Manganese Pincer Catalyzed Organic Transformations

By

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List of Publications arising from the thesis

Journal

1. **Pandia, B. K.**; Gunanathan, C. Manganese(I) Catalyzed *α*-Alkenylation of Amides Using Alcohols with Liberation of Hydrogen and Water. *J. Org. Chem.* **2021**, *86*, 9994-10005.
2. **Pandia, B. K.**; Pattanaik, S.; Gunanathan, C. Manganese(I) Catalyzed Alkenylation of Phosphine Oxides Using Alcohols with Liberation of Hydrogen and Water *J. Org. Chem.* **2021**, *86*, 17848-17855.
3. **Pandia, B. K.**; Pattanaik, S.; Gunanathan, C. Manganese(I) Catalyzed Cross-coupling of Secondary Allylic Alcohols and Primary Alcohols. *Tetrahedron* **2021**, *101*, 132472 (*Invited Article in Special Issue: "Earth Abundant Metal-Catalyzed Sustainable Organic Transformations*).

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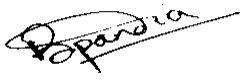
2. Gawali, S. S.; Pandia, B. K.; Pal, S.; Gunanathan, C. Manganese(I)-Catalyzed Cross-Coupling of Ketones and Secondary Alcohols with Primary Alcohols. *ACS Omega* **2019**, *4*, 10741-10754 (Invited Article).

Conferences:

1. **Oral Presentation**: Smart Materials Chemistry (CHEMSMAT-21) at Department of Chemistry, St.Joseph's College, Tiruchirappalli during 29^{th}-31^{st} July 2021. Title:

Manganese(I) Catalyzed Alkenylation of Amides Using Alcohols with Liberation of Hydrogen and Water (*Awarded second prize*)

2. **Oral Presentation**: Modern Trends in Chemistry (MTC-27) at Department of Chemistry Vivekananda College, Madurai during 9^{th}-10^{th} November 2021. Title: Manganese(I) Catalyzed Alkenylation of Amides Using Alcohols with Liberation of Hydrogen and Water
3. **Oral Presentation**: Main Group Molecules to Materials (MMM-II) at NISER, Bhubaneswar during 13^{th}-15^{th} December 2021. Title: Manganese(I) Catalyzed Alkenylation of Amides and Phosphine Oxides Using Alcohols with Liberation of Hydrogen and Water
4. **Oral Presentation**: Recent Advances in Heterocyclic Chemistry (RAHC) at Department of Chemistry, Ravenshaw University, Cuttack during 15^{th}-16^{th} January 2022. Title: Manganese(I) Catalyzed Alkenylation of Amides and Phosphine Oxides Using Alcohols with Liberation of Hydrogen and Water



Biplab Keshari Pandia

Dedicated to....

To my parents

&

Dr. C. Gunanathan

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…Biplab Keshari Pandia

SYNOPSIS

1. **Name of the Student**	: Mr. Biplab Keshari Pandia
2. **Name of the Constituent Institution**	: National Institute of Science Education and Research (NISER)
3. **Enrolment No.**	: CHEM11201604032
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Introduction

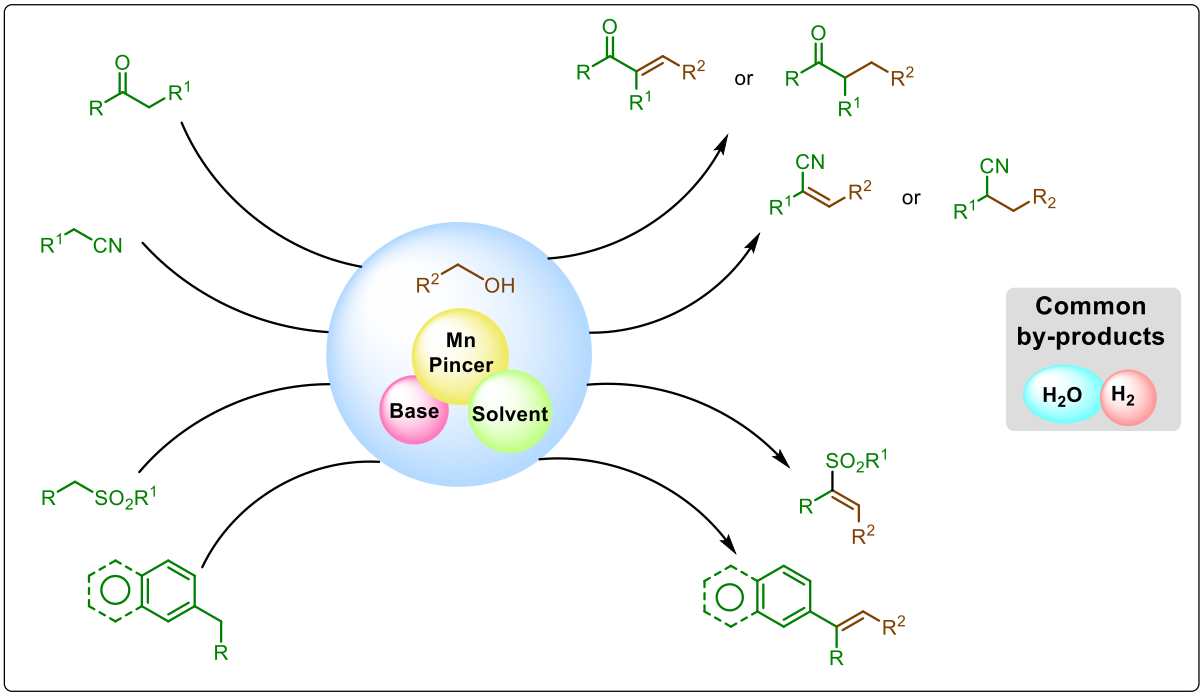
Pincer complexes are composed of tridentate ligands, which possess unique balance of stability and reactivity. The steric and electronic properties of the pincer ligands can be modularly tuned to impart enhanced stability, and well-defined reactivity on pincer complexes.[1-2] In recent years diverse manganese pincer complexes and their catalytic applications have been reported.[4-6] Manganese pincer complexes catalyze a wide range of chemical transformations with high efficiency and selectivity especially via borrowing hydrogen, and acceptorless dehydrogenation pathways.[7-8]

Scope and Organization of Present Thesis

A manganese pincer complex derived from PNP-2,6-diamino triazine backbone (Kempe's catalyst) was prepared, which exhibited the dearomatization-aromatization metal ligand cooperation. Using this manganese pincer catalyst different alkenylation reactions were developed in which alcohols were used as direct alkenylation reagent. Manganese pincer catalyzed α-alkenylation of amides to α,β-unsaturated amides, and α-alkenylation of methyldiphenylphosphine oxides were attained. Catalytic cross coupling of secondary allylic alcohols and primary alcohols to α-alkenylation and α-alkylation was also developed. Remarkably, water and/or liberated molecular hydrogen are the only byproducts, which

make these transformations atom-economical and environmentally benign. The detailed mechanistic studies, substrate scope, are shown in each chapter. The current thesis is classified into four chapters. Chapter-wise discussions are shown below.

Chapter 1: Introduction



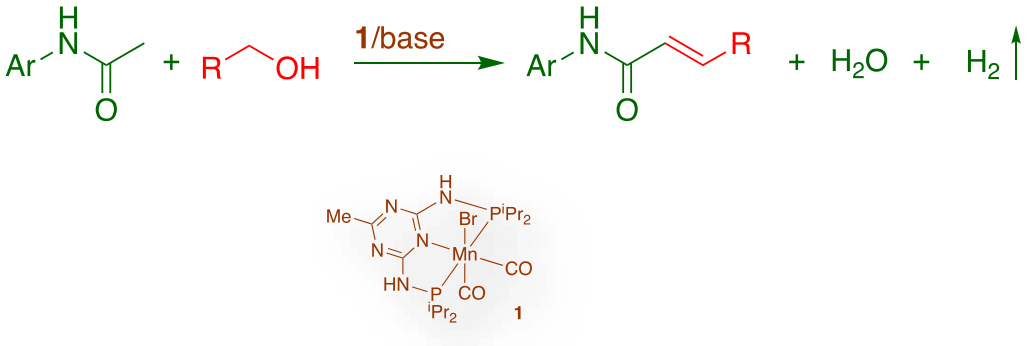
Scheme 1: Manganese Pincer Catalyzed Alkenylation and Alkylation of Organic Compounds

Pincer complexes are composed of tridentate pincer ligands that upon complexation with metal attain a meridional geometry. Due to their unique structure, they exhibit balance in stability and reactivity. They can withstand high temperature making them useful in homogeneous catalysis. The electronic and steric properties can be fine-tuned by changing the substituents present on the pincer backbone as well as the metal thereby imparting diverse reactivity to the pincer complex.[1-2] The metal-ligand cooperation operative in the pincer complexes allows them to activate small molecules and inert chemical bonds. In recent years, various manganese pincer complexes have been synthesised and their reactivity has been thoroughly explored. By following the acceptorless dehydrogenative

coupling and borrowing hydrogen strategies[3] a range of chemical transformations have been developed using alcohols.[4-8] Chapter 1 will describe the summary of literature reports on manganese pincer catalyzed organic transformations with particular focus on alkenylation and alkylation reactions.

