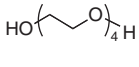
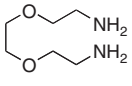
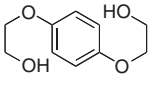
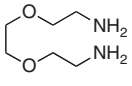
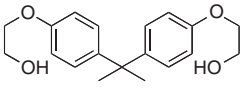
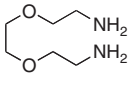
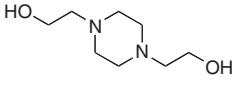
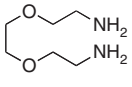
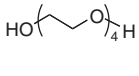
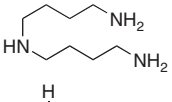
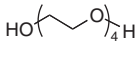
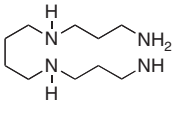
The aminolysis of esters catalyzed by complex **8** is possibly initiated by N–H activation of the amine by metal–ligand cooperation involving **8**. Ester coordination followed by intramolecular nucleophilic attack by the amido ligand at the acyl functionality is thought to be a key step [15]. Overall, in one catalytic cycle, two molecules of amide and of H_2 are formed from one ester molecule.

1.4.3
Synthesis of Polyamides from Diols and Diamines

Polyamides are an important class of polymers in chemistry and biology, including biomolecules such as peptides and proteins. Synthetic polyamides have found numerous applications [53, 54] in fiber products, engineering plastics, and biomaterials. They possess high strength, toughness, and stability, and have good biocompatibility and degradability. Generally, polyamides are synthesized by

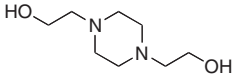
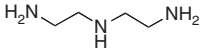
Table 1.11 Catalytic dehydrogenative polyamidation.[a]



Entry	Diol	Diamine	Conversion[b] (yield[c]) %	M_n (10^3)	PDI
1[d]			99 (89)	11.9	3.09
2[d]			>99 (87)	12.7	2.80
3[d]			>99 (84)	19.8	1.86
4[e]			>99 (88)	28.4	1.75
5[e]			>99 (73)	19.4	1.59
6[e]			>99 (78)	22.1	1.56
7[e]			99 (85)	15.0	1.59
8[e]			>99 (79)	16.5	1.69
9[e]			>99 (76)	19.5	1.65
10[e]			97 (65)	6.8[f]	2.56
11[e]			99 (70)	9.6[f]	1.65

(continued overleaf)

Table 1.11 (*Continued*)

Entry	Diol	Diamine	Conversion[b] (yield[c]) %	M_n (10^3)	PDI
12[e]			99 (72)	11.3[f]	3.06

Taken from Guan *et al.* [21]
[a] Reaction conditions: 1.0 mmol diol, 1.0 mmol diamine, and the Ru catalyst were premixed in 1.5 ml solvent in a glovebox, then heated under N_2 flow for 48 h.
[b] Determined by ^{1}H NMR of the crude reaction mixture.
[c] Isolated yield after precipitation from toluene.
[d] In anisole/DMSO (4 : 1), 2 mol% catalyst loading.
[e] In anisole, 1 mol% catalyst loading.
[f] GPC taken after acylation by Ac_2O to avoid strong interaction with the GPC column gel material.

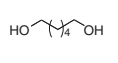
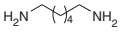
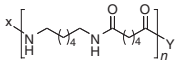
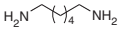
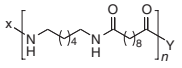
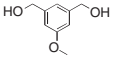
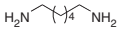
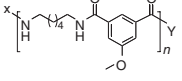
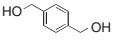
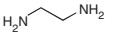
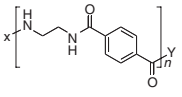
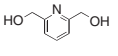
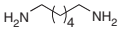
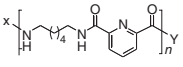
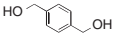
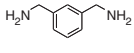
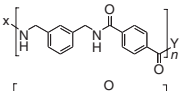
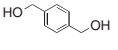
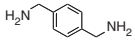
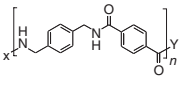
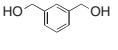
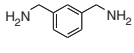
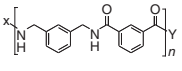
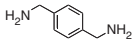
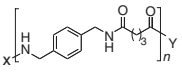
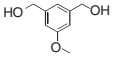
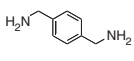
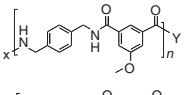
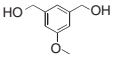
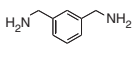
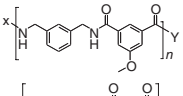
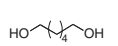
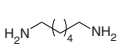
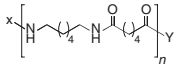
condensation of diamines and activated dicarboxylic acid derivatives [54, 55] and/or in the presence of coupling reagents [56]. In some cases, ring opening of small-ring lactams at high temperatures leads to the formation of polyamides [57]. To avoid the use of activators, waste generation, or harsh conditions, the development of atom-economical, efficient, and environmentally benign protocols are desirable.

