

Introduction

"Catalysis, whether homogeneous or heterogeneous, lies at the heart of many industrial processes, enabling reactions to occur under milder conditions, with higher selectivity and efficiency."

-Henry J. Breen

Historically, chemistry has been essential for meeting basic human requirements such as food, medicine, fertilizer, and materials for contemporary society. Over the years, synthetic chemistry has evolved to create more efficient, cost-effective, and environment-friendly methods for producing these essential products. Catalysis has emerged as one of the most powerful tools for these types of transformations. By tuning reactions to occur more efficiently and with fewer waste products, catalysis has the potential to make chemical synthesis more sustainable, a goal that has been central to several Nobel Prize-winning discoveries.¹ As the demand for sustainable chemical processes continues to rise, the creation of efficient catalytic processes that also environmentally benign has become increasingly important.²

Palladium, platinum, rhodium, ruthenium, and iridium are among the precious metals that have historically been used most frequently in homogeneous catalysis.^{3,4} Key catalytic reactions (such as hydrogenation, C-C and C-N coupling, and dehydrogenation) have relied heavily on homogenous transition metals (Figure 1.1).^{5,6} Their high catalytic activity, robustness, and versatility have made them indispensable in both industries and academia. However, despite their remarkable performance, the widespread use of precious metals has raised significant concerns regarding their cost, limited natural abundance, and environmental impact. Extraction and refining of these metals are energy-intensive processes that contribute to environmental degradation. Furthermore, their toxicity and high price limit their long-term sustainability as catalytic materials, prompting the need for alternatives that are both economically viable and environmentally friendly.⁷

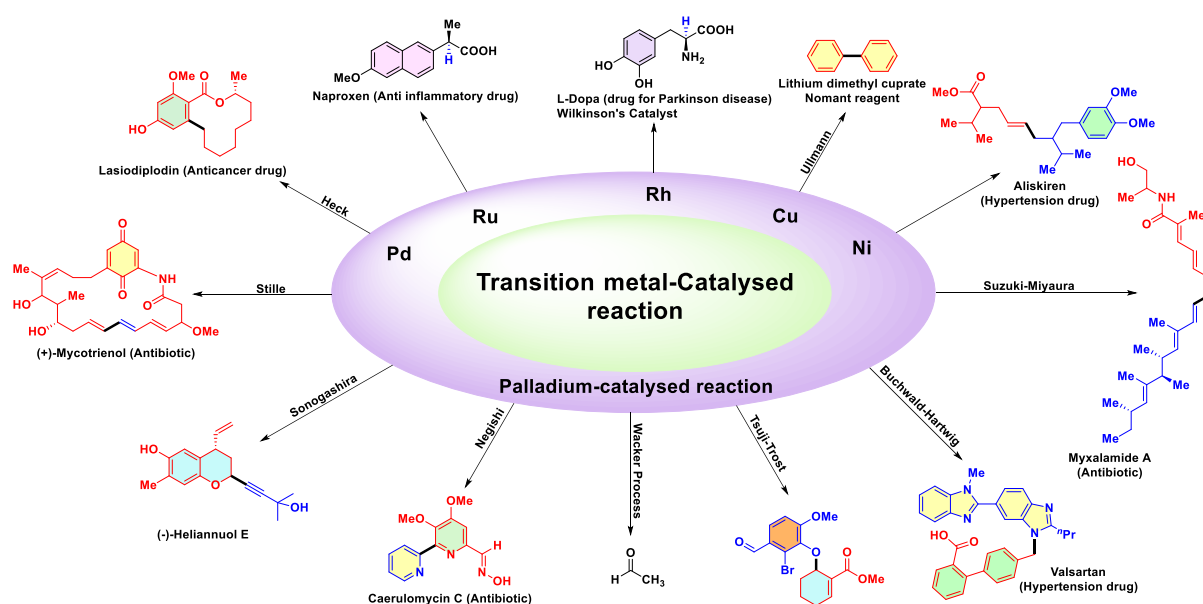


Figure 1.1. Representative examples of transition-metal-catalysed synthetic methods.

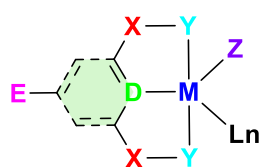
As a result, there has been a revived interest in 1st row transition metals (such as manganese, iron, cobalt, and nickel), which are inherently more abundant, less toxic, and generally more cost-

effective than precious metals. Besides their positive economic and environmental characteristics, these metals possess a variety of oxidation states and coordination geometries, which make them extremely adaptable for use in catalysis.⁸ The ability to switch between different coordination modes and spin states facilitates evolution as it occurred of groundbreaking systems of catalysis that are distinguished by unique reactivity and selectivity, opening up exciting avenues for a diverse array of organic transformations.⁹

Among the first-row transition metals, manganese has garnered significant attention due to its abundance and favourable properties. With a concentration of around 950 mg/kg, manganese is the 3rd most prevalent transition metal in the earth crust. It is also less toxic than heavier transition metals such as platinum and palladium, which makes it an attractive candidate for environmentally friendly catalytic processes. Furthermore, manganese plays crucial roles in biological systems, including in enzymes like manganese superoxide dismutase, which protects against oxidative stress. Manganese's ability to exist in multiple stable oxidation states, further enhances its suitability for catalytic applications. Its flexibility in oxidation states, coupled with its ability to form stable complexes with various ligands, makes manganese a highly promising metal for catalysis.^{10,11}

While manganese catalysis has traditionally been associated with oxidative reactions using higher-valent manganese complexes, recent advancements have shifted focus to low-valent manganese species. These low-valent manganese complexes, often stabilized by pincer or non-pincer ligands, are now being investigated for a variety of reactions, including hydrogenation, dehydrogenation, cross-dehydrogenative coupling (CDC), hydroelementation, and C-H activation.¹² This shift towards low-valent manganese complexes represents a significant advancement in manganese catalysis, opening up new possibilities for reactions that were once dominated by precious metals. Since the ligand selection is crucial in defining the metal complex's reactivity, selectivity, and efficiency, progress in ligand design have made it easier to construct these novel manganese-based catalysts.¹³

A major challenge in the development of 1st row transition metal catalysts, including manganese, lies in their higher reactivity compared to late-transition metals. This increased reactivity can lead to catalyst instability and difficulties in controlling the reaction. To address this issue, researchers have turned to the design of multifunctional ligands that can stabilize the metal center while also promoting catalysis.¹⁴