Chapter 2: Manganese(I) Catalyzed α-Alkenylation of Amides Using Alcohols with Liberation of Hydrogen and Water

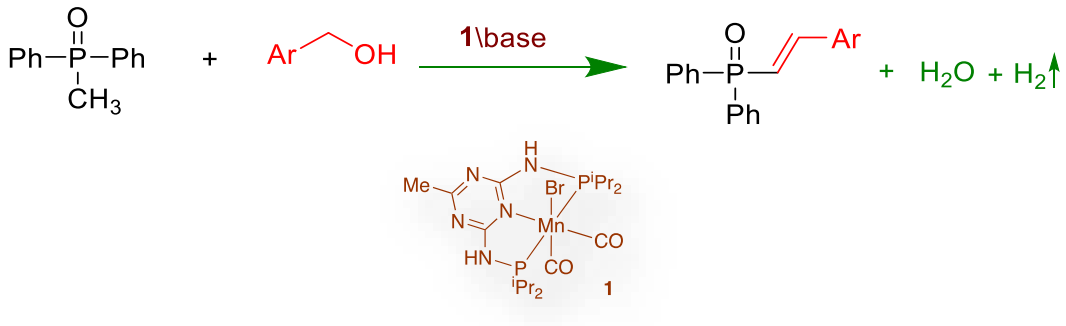
In this chapter an unprecedented manganese-catalyzed direct α-alkenylation of amides using alcohols is reported.[14] Aryl amides are reacted with diverse primary alcohols, which provided the α,β -unsaturated amides in moderate to good yields with excellent selectivity. Mechanistic studies indicate that Mn(I) catalyst oxidizes the alcohols to their corresponding aldehydes and also plays an important role in efficient C=C bond formation through aldol condensation. This selective alkenylation is facilitated by metal−ligand cooperation by the aromatization-dearomatization process operating in the catalytic system. Biorenewable alcohols are used as alkenylation reagents for the challenging α-alkenylation of amides with the highly abundant base metal manganese as a catalyst, which results in water and dihydrogen as the only byproduct, making this catalytic transformation attractive, sustainable, and environmentally benign.



Scheme 2: Manganese Catalyzed *α*-Alkenylation of Amides Using Alcohols

Chapter 3: Manganese(I) Catalyzed Alkenylation of Phosphine Oxides Using Alcohols with Liberation of Hydrogen and Water

In this chapter the catalytic cross-coupling of methyldiphenylphosphine oxide with arylmethyl alcohols leading to the alkenylphosphine oxides is reported.[15] A manganese pincer catalyst catalyzes the reactions, which provides exclusive formation of trans-alkenylphosphine oxides. Mechanistic studies indicate that reactions proceed via aldehyde intermediacy and the catalyst promotes the C=C bond formation. Reactions are facilitated by dearomatization, and aromatization metal-ligand cooperation operates in catalyst. Use of abundant base metal catalyst and formation of water and H_2 as the only byproducts, which make this catalytic protocol sustainable and environmentally benign.



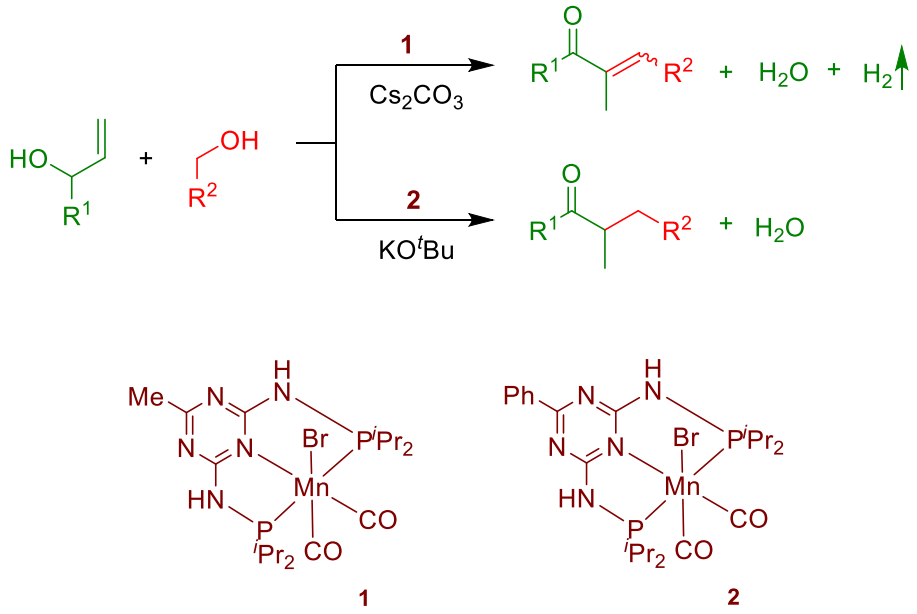
Scheme 3: Manganese Catalyzed *α*-Alkenylation of Phosphine Oxides Using Alcohols

Chapter 4: Manganese(I) Catalyzed Cross-Coupling of Secondary Allylic Alcohols and Primary Alcohols

Cross-coupling of alcohols to value-added products by using sustainable catalytic reactions has gained attention in recent years. Isomerization of secondary allylic alcohol to the corresponding enolizable ketone is an atom economical and known transformation. Herein, a selective cross-coupling of secondary allylic alcohol and primary alcohol is reported to afford the corresponding *α*-alkenyl or alkylation products. [16]

These catalytic protocols proceed via acceptorless dehydrogenative coupling (ADC) or borrowing hydrogen (BH) strategies, which liberates water and/or hydrogen as the only

byproducts. Highly abundant manganese-based pincer catalysts catalyze the reactions.



Scheme 4: Manganese(I) Catalyzed Cross-Coupling of Secondary Allylic Alcohols and Primary Alcohols

References:

1. (a) K.J. Szabo, O.F. Wendt, *Pincer and Pincer-type complexes*, **2014**, Wiley-VCH, Germany. (b) Peris, E.; Crabtree, R. H. Key Factors in Pincer Ligand Design. *Chem. Soc. Rev*. **2018**, *47*, 1959-1968.
2. Gunanathan, C.; Milstein, D. Bond Activation and Catalysis by Ruthenium Pincer Complexes. *Chem. Rev*. **2014**, *114*, 12024-12087.
3. Gunanathan, C.; Milstein, D. Applications of Acceptorless Dehydrogenation and Related Transformations in Chemical Synthesis. *Science* **2013**, *341*, 1229712.
4. Mukherjee, A.; Milstein, D. Homogeneous Catalysis by Cobalt and Manganese Pincer Complexes. *ACS Catal*. **2018**, *8*, 11435-11469.
5. Elangovan, S.; Topf, C.; Fischer, S.; Jiao, H.; Spannenberg, A.; Baumann, W.; Ludwig, R.; Junge, K.; Beller, M. Selective Catalytic Hydrogenations of Nitriles, Ketones, and Aldehydes by Well-Defined Manganese Pincer Complexes. *J. Am.*

Chem. Soc. **2016**, *138*, 8809-8814.

6. Mastalir, M.; Glatz, M.; Pittenauer, E.; Allmaier, G.; Kirchner, K. Sustainable Synthesis of Quinolines and Pyrimidines Catalyzed by Manganese PNP Pincer Complexes. *J. Am. Chem. Soc*. **2016**, *138*, 15543-15546.
7. Irrang, T.; Kempe, R. 3d-Metal Catalyzed N- and C-Alkylation Reactions via Borrowing Hydrogen or Hydrogen Autotransfer. *Chem. Rev*. **2019**, *119*, 2524-2549.
8. Das, K.; Barman, M. K.; Maji, B. Advancements in Multifunctional Manganese Complexes for Catalytic Hydrogen Transfer Reactions. *Chem. Commun*. **2021**, *57*, 8534-8549.
9. Gawali, S.S.; Pandia, B. K.; Gunanathan, C. Manganese(I)-Catalyzed α-Alkenylation of Ketones Using Primary Alcohols. *Org. Lett.* **2019**, *21*, 3842-3847.
10. Gawali, S.S.; Pandia, B. K.; Pal, S.; Gunanathan, C. Manganese(I)-Catalyzed Cross-Coupling of Ketones and Secondary Alcohols with Primary Alcohols. *ACS Omega.* **2019**, *4*, 10741-10754.
11. Yadav, V.; Landge, V.G.; Subaramanian, M.; Balaraman, E. Manganese-Catalyzed α-Olefination of Nitriles with Secondary Alcohols. *ACS Catal*. **2020**, *10*, 947-954.
12. Zhang, G.; Irrgang, T.; Dietel, T.; Kallmeier, F.;Kempe, R. Manganese-Catalyzed Dehydrogenative Alkylation or α-Olefination of Alkyl-Substituted N-Heteroarenes with Alcohols. *Angew. Chem. Int. Ed*. **2018**, *57*, 9131-9135.
13. Borghs, J. C.; Tran, M. A.; Sklyaruk, J.; Rueping, M.; El-Sepelgy, O. Sustainable Alkylation of Nitriles with Alcohols by Manganese Catalysis. *J. Org. Chem*. **2019**, *84*, 7927-7935.
14. Pandia, B. K.; Gunanathan, C. Manganese(I) Catalyzed *α*-Alkenylation of Amides Using Alcohols with Liberation of Hydrogen and Water. *J. Org. Chem*. **2021**, *86*, 9994-10005.

15. Pandia, B. K.; Pattanaik, S.; Gunanathan, C. Manganese(I) Catalyzed Alkenylation of Phosphine Oxides Using Alcohols with Liberation of Hydrogen and Water *J. Org. Chem.* **2021**, *86*, 17848-17855.

16. Pandia, B. K.; Pattanaik, S.; Gunanathan, C. Manganese(I) Catalyzed Cross-coupling of Secondary Allylic Alcohols and Primary Alcohols. *Tetrahedron* **2021**, *101*, 132472.