Thus, we have developed the catalytic synthesis of polyamides [20] from diols and diamines using complex **8** as a catalyst. Prior to us, Zeng and Guan [21] reported such a transformation using (the now commercially available) complex **8**. Extensive optimization studies carried out by Zeng and Guan [21] revealed the need for polar solvents for successful polymerization of diols and diamines, and anisole was found to be a suitable polar solvent in which the catalyst remained highly active and the number averaged molecular weights (M_n) of the polyamides were dramatically increased. M_n of the polyamides was further improved by the addition of small amounts of dimethylsulfoxide (DMSO).

Using the optimized conditions, Guan and coworkers prepared a series of polyamides using various diols and diamines; selected examples are shown in Table 1.11. The anisole/DMSO mixed solvent provided better polymerization for less soluble polyamides (Table 1.11, entries 1–3), but decreased the catalytic activity of the complex **8**. Polymerizations in anisole gave longer polymers for more soluble polyamides (entries 4–12). As described in Section 1.4.1, the amidation reaction catalyzed by complex **8** is highly selective to primary amines and this offered excellent opportunity for the direct synthesis of functional polyamides containing secondary amino groups (entries 10–12) circumventing tedious protection and deprotection steps.

While Guan *et al.* disclosed the preparation of a variety of polyamides, many bearing ether spacers, with M_n in the range of 10–30 kDa, we reported the application of the amidation reaction to the synthesis of a variety of polyamides not bearing ether spacers, from simple diols and diamines, under different conditions,

Table 1.12 Catalytic polyamidation using diols and diamines.[a]

Entry	Diols	Diamines	Polyamides	Isolated yield (%)	Highest *Mw*: MALTI-TOF (Da)	M_n (10^3)	PDI
1				82	4195	16.6[b]	—
2				88	5000	10.3[b]	—
3				86	7199	18.7	2.08
4				63	1849	ND	—
5				74	4583	26.9[c]	—
6				86	3861	ND	—
7				84	3734	ND	—
8				78	1467	ND	—
9				80	5200	ND	—
10				76	4450	5.3[c]	3.20
11				88	—	11.3[c]	2.18
12				84	4951	ND	—

[a] Complex **8** (0.01 mmol), diol (1 mmol), diamine (1 mmol), and 1,4-dioxane (2 ml) were refluxed at an oil bath temperature of 135 °C in a Schlenk tube under argon for 3 days.
[b] M_n was calculated from ^{1}H NMR.
[c] M_n was obtained from GPC analysis.
[d] Catalyzed by complex **11** under solvent-free condition. ND means GPC was not performed because of insolubility in dimethyl formamide (DMF).

using 1,4-dioxane as a solvent (Table 1.12). Both complexes **8** and **11** were used as catalysts. Remarkably, using complex **11** as catalyst, the polyamidation reaction proceeded under solvent-free conditions, and only 0.2 mol% of catalyst was required, representing a perfect ''green'' reaction [20].

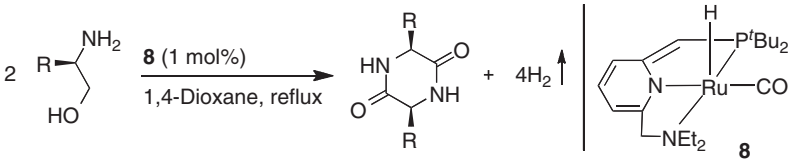
Notably, the potentially competing polyester formation [19] by dehydrogenative self-coupling of diols was not observed under these conditions. This is probably because the intermediate aldehyde reacts preferentially with the amine, which is a better nucleophile than the alcohol, forming a hemiaminal intermediate [14] (rather than a hemiacetal [11]) followed by its dehydrogenation to the amide (Schemes 1.6 and 1.11). In addition, it should be noted that complex **8** also catalyzes the formation of amides by coupling of esters with amines (Section 1.4.2) [15]; hence, even if some ester (or oligoester) were to be initially formed, it would be converted to the polyamide.