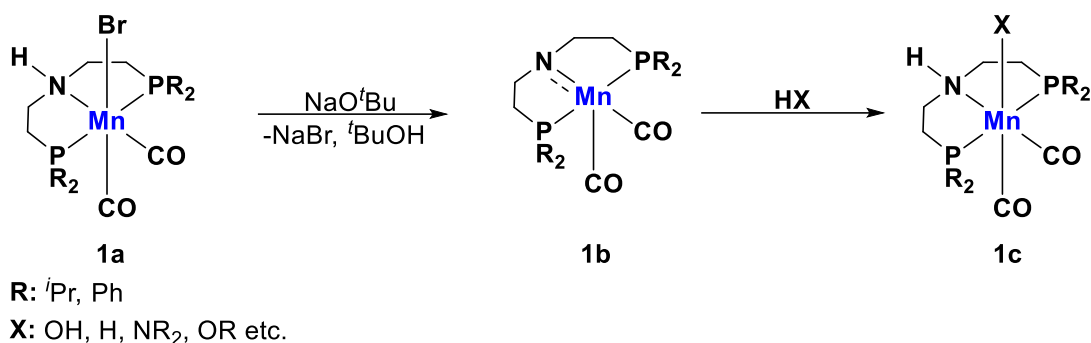


X: NR, O, CR₂
Y: NHC, PR₂, NR₂, SR, OR
Z: Halogen, CO, H, H₂
M: Ir, Rh, Pd, Pt, Fe, Ru, Mn, Ni, Co etc.
D: C, N, NH, B, Si, P, O, S
E: electron donating, electron withdrawing group

Figure 1.2. General structure of transition metal-based pincer complexes.

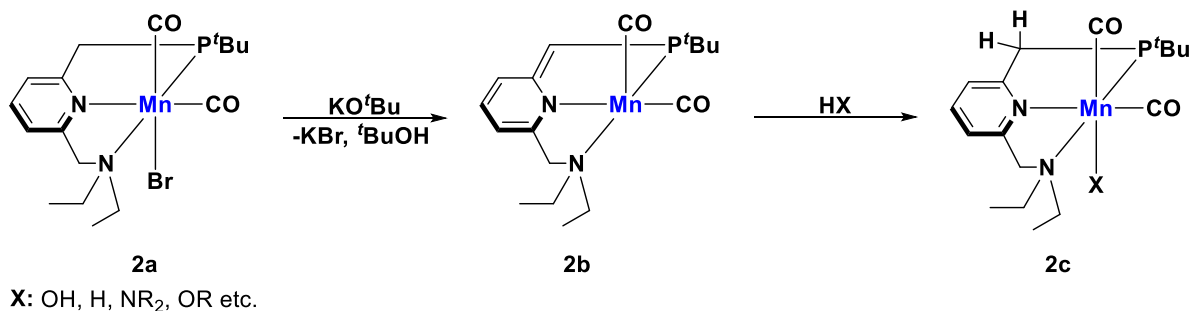
Pincer ligands have been particularly important in the design of manganese catalysts due to their strong binding affinity for the metal center and their ability to facilitate various catalytic processes. Pincer ligands typically feature a tridentate structure, with a central donor atom and two side arms that can coordinate with the metal.¹⁵⁻¹⁷ These ligands can be tailored to incorporate different donor atoms—such as nitrogen, phosphorus, and sulfur—allowing the fine-tuning of the metal's electronic properties. The design of pincer ligands for manganese complexes often draws inspiration from similar ligands used in catalysts based on higher transition metals. By incorporating multifunctional groups into these ligands, it is possible to enhance metal-ligand cooperativity, thereby improving the efficiency and selectivity of the catalytic process.¹⁸ A pincer complex features a central metal atom coordinated by a rigid, multidentate ligand with a 1,3-

disubstituted aryl ring and two chelating side arms. These arms, containing donor atoms like nitrogen or phosphorus, where all donor atoms lie in a single plane to establish a stable geometry. Pincer complexes are often palindromic (e.g., NNN, PNP, PCP), though non-palindromic versions (e.g., NNP, PNN) are also studied.^{19–21} Figure 1.2 shows a generic representation of the pincer complex.



Scheme 1.1. Amine-amide mode of MLC.

Natural enzymes work with ligands and metal centers to cooperatively activate inert bonds.^{22,23} In a similar fashion, metal-ligand cooperation is evident in reactions catalyzed by transition metals. Shvo and Noyori were pioneers in this area, coining the term "bifunctional catalysis" to describe it. In the type of catalyst developed by Noyori, the chelating amine ligand actively engages in the reaction through a reversible proton transfer process, which boosts the reactivity at the metal center.^{24,25} Noyori and his collaborators showcased the application of bifunctional catalysis by employing ruthenium catalysts to facilitate the hydrogenation of carbonyl compounds.^{18,26,27} In 2005, Milstein and his team were the first to observe metal-ligand cooperativity in pyridine-based pincer complexes. The distinctive reactivity of these complexes is attributed to the active participation of their ligands in reaction chemistry through metal-ligand cooperation. Pincer complexes exhibit two main types of MLC: amine-amide MLC (refer to Scheme 1.1) and dearomatization-aromatization MLC (refer to Scheme 1.2).^{28–33} The amine functionality is dehydrohalogenated in the first mode of complex **1a**'s reaction with a base, resulting in a coordinatively unsaturated intermediate (**1b**), which changes the amine into an amide. The amine functionality can then be restored in a coordinatively saturated complex (**3**), this occurs by the activation of inactive bonds (H_2 , H_2O , alcohols, or amines) 16-electron species. The deprotonation at the methylene carbon of a pyridinyl group caused by complex **2a**'s reaction with a base in another mode yields a dearomatized intermediate (**2b**), which is likewise a 16-electron species. These intermediate forms 18 electron species via activation of a wide variety of tiny molecules (such as H-X , where $\text{X} = \text{OH}$, OR, H, NH_2 , NR_2), (refer to Scheme 1.2). Numerous types of reactions have been created by these MLC interactions.

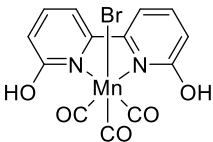
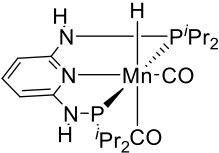
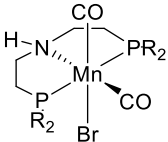
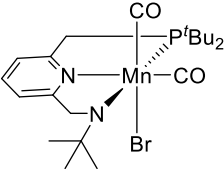
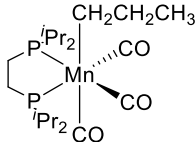
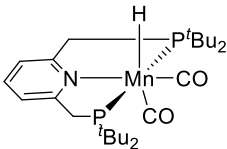
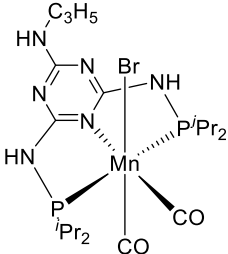


Scheme 1.2. Dearomatization-aromatization mode of MLC

Recent investigations have brought to light the effectiveness of manganese-based catalysts in a variety of reactions (hydrogenation, dehydrogenation, and C-H activation). Manganese pincer complexes, for example, have been applied in the dehydrogenative synthesis of imines, where

the metal and ligand collaborate to enable the transfer of protons and hydrides. The integration of multifunctional ligands, which can undergo protonation/deprotonation or redox transformations, has been pivotal in enhancing catalytic performance. These advancements underscore the potential of manganese catalysis as a promising and sustainable alternative to precious metals in chemical processes.³⁴

Table 1.1. Manganese catalysed hydrogenation of CO₂ and bicarbonate to formate.