List of Schemes

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List of Abbreviations Used

Å	Angstrom
Anal.	Analytically
Anhyd	Anhydrous
aq	Aqueous
bp	Boiling Point
br	Broad
°C	Degree Celcius
Calcd	Calculated
cm	Centimeter
Conc	Concentrated
conv	Conversion
d	Doublet, Days
DCM	Dichloromethane
dd	Doublet of a Doublet
DMF	N,N-Dimethyl Formamide
eq	Equation
equiv	Equivalent
Et	Ethyl
g	Grams
h	Hours
HRMS	High-resolution Mass Spectrometry

IR	Infrared
K	Kelvin
kcal	Kilo calories
lit	Liter
m	Multiplet
M	Molar
MeCN	Acetonitrile
mp	Melting point
Me	Methyl
MHz	Mega Hertz
Min	Minutes
mL	Milliliter
mM	Millimolar
mmol	Millimole
mol	Mole
MS	Mass Spectra
N	Normal
NMR	Nuclear Magnetic Resonance
ppm	Parts per Million
rt	Room Temperature
s	Singlet, Seconds
TLC	Thin Layer Chromatography
TOF	Turn Over Frequency
TON	Turn Over Number
XRD	X-Ray Diffraction
NaOMe	Sodium methoxide

Table of Contents

CHAPTER 1

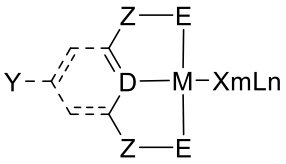
Introduction-Manganese Pincer Complexes and Their Reactivity

Chemists have made relentless efforts to develop greener chemical protocols. The principles of green chemistry aim to minimize pollution at its source by eliminating toxic chemicals, reagents and deleterious side wastes. Catalysis is an important aspect of green chemistry.[1] It helps to achieve important chemical transformations which would be difficult to perform by traditional methods and circumvents or reduces the amount of byproducts formed. A catalyst enhances the rate of slow chemical reactions by reducing their activation energy. In catalytic amount, it helps to carry out chemical transformations where the catalyst itself is not consumed in the process.[2] Catalysis plays a vital role in modern industry, which involves production of commodity chemicals, petrochemicals, polymers and pharmaceuticals. Catalysis played important role in devising sustainable and environmentally friendly synthetic protocols.[3]

Transition metal catalyzed activation of small molecules is of utmost importance in the field of homogeneous catalysis. In this direction, transition metal-based pincer complexes have been extensively studied. Pincer complexes contain a tridentate pincer ligand, which upon complexation with metal adopt a meridional geometry. The pincer-ligation imparts unique thermal stability to the resulting complex and makes them efficient in high temperature reactions. Modular fine-tuning of the pincer ligand by changing its steric and electronic properties can induce different reactivity at the metal center of the resulting pincer complex.[4,5] Pincer complexes contain a central aryl ring (phenyl, pyridinyl, pyrazinyl, triazinyl, etc.) which is 1,3-disubstituted with two chelating side arms. The resulting complex is attained in a meridional geometry with all the donor atoms present in a single plane. Pincer complexes with an aliphatic backbone are also reported. The pincer complexes are named according to the three donor atoms and majority of them reported in literature are palindromic (i.e., NNN, PNP, PCP,

NCN, etc.). However, non-palindromic pincer complexes are also studied (i.e., NNP, PNN, etc.).[5] The general depiction of the pincer complex is presented in Figure 1.1.

Figure 1.1. General Structure of Transition Metal Based Pincer Complexes



E = PR_2, NR_2, SR, OR, NHC
Z = CR_2, NR, O
D = N, NH, C, B, S, Si, P
M = Ru, Ir, Rh, Pd, Pt, Fe, Mn, Ni. etc.
X = CO, Halogen, H, H_2, etc.
Y = CO_2^-, SO_3^- , electron donating, electron withdrawing group

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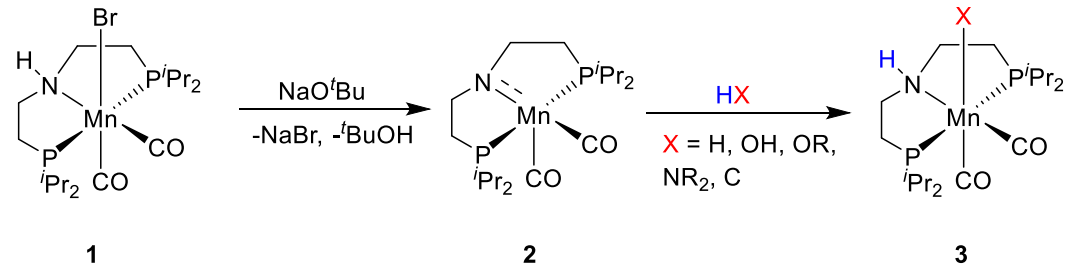
In nature enzymes are known to activate inert bonds by cooperative effect of both ligand and metal center.[6] In transition metal catalyzed reactions, such metal ligand cooperation is also observed. Shvo and Noyori were the pioneers of this concept and termed this phenomenon as "bifunctional catalysis". In Noyori type catalyst, the chelating amine ligand is directly involved in the reaction via reversible proton (H^+) transfer mechanism, which in turns promotes reaction at the metal center.[7] Applying the concept of bifunctional catalysis Noyori and coworkers reported the ruthenium catalyzed hydrogenation of carbonyl compounds.[8] The metal-ligand cooperativity in pincer complexes was first observed by Milstein and coworkers in 2005. The unusual reactivity of pincer complexes originates from the non-innocent behaviour of their pincer ligands. They take part directly in the reaction chemistry via metal-ligand cooperation (MLC). There are mainly two modes of metal-ligand cooperation operative in pincer complexes; dearomatization-aromatization MLC and amine-amide MLC (**Scheme 1.1**).[4,9] When complex **1** is reacted with base, it undergoes dehydrohalogenation of coordinated amine functionality to generate coordinatively unsaturated intermediate **2**. This process converts the amine ligand to an amide ligand. The 16 electron species, intermediate **2** can activate inert chemical bonds present molecules like H_2, H_2O, ROH, RNH_2, sp^3 C-H to provide coordinatively saturated complex **3** where the amine functionality is regenerated in the pincer

backbone. Similarly, the pincer complex **4** upon reaction with base undergoes deprotonation at the pyridinyl-methylene carbon to generate dearomatized intermediate **5**, which is a 16 electron species. The coordinatively unsaturated intermediate **5** reacts with various small molecules (H–X; X = H, C, OH, OR, NH_2, NR_2) where the unsaturated methine carbon accepts a proton and the X-fragments form bond with metal center to generate 18 electron intermediate **6**. Based on such metal ligand cooperation, plethora of reactions have been developed.

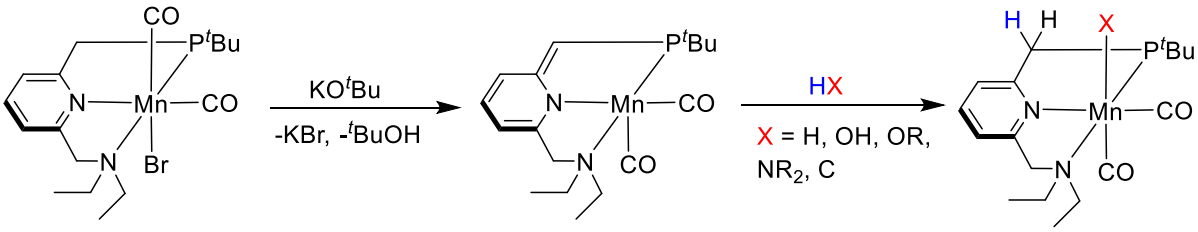
Scheme 1.1. Different Modes of MLC: (a) MLC Based on Amine-Amide, (b) MLC Based on Dearomatization-Aromatization

(a) Amine-Amide MLC:



1 **2** **3**

(b) Dearomatization-Aromatization MLC:



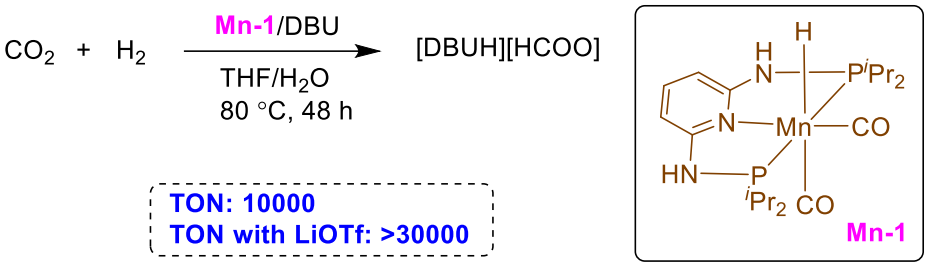
4 **5** **6**

The high cost and toxicity of precious transition metals are unsuitable to achieve low cost and sustainability goals in chemical synthesis. Therefore, homogeneous catalysis based on abundant and environmentally benign first row transition metals have emerged as an attractive alternative. Manganese being the third most abundant transition metal in earth's crust, synthesis and reactivity of their corresponding pincer complexes have been extensively studied in recent times. A range of manganese pincer complexes bearing aliphatic and aromatic backbones were

synthesized and were employed for chemoselective hydrogenation as well as hydrogen auto transfer reactions.[10]

Carbon dioxide is a valuable carbon feedstock and recently, Gonsalvi and coworkers reported the catalytic reduction of carbon dioxide to formic acid salt. The reaction was catalyzed by **Mn-1** hydride pincer complex (0.002 mol %) where DBU was used as base. This catalyst performed better than its Fe analogue. With 80 bar total pressure of H_2 and CO_2 and DBU as base the reaction produced turn over number (TON) up to 10000. When LiOTf was used as a cocatalyst TONs greater than 30000 was attained. Mechanistic studies revealed that the reaction proceeded via mental-centered or a ligand assisted mechanism.[11]