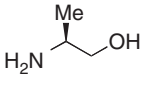
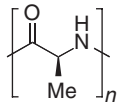
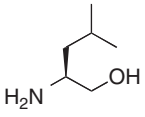
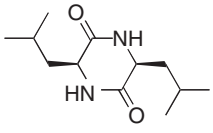
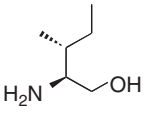
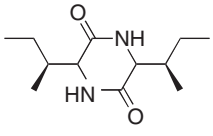
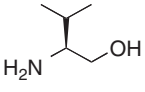
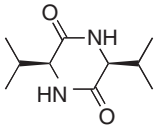
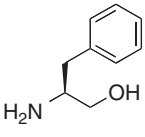
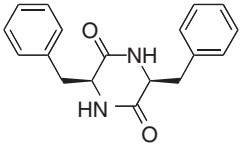
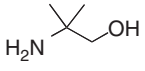
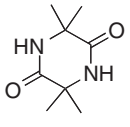
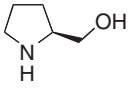
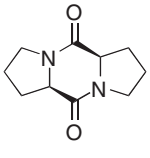
In general, an assortment of polyamides having aliphatic–aliphatic, aromatic–aromatic, aliphatic–aromatic, and aliphatic–heteroaromatic spacers were obtained in good yields using nonactivated and ether-linked/non-ether-linked diols and diamines, with liberation of H_2. Under our conditions, using dioxane as a solvent, polyamides were obtained with M_n in the range of 19–29 kDa, and, under the conditions of Zeng and Guan [21] using anisole or anisole/DMSO as solvents, $M_n = 10–30$ kDa was obtained. Both polymerization conditions catalyzed by complex **8** (as well as by complex **11**) provide synthetically useful and general methods for the preparation of a variety of polyamides under mild, neutral conditions, using no toxic reagents, not requiring preactivation of the substrates, and generating no waste.

1.5
Synthesis of Peptides from β-Amino Alcohols

Peptides constitute one of the most important families of compounds in chemistry and biology and play vital roles in living systems. Short peptides have found interesting biological and synthetic applications. For example, the conformational rigidity of cyclic peptides makes them attractive candidates for drug discovery and biomedical research [58]. Several cyclic peptides that show intriguing biological activity are found in nature [59]. Cyclic peptides have interesting applications as antibiotics [60], enzyme inhibitors [61], and receptor antagonists. Among them are the smallest cyclic peptides, 2,5-diketopiperazines derivatives, which are commonly found as natural products [62]. These peptides exhibit high-affinity binding to a large variety of receptors and show a broad range of biological activities [63], including antimicrobial, antitumor, antiviral, and neuroprotective effects. In general, 2,5-diketopiperazine derivatives are synthesized in solution or on the solid phase from commercially available and appropriately protected chiral α-amino acids in processes that are usually not atom-economical and generate considerable amounts of waste. Large libraries of cyclic peptides are accessible through solid-phase split-and-pool synthesis [64], and various methods have been developed for

Table 1.13 Synthesis of cyclic dipeptides from β-amino alcohols.[a]



Entry	β-Amino alcohol	Peptides	Yield[b] (%)
1			72[c]
2			64
3			72
4			78
5			72
6			92
7			99

[a] Complex **8** (0.02 mmol), amino alcohol (2 mmol), and 1,4-dioxane (2 ml) were heated to reflux in argon (oil bath temperature of 135 °C) for 19 h.
[b] Yield of isolated product.
[c] Including a minor amount of the dipeptide.

their syntheses [65]. Thus, green, atom-economical methods for the generation of peptides are highly desirable.

As complex **8** catalyzes the amidation of amines by amino alcohols with retention of configuration, we reasoned that use of amino alcohols alone might result in linear or cyclic peptides from the self-coupling reactions. Refluxing a 1,4-dioxane solution containing (*S*)-(+)-2-amino-1-propanol and complex **8** (1 mol%) for 19 h under argon flow provided a mixture of oligo-alanines containing a small amount of the cyclic dipeptide amounting together giving 72% yield (Table 1.13, entry 1). Interestingly, similar reactions of amino alcohols bearing larger substituents at the α-position of the amine group provided the corresponding cyclic dipeptides (diketopiperazines) as the only products (Table 1.13, entries 2–7) in very good yields with liberation of H_2 as the only byproduct.

1.6 Concluding Remarks

The chemistry illustrated in this chapter outlines the outstanding potential of pincer complexes for the catalytic synthesis of esters, amides, and peptides. These commonly used fine and bulk chemicals, conventionally prepared from carboxylic acids and their derivatives in multistep processes, can now be produced atom-economically directly from alcohols with liberation of molecular hydrogen (*the only byproduct*), which is valuable by itself. In addition to the higher stability associated with mer-coordination, the pincer platform offers the opportunity to fine-tune the steric and electronic properties of the metal, and, importantly, provide new opportunities for efficient metal–ligand cooperation. This has resulted in hitherto-unknown, efficient, and environmentally benign catalytic processes. In addition to the processes described here, we have developed several other reactions catalyzed by PNP and PNN pincer complexes of Ru and Fe, as briefly mentioned in Section 1.1. The PNN complex **8** and its precursor complex **7**, as well as complex **13** and the associated ligands, are commercially available (from Strem Chemicals, USA). We believe that many innovative catalysts and methodologies would emerge from this stimulating research topic.

Acknowledgments

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