$\text{H}_2 + \text{CO}_2 \xrightarrow[\text{Base}]{\text{Reaction condition}} \text{H}-\overset{\text{O}}{\underset{\text{ }}{\text{C}}}-\text{O}^- + \text{H}^+ \text{Base}$									
 Khusnutdinova, 2017 C-1  Kirchner & Gonsalvi, 2017 C-2  Prakash, 2018 R = <i>i</i>Pr, C-3 R = Cy, C-4  Milstein, 2019 C-5									
 Kirchner & Gonsalvi, 2021 C-6  Saouma, 2021 C-7  Sponholz, Junge, Beller, 2022 C-8									
Entry	Catalyst	CO ₂ /H ₂ pressure (bar)	T (°C)	Solvent	base	additive	TON	TOF	Yield
1	C-1	30/30	65 °C	CH ₃ CN	DBU	-	6250	-	98%
2	C-2	40/40	80 °C	THF/H ₂ O	DBU	LiOTf	10000 1233	>99	-
3	C-3	-/50	80 °C	THF	NaOH	-	2258	31	45%
4	C-4	-/50	80 °C	THF	NaOH	-	-	33	82%
5	C-5	30/30	110 °C	H ₂ O	KOH	-	-	-	23%
6	C-6	50/25	80 °C	THF	DBU	LiOTf	1988	-	98.7%
7	C-7	15/15	100 °C	THF	KO ^t Bu	-	58	-	-
8	C-8	20/60	115 °C	H ₂ O/THF	Lys	-	230000	-	92%

Carbon dioxide is a plentiful chemical resource in the atmosphere. Despite being thermodynamically and kinetically stable, making it challenging to activate, the use of a catalyst can facilitate the process by lowering the energy barrier.³⁵ Formic acid is a vital component in the leather and textile industries, where it is applied in tanning and dyeing. It also plays a significant role in silage production and acts as a reducing agent in synthetic manufacturing processes. In the pharmaceutical sector, formic acid is utilized for various applications. Furthermore, it serves as a coagulating agent in the production of latex rubber, is used in the electroplating of different materials, and contributes to the manufacturing of resins, varnishes, plasticizers, and glass.³⁶

Since 2017, various research teams have explored the manganese-catalysed conversion of CO₂ into formate, building on the findings of Nervi and Khusnutdinova. They showed that the 2,2'-bipyridine based Mn(I) catalyst **C-1** (refer to Table 1.1), is highly effective in facilitating this reaction. By employing a catalyst loading of 0.005 mmol and using DBU as the base at a temperature of 65 °C for 24-hours in acetonitrile, a 99% yield of formates is achieved. Additionally, a turnover number (TON) reaching up to 6250 was recorded (see Table 1.1, entry 1).³⁷

Gonsalvi and Kirchner also reported CO₂ hydrogenation utilizing the manganese-based PNP pincer hydride complex **C-2** (Table 1.1). The maximum TON of 10000 was achieved after carrying out the reaction for 24 hours at 80 °C using DBU as the only basic additive. The incorporation of LiOTf as a co-catalyst increased the TON to 30000 (Table 1.1, entry 2).³⁸

In 2018 group of Prakash came up with an integrated approach to capture CO₂ followed by hydrogenation to formate utilizing Ru, Mn, and Fe pincer complexes. The Mn complexes **C-3** and **C-4** revealed TON of 1233 and 2258, respectively when the hydrogenation of CO₂ was carried out in the presence of NaOH base.³⁹

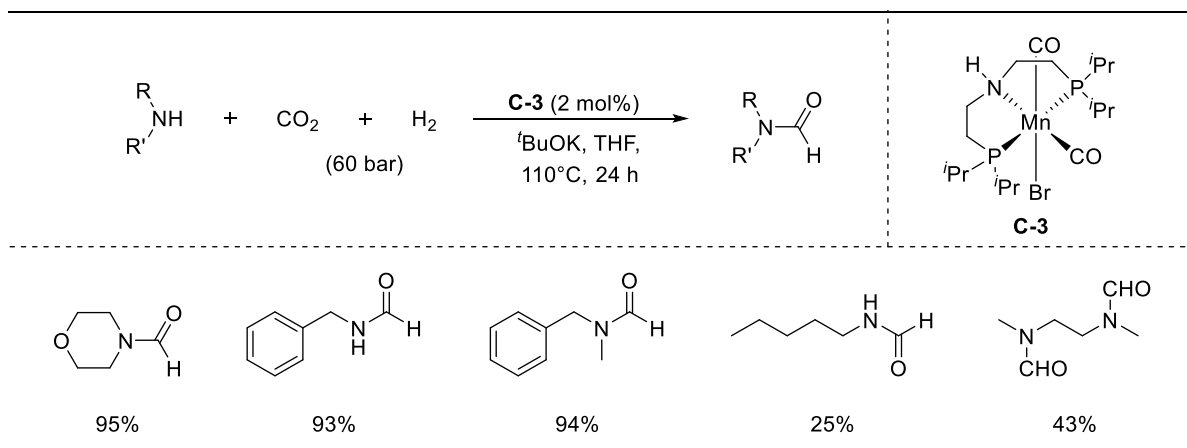
Milstein group in 2019, demonstrated activation of CO₂ using Mn-PNP type pincer complexes via different modes of metal-ligand cooperation. They explored the reactivity of the complexes with CO₂ and revealed that **C-5** was able to hydrogenate CO₂ giving low yield of 23% at 110 °C in the presence of KOH (Table 1.1, entry 5).⁴⁰

In 2021, Kirchner and Gonsalvi documented the hydrogenation of CO₂ using a Mn complex **C-6** with a bidentate dippe ligand, achieving a TON of up to 1988. This process utilized DBU as a base and LiOTf as a co-catalyst, and the reaction was conducted in THF.⁴¹

In the same year, Saouma documented the hydrogenation of CO₂ utilizing a manganese PNP pincer complex **C-7**, as shown in Table 1.1. By using 0.0005 mmol of the catalyst over an 18-hour duration with KO^tBu, formates were produced, reaching a TON of up to 58. The author suggested that due to the complex's low hydricity, it is less prone to CO₂ insertion, indicating that the reaction might proceed through an alternative pathway.⁴²

Beller and his colleagues recently introduced a manganese-based PNP pincer complex combined with the naturally occurring Lys (**C-8**), achieving a formate yield as high as 92% and a turnover number (TON) of 230,000. This catalytic system demonstrated remarkable stability, enabling it to be reused multiple times, reaching a total turnover number (TTON) of up to 2,000,000. Notably, this catalyst system also facilitates hydrogen production from formic acid (FA).⁴³

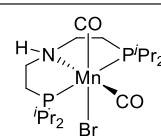
Table 1.2. Mn (**C-3**) catalysed *N*-formylation of amine with CO₂ and H₂.