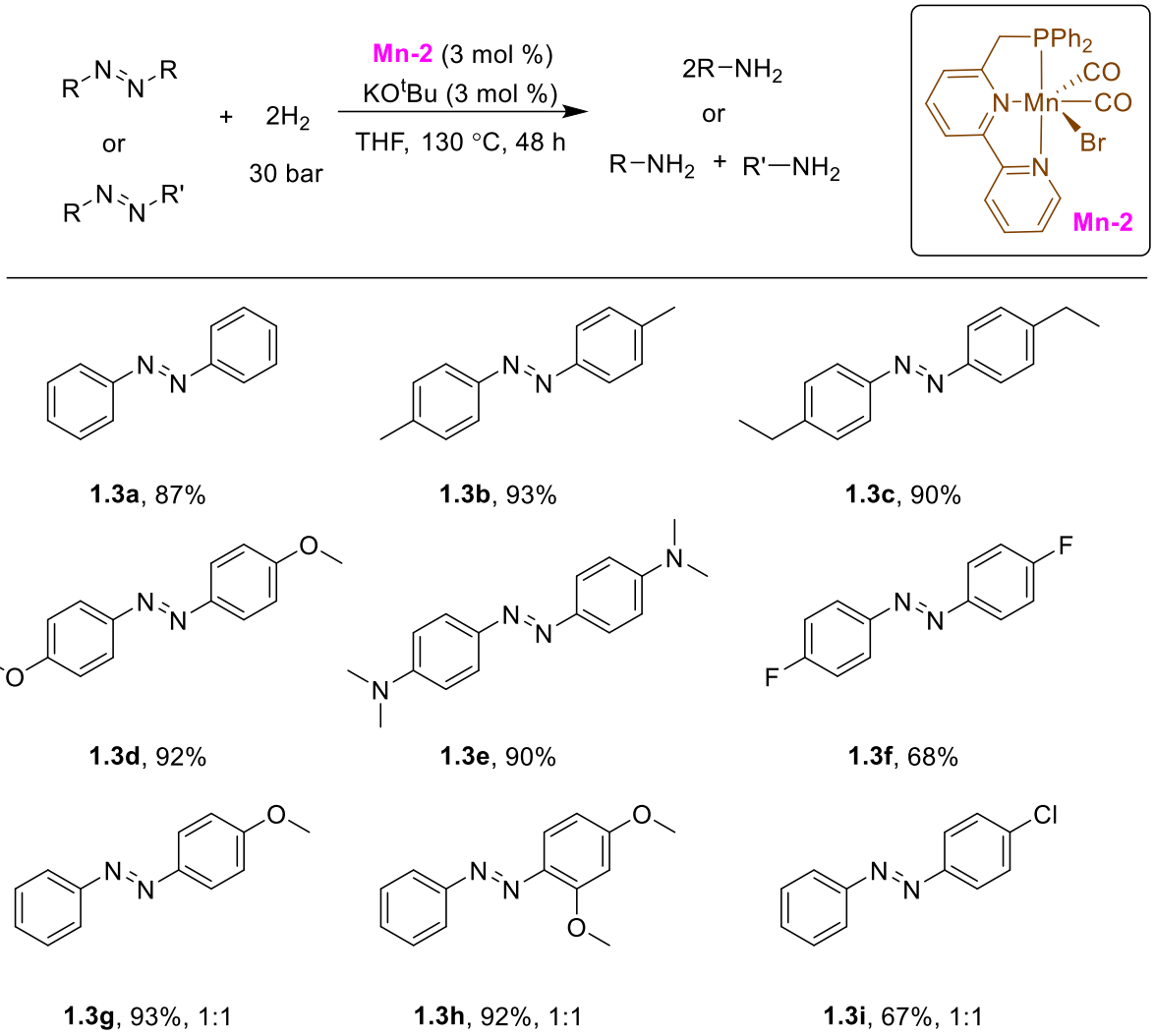
Scheme 1.2. CO_2 Hydrogenation Catalyzed by Mn-1 PNP Pincer Catalyst



Later, manganese catalyzed hydrogenation of azo compounds to corresponding amines was reported by Milstein and coworkers. The reaction was catalyzed by manganese complex **Mn-2** and catalytic amount of base, potassium *tert*-butoxide. Hydrogen pressure (30 bar) was used to cleave the non-polar N=N. Symmetrical azo compounds bearing electron donating groups provided better yield of corresponding amines than those bearing electron withdrawing groups. Unsymmetrical azo compounds bearing different aromatic rings also underwent facile hydrogenation to the corresponding amines. Aliphatic azo compounds could not be hydrogenated following this catalytic protocol. Detailed mechanistic studies established the involvement of manganese

hydride intermediate and the hydrogenation proceeded by subsequent hydrogenation of the N=N and NH-NH bonds.[12]

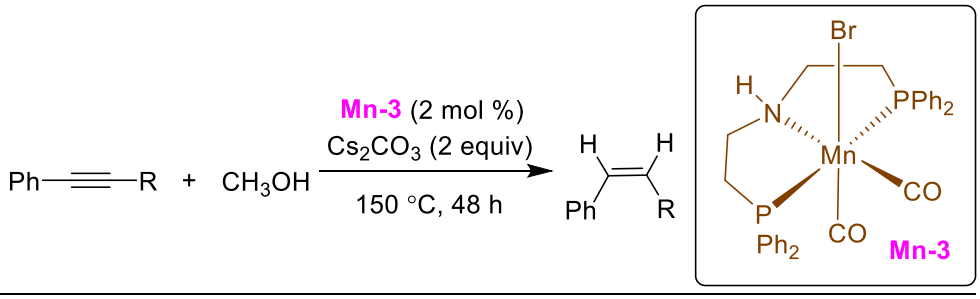
Scheme 1.3. Mn-2 Catalyzed Hydrogenation of Azo (N=N) Bonds to Amines

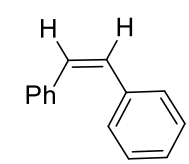


In 2020, Rueping and coworkers reported the manganese catalyzed transfer hydrogenation of internal alkynes to *Z*-alkenes. This semihydrogenation was furnished using methanol as transfer hydrogenation reagent as methanol is a potential hydrogen storage chemical. The reaction was catalyzed by an air and moisture stable manganese pincer complex, **Mn-3**. Alkynes bearing both electron donating and withdrawing groups underwent facile semihydrogenation to produce the *Z*-alkenes with excellent stereoselectivity and yield. Gram

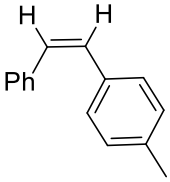
scale synthesis of *Z*-stilbene was accomplished by this method with excellent yield. Deuterium labelling experiment with methanol-d_4 confirmed cis-selective hydrogen incorporation. The catalytic cycle proposed for this reaction hypothesized the involvement of manganese hydride intermediate.[13]

Scheme 1.4. Mn-3 Catalyzed Transfer Hydrogenation of Alkynes to *Z*-Alkenes Using Methanol

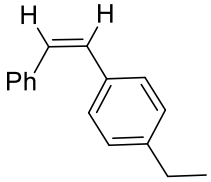




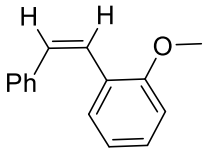
1.4a, 98%, 97:3 *Z/E*



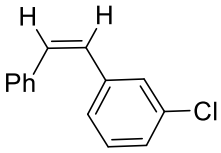
1.4b, 94%, 99:1 *Z/E*



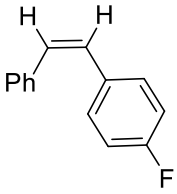
1.4c, 96%, 95:5 *Z/E*



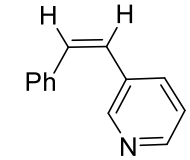
1.4d, 86%, 99:1 *Z/E*



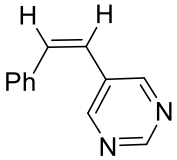
1.4e, 98%, 99:1 *Z/E*



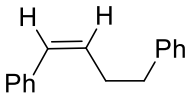
1.4f, 99%, 91:9 *Z/E*



1.4g, 75%, 99:1 *Z/E*



1.4h, 35%, 91:9 *Z/E*

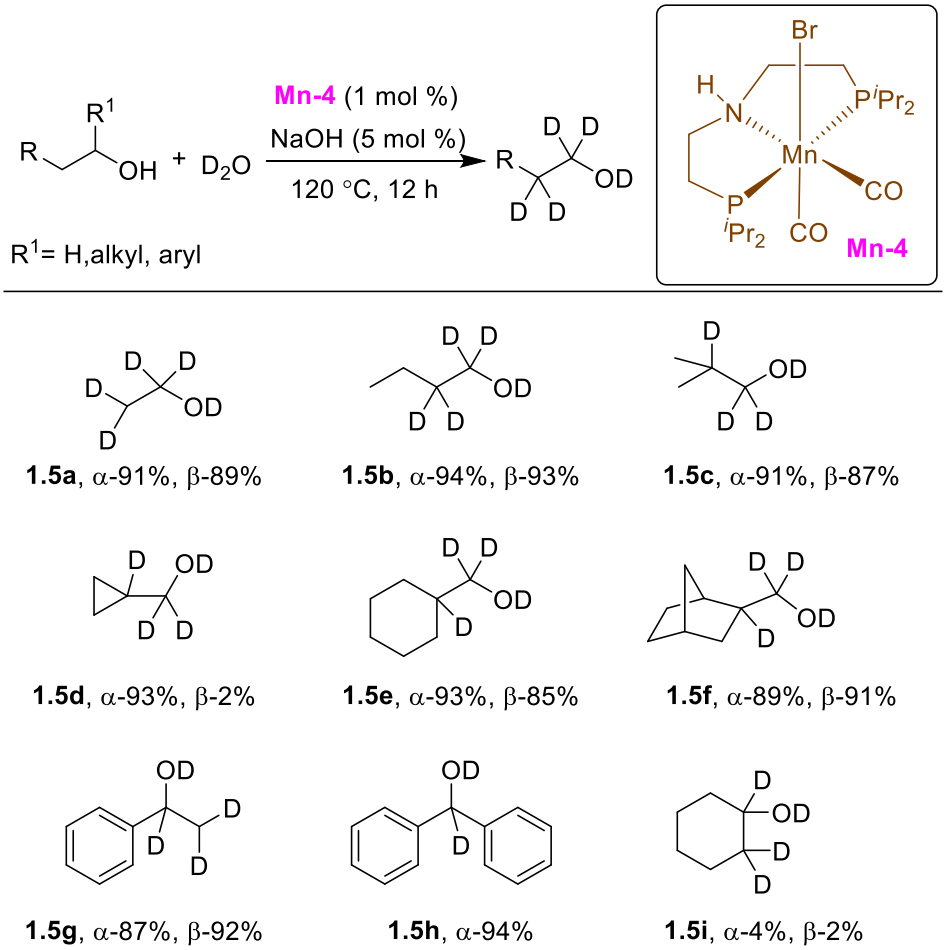


1.4i, 99%, 97:3 *Z/E*

Deuterated compounds are highly valuable and their synthesis is an important chemical transformation in organic synthesis. Deuterated compounds find numerous applications in