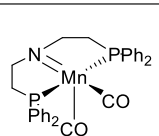
Suryaprakash and his team explored the Mn-pincer complex **C-3** to evaluate its role in the *N*-formylation of amine using CO₂ and H₂, marking the first phase in the stepwise transformation of CO₂ into methanol. Their findings revealed that **C-3** effectively converts CO₂ into formamide, achieving a yield of up to 94% with *N*-methylbenzylamine after a 24-hour reaction at 110 °C in THF (Table 1.2).⁴⁴

Table 1.3. Direct hydrogenation of CO₂ to methanol using manganese catalysts.

$$3\text{H}_2 + \text{CO}_2 \xrightarrow[\text{Base}]{\text{Reaction condition}} \text{CH}_3\text{OH} + \text{H}_2\text{O}$$



Prakash, 2017 & 2018
C-3

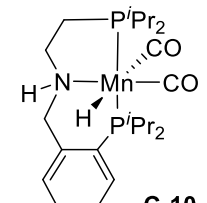
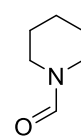
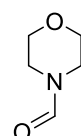
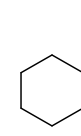
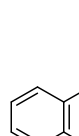
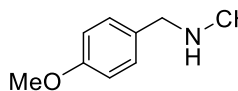
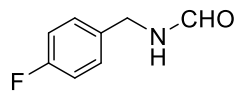
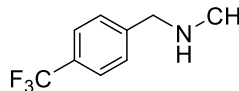


Leitner, 2021
C-9

Entry	catalyst	CO ₂ /H ₂ pressure (bar)	T (°C)	solvent	amine	additive	TON	Yield
1	C-3	-/80	150 °C	THF	morpholine	KO ^t Bu	-	71%
2	C-3	-/70	145 °C	THF	PEHA	-	25	5%
3	C-9	5/160	150 °C	1,4-dioxane/EtOH	-	Ti(O ⁱ Pr) ₄	160	-

In 2017, Prakash achieved the stepwise hydrogenation of CO₂ into methanol via formamide. The team utilized an air-stable pincer complex of PNP Mn(I), specifically **C-3**, to perform this process. By employing a 2 mol% of catalyst in the presence of KO^tBu as a base in THF, they obtained 4-formyl morpholine with a 95% yield after 36 hours at 110 °C, using a total pressure of 60 bar of CO₂ and H₂ in a 1:1 ratio. Following this, methanol was generated with a 71% yield relative to the amine under 80 bar of hydrogen after another 36 hours (Table 1.3, entry 1).⁴⁴

Table 1.4. Mn (**C-10**) catalysed acceptorless dehydrogenative coupling of methanol with amine.

$\text{CH}_3\text{OH} + \text{R}^1\text{NH}_2 \xrightarrow[\text{MeOH, 110 °C}]{\text{C-10 (2 mol\%)}} \text{H}-\text{C}(=\text{O})-\text{NH}-\text{CH}_2-\text{R}^1 + 2\text{H}_2 \uparrow$				 C-10
Selected examples				
				
Yield: 86%	50%	66%	62%	
				
Yield: 78%	70%	64%	53%	
				
Yield: 67%	57%	71%		

The following year, they demonstrated that, in the presence of pentaethylenehexamine (PEHA), **C-3** may be utilized to capture CO₂ and then hydrogenate it to methanol. Even though ruthenium

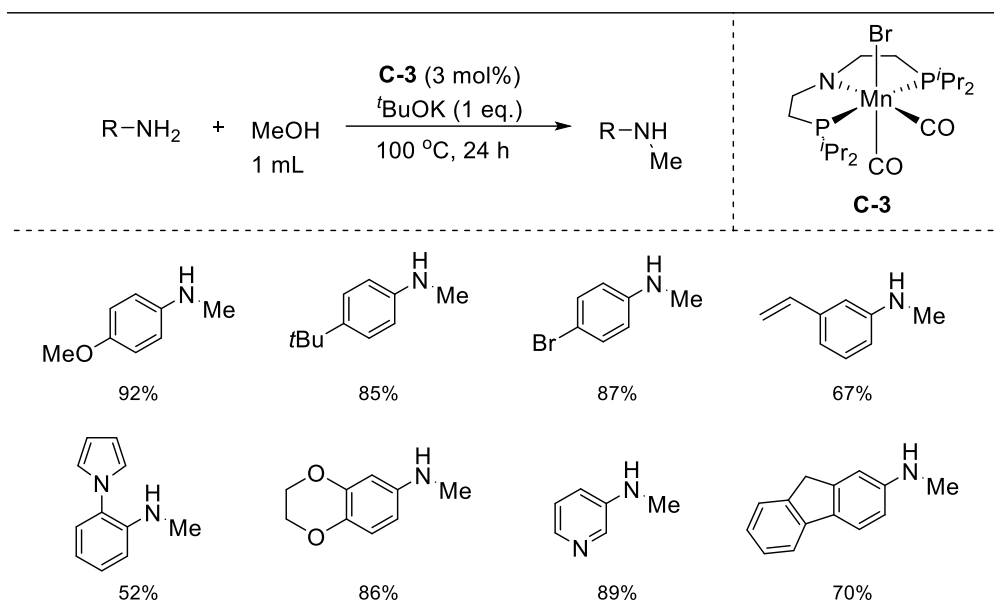
pincer complexes worked best in this instance, 20 μmol of Mn catalyst with 1 mmol K_3PO_4 produced 5% methanol after 72 hours at 145 $^\circ\text{C}$ using 70 bar dihydrogen, and a TON of 25 was noted (Table 1.3, entry 2).⁴⁵

Furthermore, in 2021, Leitner and coworkers explored methanol synthesis from CO_2 using Mn PNP pincer catalyst **C-9**. In cooperation with $\text{Ti}(\text{O}^i\text{Pr})_4$, a 10 μmol Mn catalyst hydrogenated 5 bar CO_2 at 150 $^\circ\text{C}$ at the cost of 160 bar H_2 pressure after 68 h. A maximum of 160 TON was noted.⁴⁶

Another industrially produced biofuel that works well as a stand-in for internal combustion is methanol. The non-renewable syngas route is converted from gas to liquid to produce methanol. In a wide range of medications, agrochemicals, and biomolecules, methyl groups have been discovered to have an appealing and common activity. The methyl group appears to be a minor motif, yet it plays a crucial part in regulating the biological and medicinal effects of any medication.⁴⁷

Milstein and colleagues⁴⁸ pioneered the development with the introduction of a useful and effective manganese PNP pincer catalyst (**C-10**) in 2017. While homogeneous precious metal catalyzed dehydrogenative coupling of methanol and amines to furnish *N*-formamides was reported since 2013 by Glorius⁴⁹ and later in 2015 by Hong,⁵⁰ the use of non-noble metal for the same was not reported until then. When alcohol and amine undergo a modest dehydrogenative coupling process without the need for an additive, the catalyst **C-10** is efficient in producing formamide. For the reaction to provide moderate to good yields, a variety of primary and secondary amine types were tolerated (Table 1.4). Based on in-depth mechanistic research and DFT analyses, the authors offered a tenable explanation for the reaction.

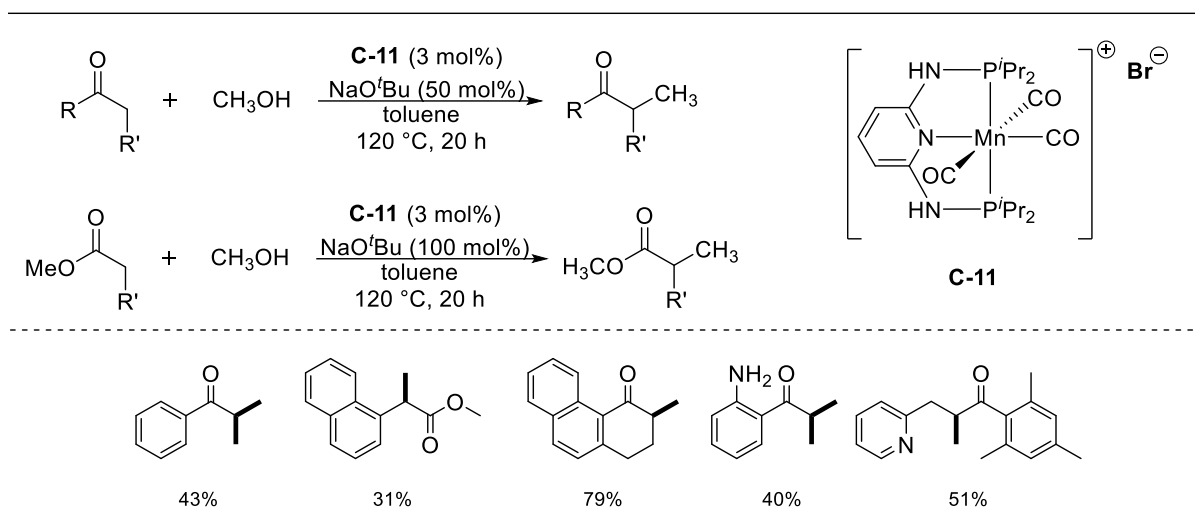
Table 1.5. **C-3** catalysed *N*-monomethylation of primary aniline by methanol and selected examples.



The main structural elements of many naturally occurring bioactive compounds are *N*-methylated amines. A green method for producing a variety of useful methylated chemical compounds is the dehydrogenative coupling of methanol with amines, followed by hydrogen auto-transfer. It is also very desirable to build earth-abundant metal-based catalytic systems for the aforementioned objective. An elegant, earth-abundant manganese-based PNP pincer catalyst **C-3** (Table 1.5) for the mono *N*-methylation of amines utilizing methanol as a methylating agent was revealed in a groundbreaking study by Beller and colleagues⁵¹ in 2016. Using a borrowed hydrogen/hydrogen autotransfer technique, this was the first instance of a C-N coupling reaction based on a non-noble metal catalyst under moderate circumstances. It can withstand a wide variety of sensitive functional groups, including heterocycles and alkenes. Nevertheless, one base

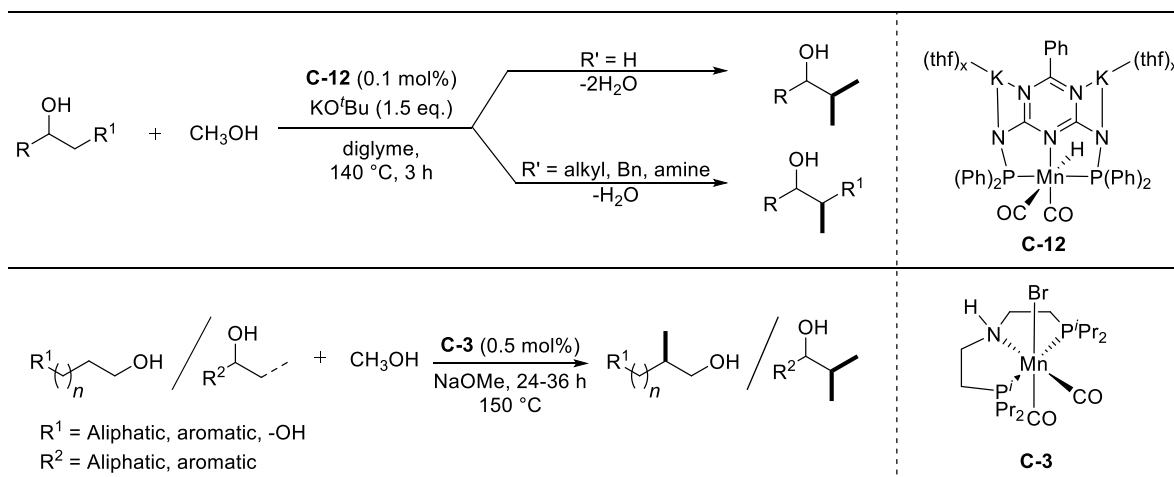
comparable in relation to substrates is needed for this procedure. Table 1.5 displays reaction conditions, isolated yields, and representative cases. This catalyst has broad application for *N*-alkylation of different amines with different alcohols in addition to methylation.

Table 1.6. C-11 catalysed BH methylation of ketones and esters.



A promising method for the effective production of physiologically active compounds is direct C-H bond functionalization. Because of the atom-economy, C-H methylation has garnered a lot of interest in the synthesis of novel therapeutic compounds. C-methylation is often accomplished using hazardous or explosive chemicals such as dimethyl sulfate, iodomethane, or diazomethane. One useful substitute for C-methylation processes is thought to be methanol. Under hydrogen borrowing circumstances, Sortais and colleagues⁵² reported using a manganese-based pincer complex **C-11** as a pre-catalyst and NaO^tBu (50 mol%) as the base for α-methylation of a range of ketones. Esters were also used to assess the reaction's scope. A variety of electron withdrawing to electron rich groups were also tolerated well to yield moderate to excellent yield. Representative examples of the substrates scope and isolated yields are shown in Table 1.6.

Additionally, at low catalyst loading, Kempe and his colleagues⁵³ showed the manganese-based pincer catalyst **C-12** for mono- and di-methylation of alcohols with a moderate to good yield of several primary and secondary alcohols as well. Additionally, a wide range of functional groups showed good tolerance. A bimetallic K-Mn catalyst is involved in the borrowing hydrogen process, according to the mechanistic pathway analysis (Scheme 1.3).

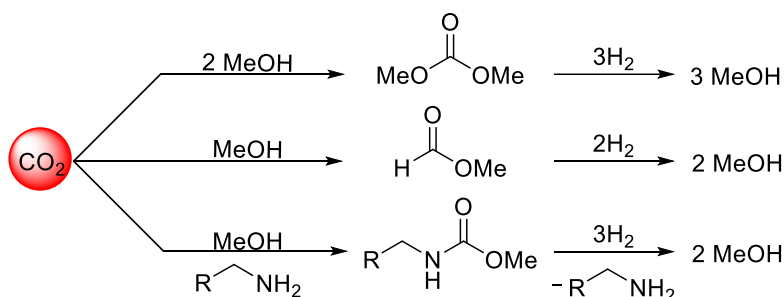


Scheme 1.3. Mn catalysed β-methylation of alcohols by methanol.