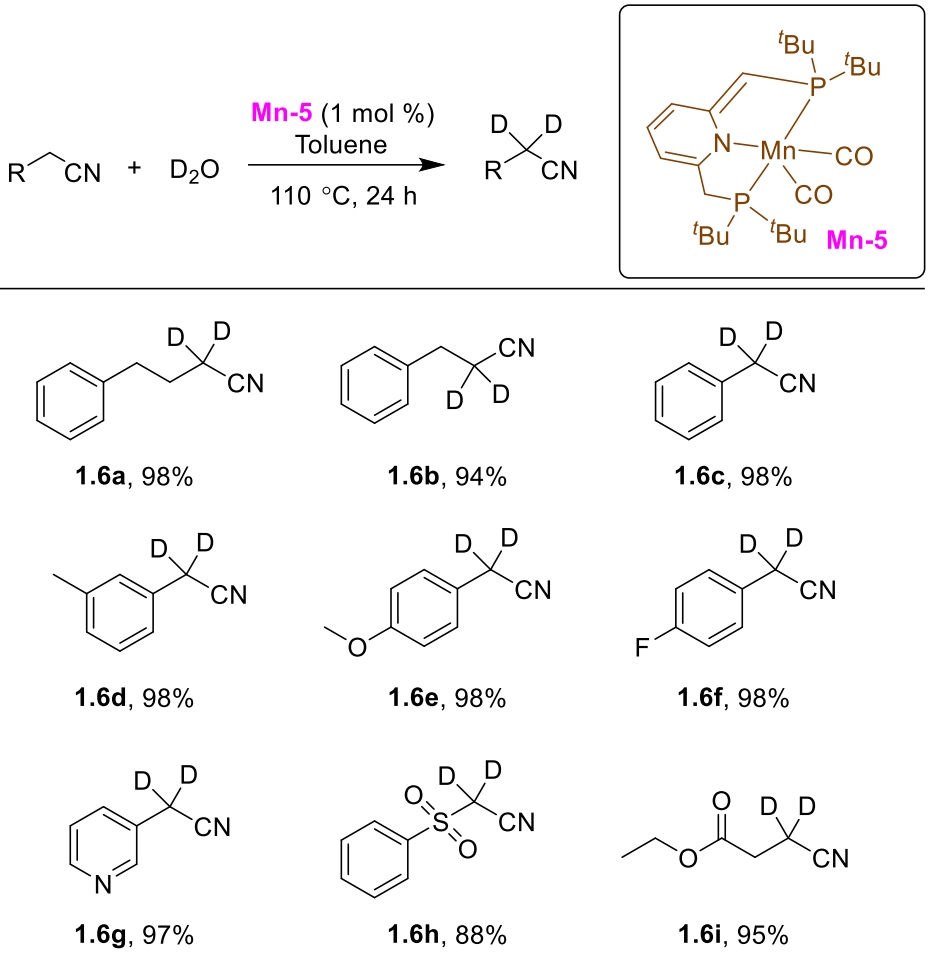
organic synthesis. Deuterated pharmaceuticals and biologically active compounds are valuable targets.[14] Using deuterium oxide as deuterium source, Gunanathan and coworkers reported various deuteration reactions of organic compounds catalyzed by a ruthenium pincer complex.[15] Similarly, Surya Prakash and coworkers reported the **Mn-4** catalyzed α,β-deuteration of primary and secondary alcohols. A range of aliphatic primary alcohols bearing small chain, long chain as well as cyclic rings were efficiently deuterated at both α and β positions. Secondary alcohols bearing an aryl ring were also efficiently deuterated whereas minor deuterium incorporation was observed in secondary alcohols bearing saturated rings. The catalytic cycle proposed the involvement of metal-alkoxide and metal-deuteroxide intermediates.[16]

Scheme 1.5. Mn-4 Catalyzed α, β-Deuteration of Primary and Secondary Alcohols Using D_2O



In 2021, Milstein and coworkers reported the α-deuteration of nitriles, which was catalyzed by a manganese pincer complex **Mn-5**. The same complex furnished the corresponding amide in *tert*-butanol whereas deuteration was accomplished by changing solvent to toluene. Excellent α-deuteration was observed in aliphatic as well as aromatic nitriles. The possible pathway for the reaction involved the formation of [2+2] cycloadduct by addition of nitrile to the dearomatized **Mn-5** followed by deuterium exchange.[17]

Scheme 1.6. Mn-5 Catalyzed α-Deuteration of Nitriles

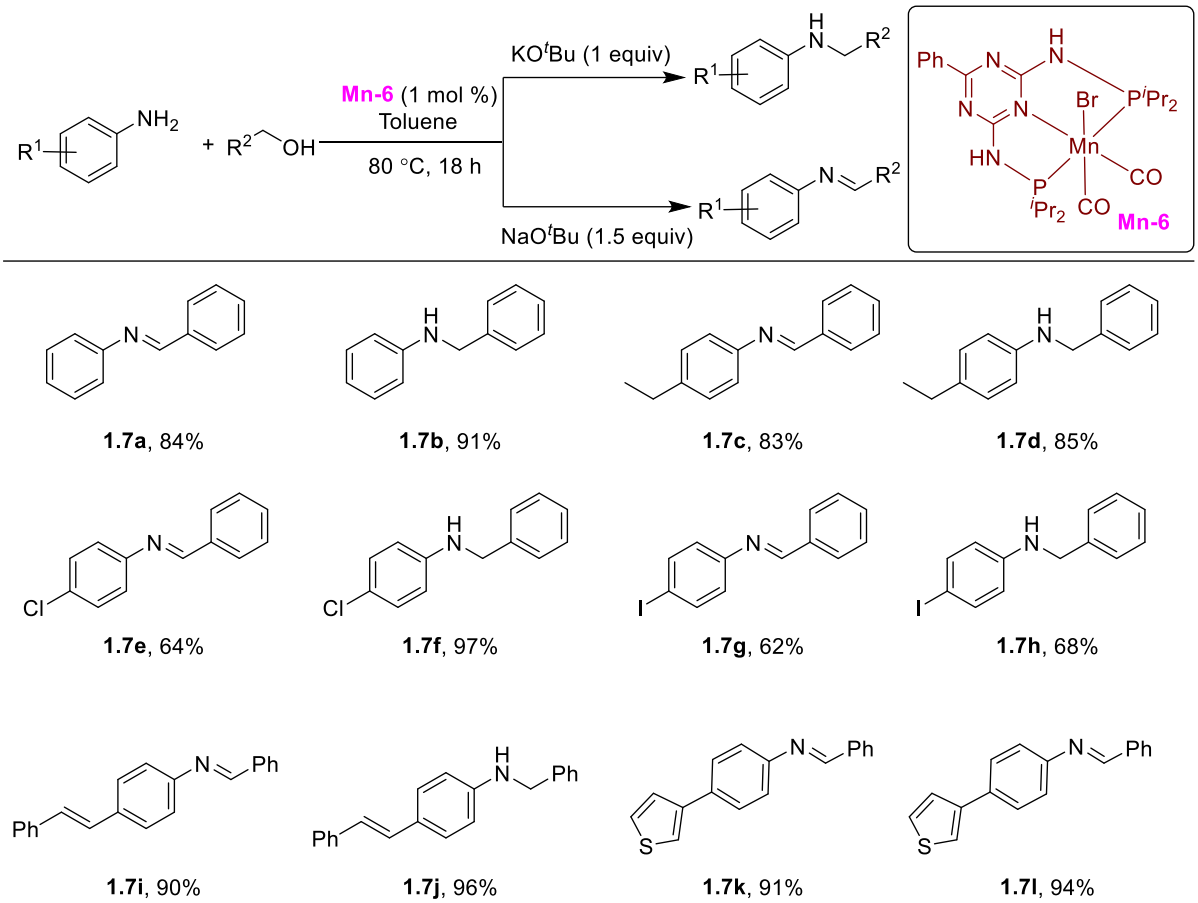


Alcohols are cheap source of carbon since they are abundantly available in nature in the form of biomass. In recent times, alcohols have been used extensively to produce bulk and fine chemicals since they do not produce hazardous byproducts. This makes them useful in developing green and sustainable chemical protocols.[10a] Alcohols have been extensively used in C–C and C–N coupling reactions, especially in alkylation and alkenylation reactions. Via metal ligand cooperation pincer catalyst promotes the acceptorless dehydrogenation of alcohol to aldehyde. The in-situ generated aldehyde can undergo further coupling reactions with carbon or nitrogen nucleophiles to form C–C or C–N coupled products. This process is known as acceptorless dehydrogenative coupling (ADC) where the only byproduct of the reaction is molecular hydrogen. Alternatively, the molecular hydrogen evolved in the reaction can

hydrogenate an unsaturated intermediate to form a saturated product. This pathway is known as borrowing hydrogen (BH) strategy.[9b] Following the ADC and BH pathways, a series of C–C and C–N bond forming reactions have been developed using manganese pincer complexes.