For the β -methylation of alcohols, Leitner and coworkers⁵² investigated the Mn-MACHO complex **C-3** based on air stable PNP ligands. A variety of aliphatic alcohols and diols generated from biomass were also chosen for methylation at the β -position with high yield. Among a variety of pre-catalysts, the **C-3** complex demonstrated the best selectivity during reaction optimization. Pharmaceutically significant compounds like naproxen and ibuprofen were synthesized using this approach (Scheme 1.3).

A number of research teams have recently investigated the "indirect" hydrogenation of CO₂ to methanol, in which easily accessible CO₂ derivatives, including urea derivatives, carbamates, formates, cyclic carbonates, and organic carbonates, can be employed as substrates (Scheme 1.4).^{54–58}

Recent research has also shown that the presence of several homogeneous earth-abundant complexes can indirectly hydrogenate CO₂ derivatives such as urea derivatives and cyclic and acyclic organic carbonates. The pyridine-based PNN pincer Mn complex **C-13** was described by Milstein as an efficient catalyst for the hydrogenation of organic carbonates to get methanol. After 30 to 50 hours at 110 °C and charging at 30 to 50 bar of hydrogen pressure, 2 mol% catalyst and 4 mol% KH as base generate 99% methanol and other alcohol as a byproduct (Table 1.7, entry 1). Moderate catalytic conditions were used to hydrogenate a broad range of carbonates, including cyclic carbonates and symmetrical and unsymmetrical acyclic carbonates. The catalyst's ability to catalytically hydrogenatively depolymerize poly(propylene carbonate) was demonstrated.⁵⁹



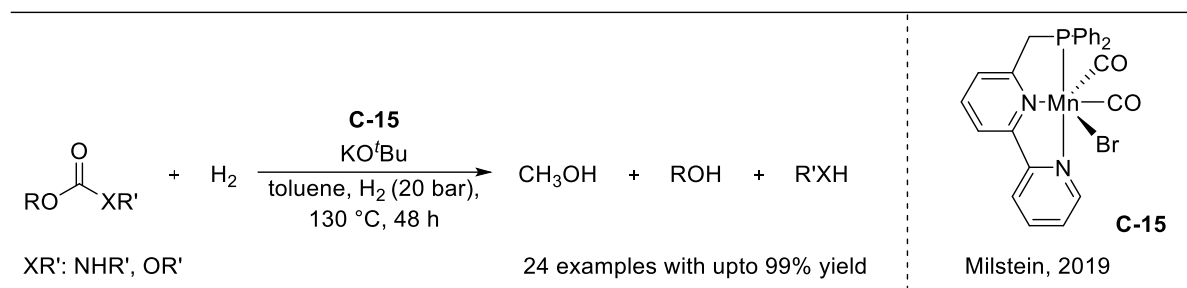
Scheme 1.4. Indirect hydrogenation of CO₂ derivatives to methanol.

Rueping and associates used the PNP-Mn complex (**C-14**) to hydrogenate polycarbonates and cyclic carbonates. After 16 hours at 140 °C in dioxane with a loading of 0.25 mol% catalyst and KO^tBu base under 50 bar H₂, methanol was generated in a 99% yield (Table 1.7, entry 2).⁶⁰

Table 1.7. Manganese catalysed hydrogenation of cyclic and acyclic carbonate.

				C-13	C-14	C-3	
Entry	catalyst	H ₂ pressure (bar)	T (°C)	solvent	base	Examples	Methanol yield
1	C-13	30	110 °C	toluene	KH	14 examples	upto 99%
2	C-14	50	140 °C	dioxane	KO ^t Bu	13 examples	upto 99%
3	C-3	30	120 °C	THF	NaO ^t Bu	11 examples	upto 94%

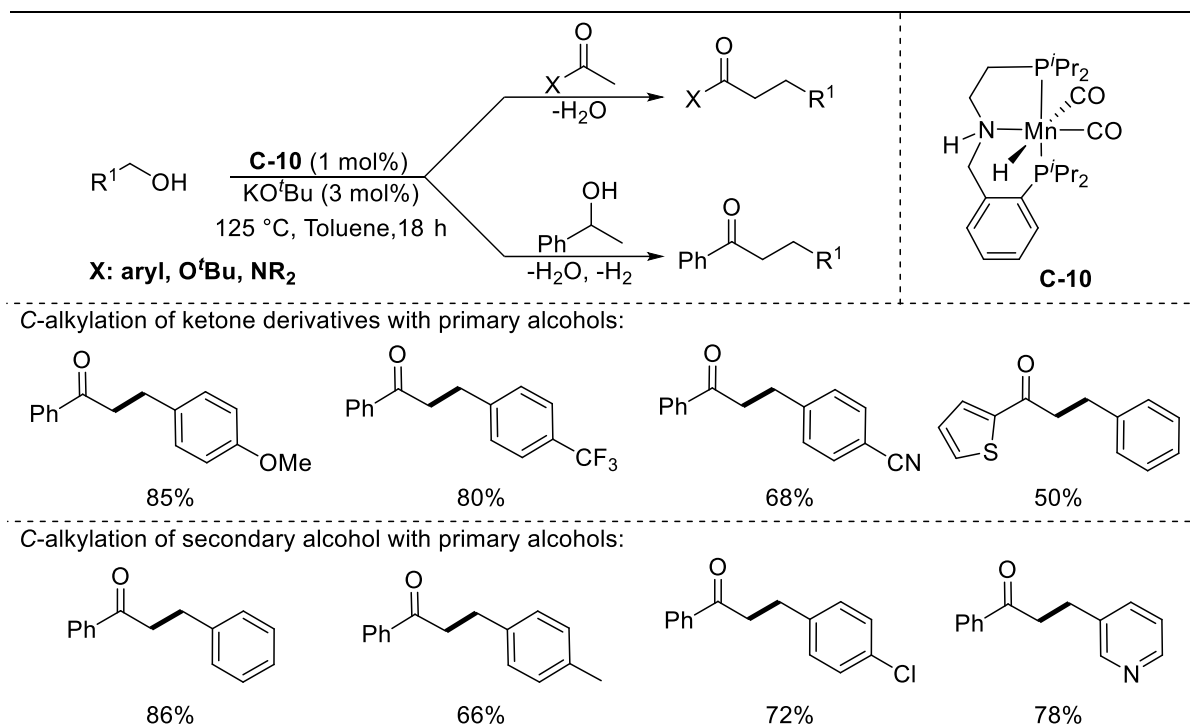
Leitner showed how to use the Mn pincer complex (**C-3**) to hydrogenate cyclic carbonates. After 40 hours at 100 °C in THF with 0.1 mol% of the catalyst loading utilizing NaO^tBu as base and 60 bar H₂ of charge, methanol (up to 92%) with a maximum TON of 400 was produced as shown in Table 1.7, entry 3.⁶¹



Scheme 1.5. C-15 catalysed hydrogenation of carbamates and urea derivatives.

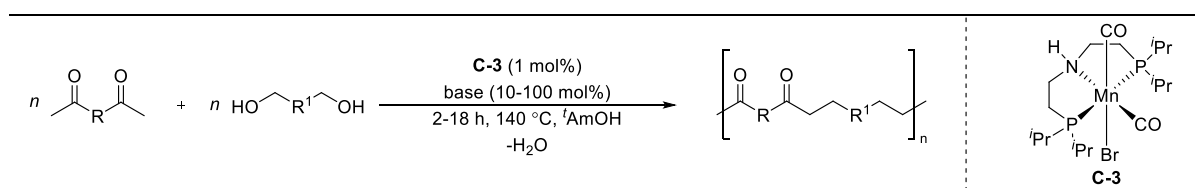
In 2019, the Milstein group announced the first hydrogenation of carbamates and urea derivatives based on earth-abundant metal complexes. Using the Mn-based PNN pincer complex **C-15**, they demonstrated the hydrogenation of carbamates. After 48 hours at 130 °C, a range of carbamates and urea derivatives were hydrogenated, with methanol as one of the byproducts, using 2 mol% of the pre-catalyst **C-15** and 3 mol% KO^tBu (Scheme 1.5). The catalyst required a remarkably low pressure of 20 bar to carry out the hydrogenation process. They suggested a process involving the aromatization and de-aromatization of the ligand backbone based on stoichiometric studies and mechanistic analysis. The cycle shows that base-based dehydrohalogenation followed by H₂ activation produces the catalytically active dearomatized complex.⁶²

Table 1.8. C-10 catalysed alkylation of ketones, amides, and esters, using primary alcohols.



The formal reverse reaction of hydrogenation involving the oxidation of organic scaffold with the elimination of H₂ is generalized as dehydrogenation. Traditionally, stoichiometric concentrations of inorganic oxidants are used in dehydrogenation/oxidation processes of organic compounds. Other additives, cocatalysts, or sacrificial hydrogen acceptors are also used, which results in the creation of several copious byproducts.³³ The release of hydrogen through acceptorless dehydrogenation (AD) reactions is becoming a potent synthetic technique that avoids the need

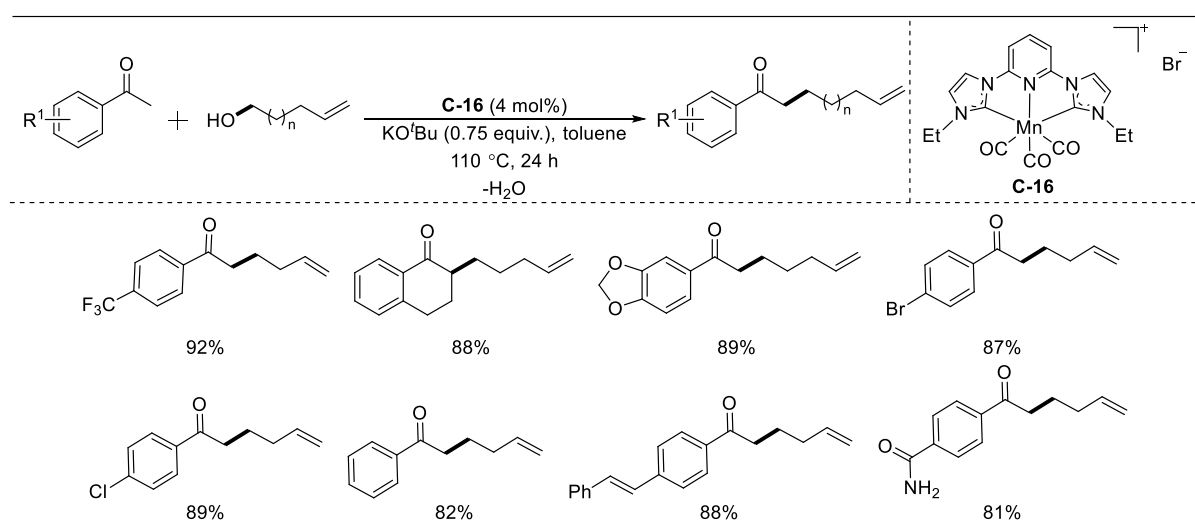
of sacrificial hydrogen acceptors or stoichiometric oxidants.⁶³ Catalytic dehydrogenation is noted for many interesting applications. Particularly noteworthy is acceptorless dehydrogenative coupling (ADC) of alcohols for the formation of vast array of C-C and C-N bonds⁶⁴ offering an attractive “green” route for the synthesis of valuable chemical product. Alcohols are a cheap, plentiful, and ecologically safe feedstock that may be bought commercially or derived from renewable resources like indigestible lignocellulosic biomass.^{65,66} Through catalytic dehydrogenation and subsequent coupling of the dehydrogenated intermediate with nucleophiles, this protocol transforms alcohols into electrophilic aldehydes or ketones. This creates new C-C and C-N bonds, enabling the conversion of alcohols into ester, acetal, imine, amine, carboxylic acid, etc., with H₂ as the sole byproduct.³³ Moreover, the evolved hydrogen gas is valuable as a potential fuel. Acceptorless dehydrogenation of small molecules like methanol, formic acid, ammonia-borane releases H₂, which is the target product of the transformation. These substrates act as hydrogen storage and carriers that produce pure H₂ with carbon dioxide (or polyborazines) being the only by-product of the dehydrogenation.⁶⁷ Such processes together with the chemical pathways to regenerate parent substrates have immense potential for energy applications.



Scheme 1.6. C-3 catalysed synthesis of polyketones.

‘Borrowing hydrogen’ (BH) or “hydrogen auto-transfer” (HA), is another elegant dehydrogenative approach enabling the functionalization of alcohols as alkylating partners in a diversity of C–C and C–N reactions that create bonds. In this process, the released H₂ from the dehydrogenative coupling reaction is transferred to unsaturated intermediates which is generated from a condensation reaction. Water is the only by-product for this one pot reaction, and the entire process is redox neutral since net hydrogen evolution is not involved.^{68–70}