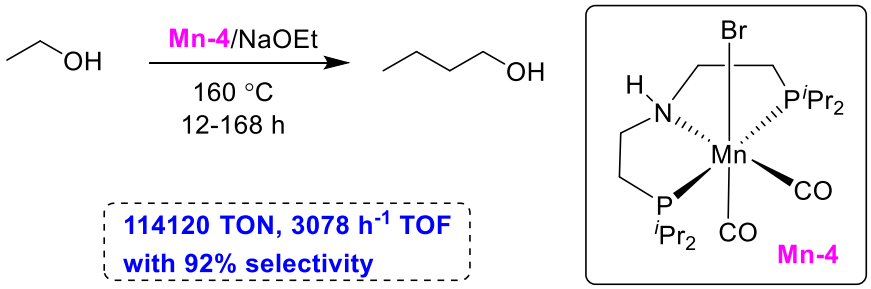
In 2018, Kempe and coworkers reported the base switchable synthesis of amines and imines catalyzed by 4-phenyl triazine based manganese pincer complex (**Mn-6**) from alcohols. Upon using strong base, potassium *tert*-butoxide N-alkylated products formed while switching to sodium *tert*-butoxide produced the imine products. The N-alkylation proceeded via BH method while the imine formation was attained by ADC pathway. A wide variety of amines were coupled with arylmethyl alcohols to furnish the amine or imine products with good functional group tolerance in moderate to good yields. Mechanistic studies confirmed the role of hydride intermediate. The N–H proton present on the side arm of **Mn-6** promoted metal ligand cooperation in presence of base thereby activating the alcohol.[18]

Scheme 1.7. Mn-6 Catalyzed Base Switchable Synthesis of Amines or Imines



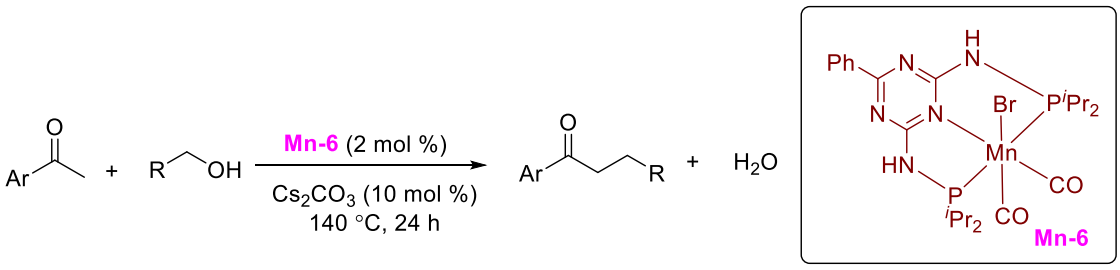
C–C coupling reactions enable chemists to synthesize higher carbon homologues. Liu and coworkers reported the manganese pincer catalyzed (**Mn-4**) Guerbet-type condensation of ethanol to form 1-butanol. This reaction proceeded smoothly in presence of ppm level of **Mn-4**. This sustainable method developed to synthesize 1-butanol exhibited a turnover number >110000 and turnover frequency (>3000 h^{-1}). Mechanistic studies highlighted the importance of amine proton present in the complex. The 16 electron species involved in the reaction was also characterized by X-ray crystallography.[19]

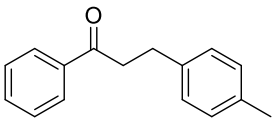
Scheme 1.8. Mn-4 Catalyzed Synthesis of 1-Butanol From Ethanol



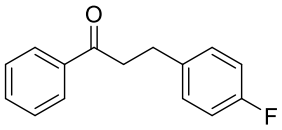
Gunanathan and coworkers reported the catalytic cross-coupling of ketones and secondary alcohols with primary alcohols. The reaction was catalyzed by Kempe's manganese pincer complex (**Mn-6**) and catalytic amount of weak base, Cs_2CO_3. Various aryl and heteroaryl alcohols bearing electron donating and withdrawing groups were coupled with primary alcohols to synthesize α-alkylated products. Using ethanol as an alkylation reagent α-ethylated products were also synthesized.