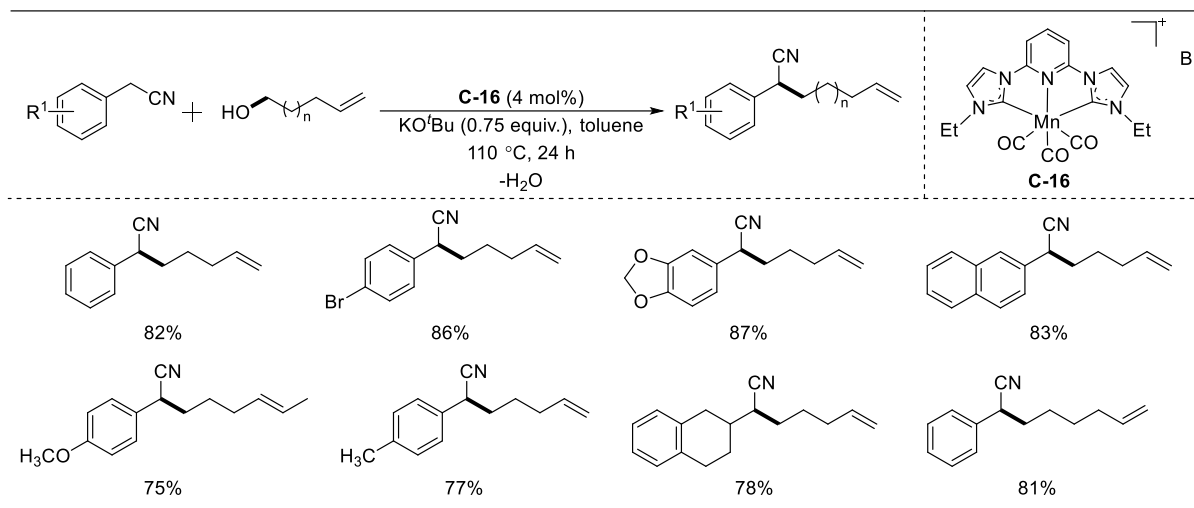
Table 1.9. C-16 catalysed alkylation of ketones derivatives with unactivated alkenyl alcohols.



Using primary alcohols, Milstein and colleagues reported manganese-catalyzed C-C bond formation processes by α -alkylation of ketones, amides, and esters and β -alkylation of secondary alcohols to produce α -alkylated ketones. The alkylation was catalyzed by a (iPr-PN^HP)Mn(H)(CO)₂ pincer complex **C-10** (1 mol%) at 125 °C in toluene for 18 h in the presence of base - Potassium *tert*-butoxide (KO^tBu: 3 mol%), liberating water for ketones and when secondary

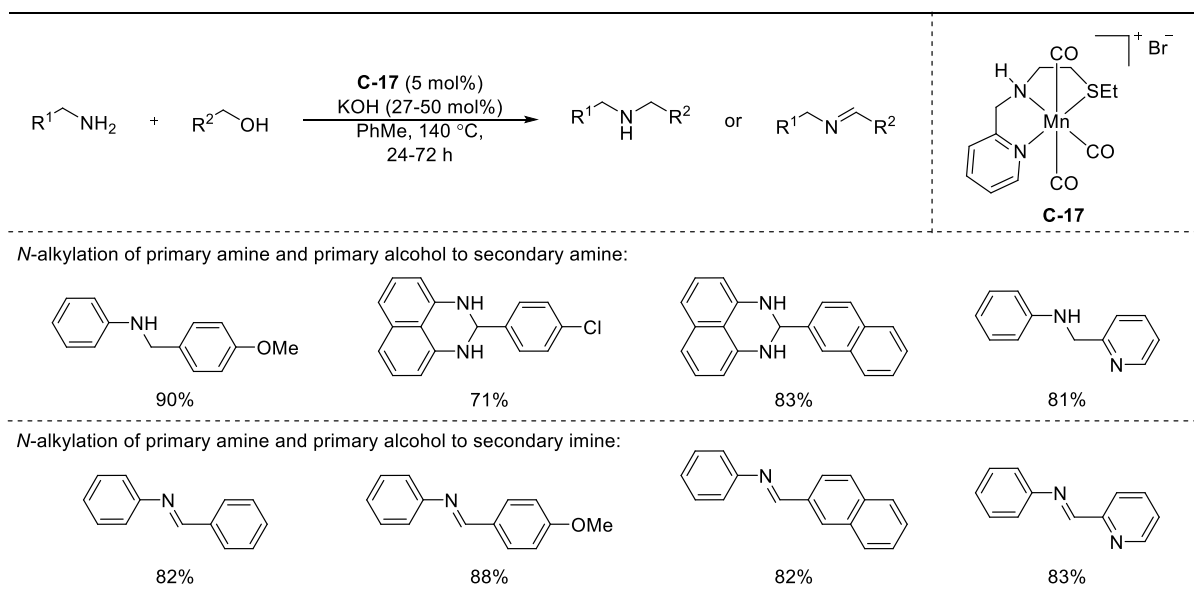
alcohol is used, the only byproduct is H₂ (see table 1.8). The C-alkylation followed borrowing hydrogen methodology and successfully applied it to 16 examples including 11 aromatic and 5 aliphatic primary alcohols with up to highest 92% conversion. Also, they covered 9 types of aromatic primary alcohols for C-alkylation of ester and amide with striking highest 99% conversion. Interestingly, the catalyst was also able to do the alkylation of secondary alcohols instead of ketones with 5 types of primary aromatic alcohols.⁷¹

Table 1.10. C-16 catalysed alkylation of nitrile derivatives with unactivated alkenyl alcohols.



Kumar and coworkers demonstrated a manganese PNP complex for the synthesis of a variety of polyketones using hydrogen-borrowing strategy. In this process, up to 12 polyketones were synthesized with a yield of up to 99% using 0.5–1.0 mol% catalytic loading and 0.05 mmol of base loading (Cs₂CO₃) in 2 hours using a variety of diketones and diols, including a renewable diol and a diol derived from the depolymerization of waste plastic bottles. (see scheme 1.6).⁷²

Table 1.11. C-17 catalysed synthesis of amine, imine, and 2,3-dihydro-1H-perimidine.



Recently, Kundu's team have explored phosphine free NHC based manganese CNC complex for selective α-alkylation of a variety of ketone derivatives with unactivated alkenyl alcohols as coupling partners. The reaction was carried out with 4 mol% catalyst loading, KO^tBu (0.75 equiv.) and toluene as solvent at 110 °C for 24 h (table 1.9). Upto 36 examples are demonstrated with the yield upto 92%. Furthermore, they have demonstrated the α-alkylation of acetonitrile derivatives

with alkenyl alcohols with similar reaction conditions and showcased upto 14 examples with the yield upto 87%. This catalytic system is particularly successful for the α -alkylation of a broad variety of ketones and acetonitriles with aromatic, heteroaromatic, and aliphatic units in the presence of numerous reducible functional groups (table 1.10). This protocol's practical usability and synthetic utility were proved by gram-scale synthesis, green chemistry metric evaluation, and alkylated product functionalization into significant compounds.⁷³

In 2019, the first phosphine-free Mn-based compound for the dehydrogenative coupling of amine and alcohol derivatives was shown by Srimani and colleagues. The selectivity and stoichiometry of the applied base played a critical role to maximize the selectivity of the product. They demonstrated the reaction with 5 mol% **C-17**, base loading 27-50 mol% at 140 °C for 24-72 h reaction time (table 1.11). Furthermore, they have corroborated their experimental data with DFT studies.⁷⁴