Scheme 1.9. Mn-6 Catalyzed Cross-Coupling of Ketones with Primary Alcohols

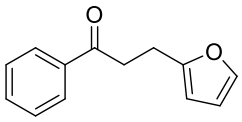




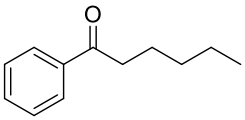
1.9a, 91%



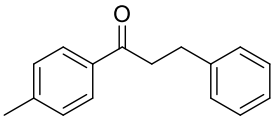
1.9b, 83%



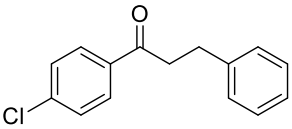
1.9c, 84%



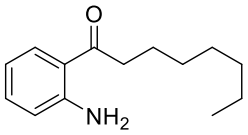
1.9d, 97%



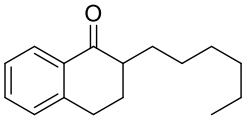
1.9e, 94%



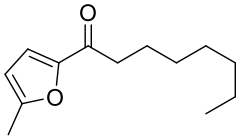
1.9f, 88%



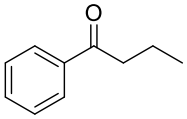
1.9g, 53%



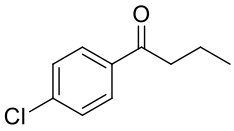
1.9h, 78%



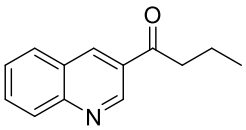
1.9i, 85%



1.9j, 58%



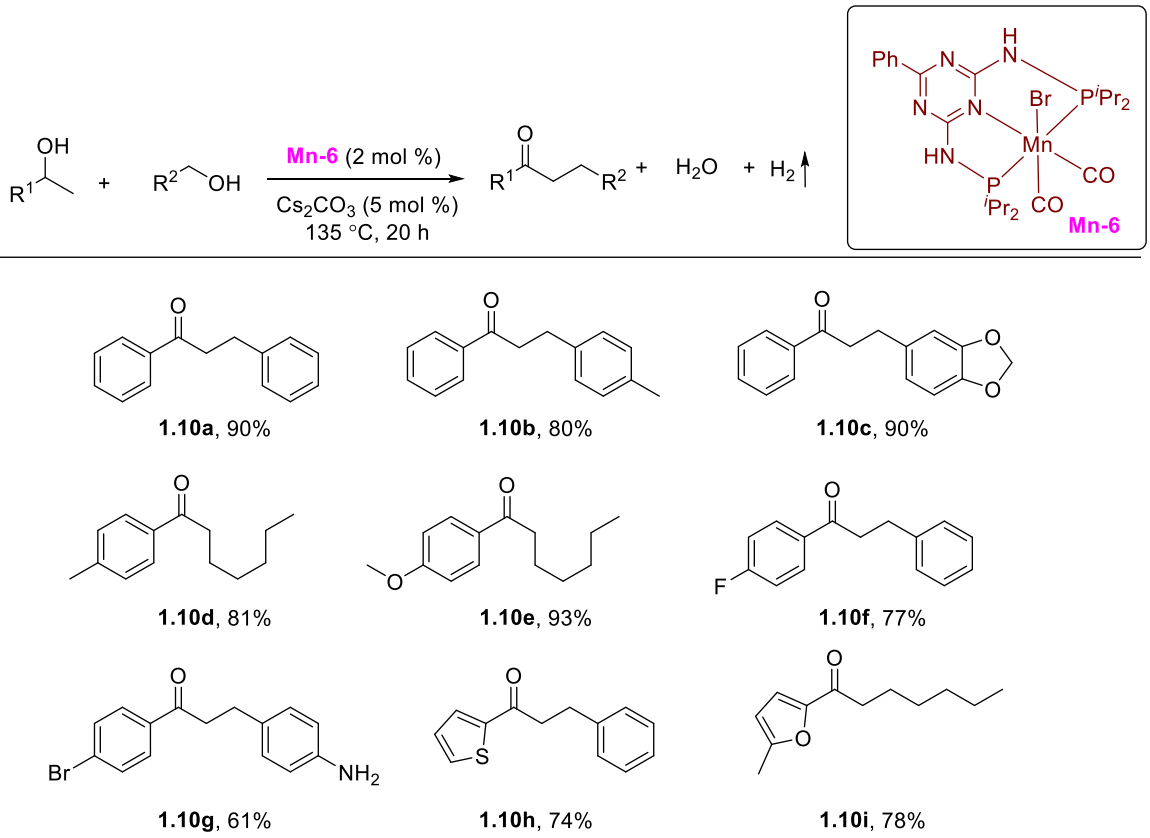
1.9k, 63%



1.9l, 23%

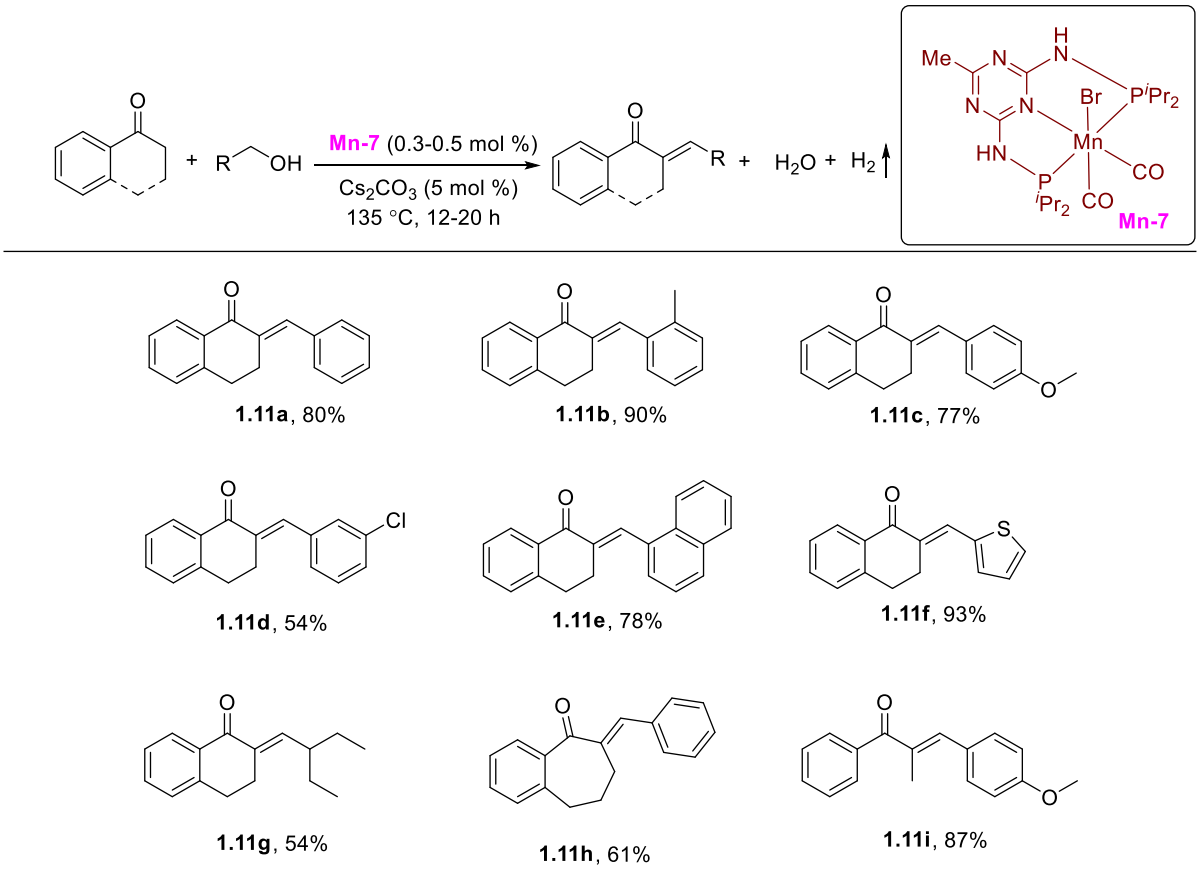
Further, direct cross-coupling of secondary alcohols with primary alcohols catalyzed by **Mn-6** was reported by Gunanathan and co-workers to attain selective β-alkylation of secondary alcohol. A variety of secondary alcohols bearing electron donating and withdrawing groups on their aromatic ring were coupled with aryl as well as aliphatic primary alcohols. Both the reactions proceeded via borrowing hydrogen pathways. The chemoselectivity of the reaction was also established by careful studies. In-situ monitoring of the reaction by GC proved that the reaction proceeds via α,β-unsaturated intermediate.[20]

Scheme 1.10. Mn-6 Catalyzed Cross-Coupling of Secondary Alcohols with Primary Alcohols



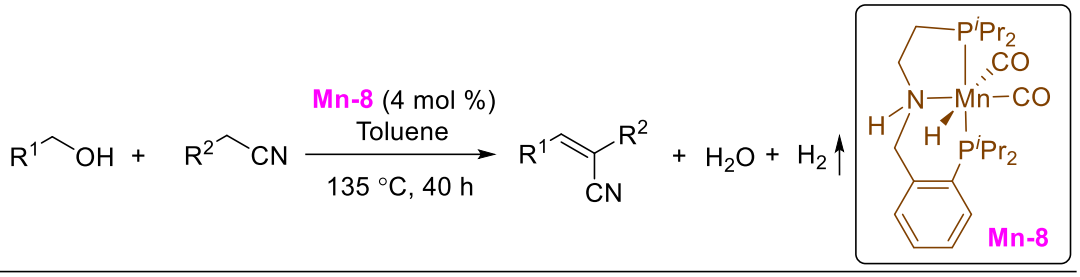
Gunanathan and co-workers also reported the selective synthesis of α,β-unsaturated ketones by coupling ketones and alcohols. The reaction was catalyzed Kempe's 4-methyl triazine based PNP manganese pincer complex (**Mn-7**) and catalytic amount of weak base, Cs_2CO_3. A range of cyclic and acyclic ketones were α-alkenylated using alcohols as the alkenylation reagent. The dearomatization-aromatization MLC operative in the catalyst enabled the reaction to proceed via acceptorless dehydrogenation pathway. Remarkably, water and molecular hydrogen are the only byproducts of this reaction.[21]

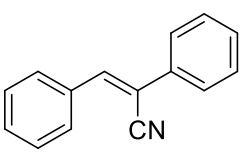
Scheme 1.11. Mn-7 Catalyzed α-Alkenylation of Ketones Using Primary Alcohols



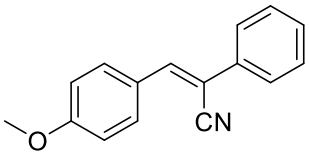
α, β-Unsaturated nitriles are important class of compounds. They are key intermediates in organic synthesis and find applications in pharmaceuticals and natural products. In this direction, greener chemical methods to synthesize such class of compounds involve direct α-alkenylation of nitriles with alcohols as alkenylation reagents. In 2017, Milstein and coworkers developed the first green protocol to synthesize α, β-unsaturated nitriles with primary alcohols. Aryl acetonitriles were reacted with diverse aryl and aliphatic primary alcohols and the corresponding unsaturated products were isolated in moderate to good yields. Remarkably, this reaction proceeds in the absence of any additives or base. The amine-amide metal ligand cooperation in **Mn-8** facilitates the reaction at the metal center.[22]

Scheme 1.12. Mn-8 Catalyzed α-Alkenylation of Nitriles Using Primary Alcohols

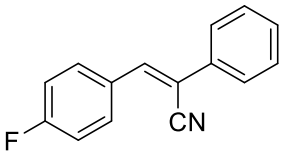




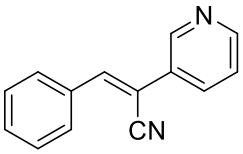
1.12a, 87%



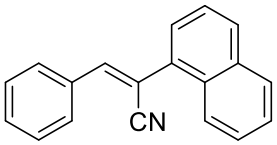
1.12b, 91%



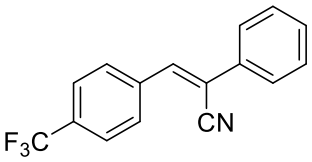
1.12c, 76%



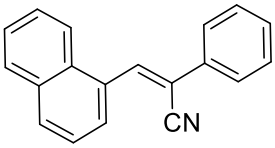
1.12d, 78%



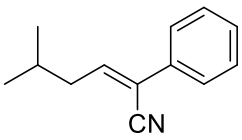
1.12e, 51%



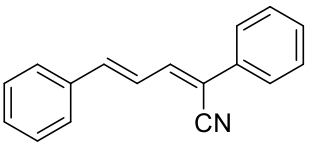
1.12f, 81%



1.12g, 58%



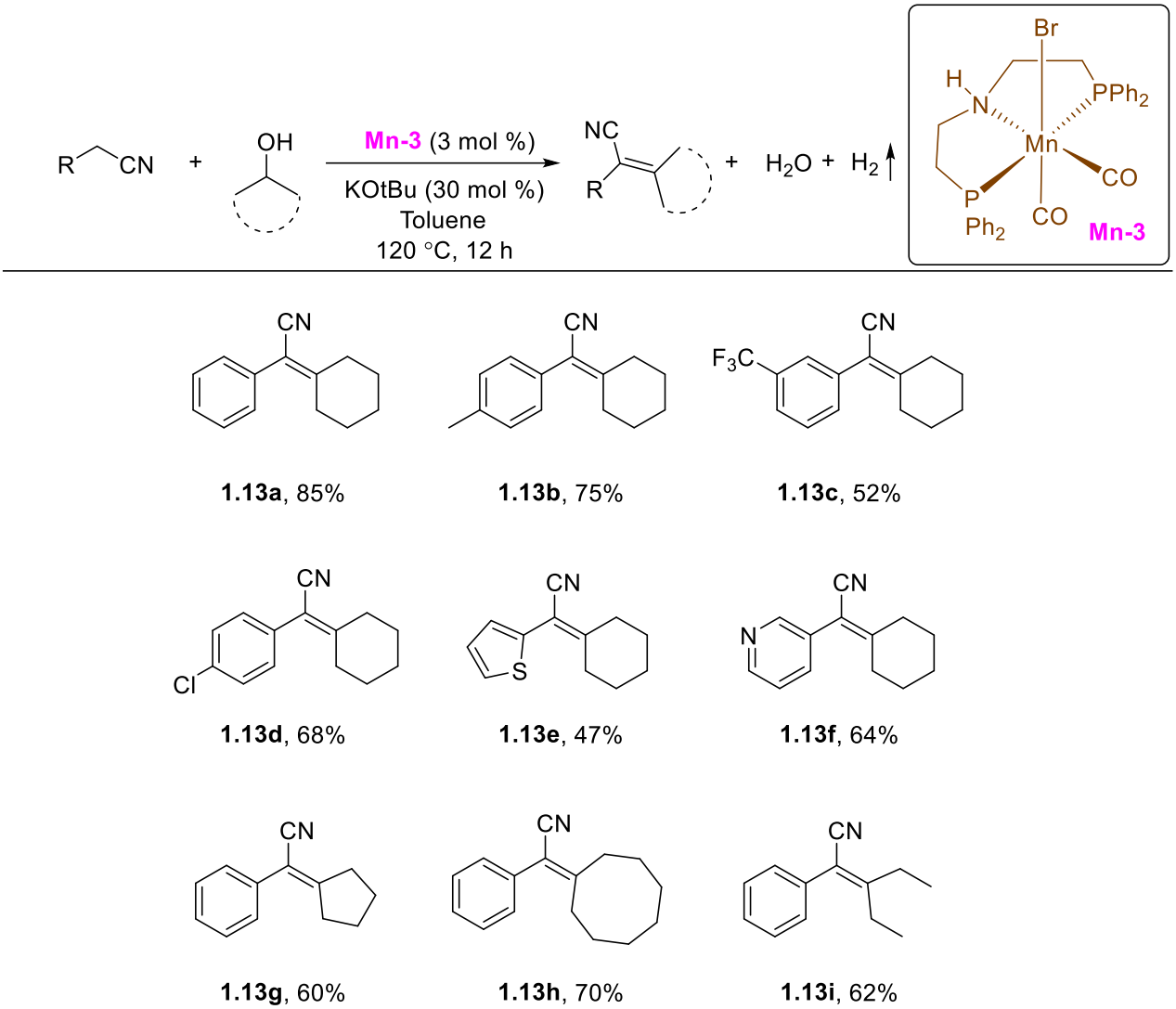
1.12h, 58%



1.12i, 81%

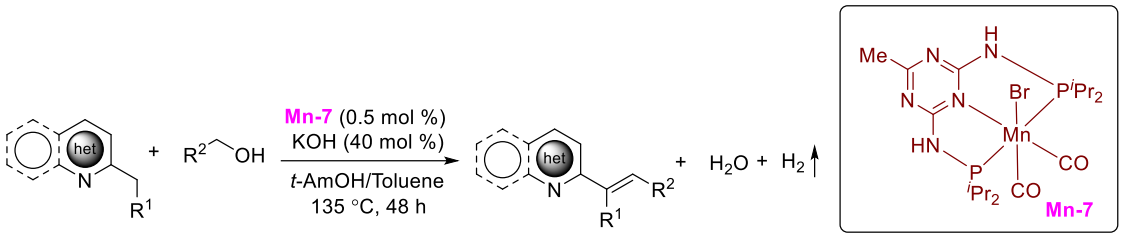
Following this report, Balaraman and coworkers reported the manganese catalyzed (**Mn-3**) α-alkenylation of nitriles with secondary alcohols. A broad range of α-vinyl nitriles in good to excellent yields were synthesized by employing cyclic, acyclic, and benzylic secondary alcohols, as well as various nitrile derivatives. Several control experiments, deuterium labeling and kinetics experiments established that the reaction proceeded via ADC pathway where water and molecular hydrogen are the only byproducts of the reaction.[23]

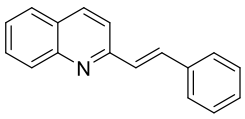
Scheme 1.13. Mn-3 Catalyzed α-Alkenylation of Nitriles Using Secondary Alcohols



Aryl-substituted olefins are highly useful compounds in organic synthesis as the olefin bond can be further functionalized. They find applications in agrochemicals and pharmaceuticals. Kempe and coworkers reported a green synthesis of such class of compounds by reacting alkyl-substituted N-heteroarenes with aryl methyl or aliphatic primary alcohols. The reaction was catalyzed by a manganese pincer complex **Mn-7**. The reaction also required a base, KOH. Following this catalytic protocol, a broad range of *E*-alkenes were synthesized. All the products were isolated in good to excellent yields. Dearomatization-aromatization MLC facilitated the reaction forward via the manganese-hydride intermediacy.[24]

Scheme 1.14. Mn-7 Catalyzed α-Alkenylation of N-Heteroarenes Using Primary Alcohols





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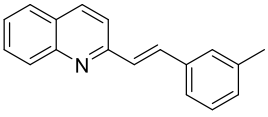

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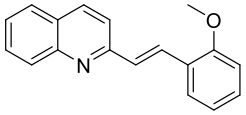

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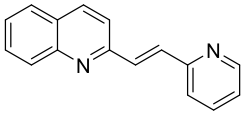

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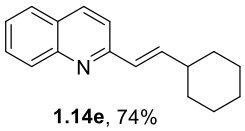
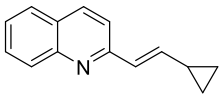
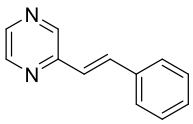


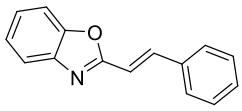
1.14e, 74%



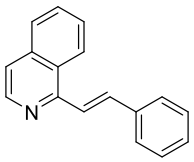
1.14f, 85%



1.14g, 81%



1.14h, 70%



1.14i, 57%

References:

(1) Anastas, P.; Eghbali, N. Green Chemistry: Principles and Practice. *Chem. Soc. Rev*., **2010**, *39*, 301-312.

(2) (a) Chorkendorff, I.; Niemantsverdriet, J. W. *Concepts of Modern Catalysis and Kinetics, Second Edition. I.* WILEY-VCH Verlag GmbH&Co. KGaA, Weinheim, 2007. (b) Schmidt, F. Baerns M. (eds) The Importance of Catalysis in the Chemical and Non-Chemical Industries. In *Basic Principles in Applied Catalysis.* Springer Series in Chemical Physics, vol 75. Springer, Berlin, Heidelberg, 2004. (c) Moulijn, J. A.; van Leeuwen, P. N. W. M.; van Santen, R. A. (Eds.), *Catalysis: an Integrated Approach to Homogeneous, Heterogeneous and Industrial Catalysis*, Elsevier, Amsterdam, 1993.

(3) (a) Catlow, C. R.; Davidson, M.; Hardacre, C.; Hutchings, G. J., Philos. Catalysis Making the World a Better Place. *Trans. A Math. Phys. Eng. Sci.,* **2016**, 374, 20150089. (b) Hagen, J. Economic Importance of Catalysts. In *Industrial Catalysis, A Practical Approach*; Hagen, J., Ed.; Wiley: 2015; Chapter 17, pp 459-462.

(4) (a) Peris, E.; Crabtree, R. H. Key Factors in Pincer Ligand Design. *Chem. Soc. Rev*. **2018**, *47*, 1959-1968. (b) Gunanathan, C.; Milstein, D. Metal-Ligand Cooperation by Aromatization-Dearomatization: A New Paradigm in Bond Activation and "Green" Catalysis. *Acc. Chem. Res.* **2011**, *44*, 588-602. (c) Gunanathan, C.; Milstein, D. Bond Activation by Metal-Ligand Cooperation: Design of "Green" Catalytic Reactions Based on Aromatization-Dearomatization of Pincer Complexes. *Top. Organomet. Chem.* **2011**, *37*, 55-84. (d) Gunanathan, C.; Milstein, D. Bond Activation and Catalysis by Ruthenium Pincer Complexes. *Chem. Rev.* **2014**, *114*, 12024-12087.

(5) (a) K. J. Szabo, O. F. Wendt, *Pincer and Pincer-type complexes*, **2014**, Wiley-VCH, Germany. (b) *The Chemistry of Pincer Compounds;* Morales-Morales, D.; Jensen, C.,

Eds.; Elsevier Science: Amsterdam, 2007. (c) Morales-Morales, D. Pincer Complexes. Applications in Catalysis. *Rev. Soc. Quim. Mex.*, **2004**, *48*, 338-346.

(6) (a) Evans, D. J.; Pickett, C. J. Chemistry and the Hydrogenases. *Chem. Soc. Rev.* **2003**, *32*, 268-275. (b) Chou, K. C. Low Frequency Resonance and Cooperativity of Hemoglobin. *Trends Biochem. Sci.* **1989**, *14*, 212-213.

(7) (a) Dub, P. A.; Gordon, J. C. The Role of the Metal-Bound N–H Functionality in Noyori-Type Molecular Catalysts. *Nat. Rev. Chem.* **2018**, *2*, 396-408. (b) Dub, P. A.; Gordon, J. C. Metal-Ligand Bifunctional Catalysis: The "Accepted" Mechanism, the Issue of Concertedness, and the Function of the Ligand in Catalytic Cycles Involving Hydrogen Atoms. *ACS Catal.* **2017**, *7*, 6635-6655.

(8) (a) Abbel, R. Abdur-Rashid, K.; Faatz, M.; Hadzovic, A.; Lough, A. J.; Morris, R. H. A. A Succession of Isomers of Ruthenium Dihydride Complexes. Which One Is the Ketone Hydrogenation Catalyst? *J. Am. Chem. Soc.*, **2005**, *127*, 1870-1882. (b) Noyori, R. Koizumi, M. Ishii, D. Ohkuma, T. Asymmetric Hydrogenation via Architectural and Functional Molecular Engineering. *Pure. Appl. Chem.* **2001**, *73*, 227-232. (c) Yamakawa, M. Ito, H. Noyori, R. The Metal-Ligand Bifunctional Catalysis: A Theoretical Study on the Ruthenium(II)-Catalyzed Hydrogen Transfer between Alcohols and Carbonyl Compounds. *J. Am. Chem. Soc.*, **2000**, *122*, 1466-1478.

(9) (a) Khusnutdinova, J. R.; Milstein, D. Metal-Ligand Cooperation. *Angew. Chem., Int. Ed.*, **2015**, *54*, 12236-12273. (b) Gunanathan, C.; Milstein, D. Applications of Acceptorless Dehydrogenation and Related Transformations in Chemical Synthesis", *Science,* **2013**, *341*, 1229712.

(10) (a) Kempe, R.; Irrang T. 3d-Metal Catalyzed N- and C-Alkylation Reactions via Borrowing Hydrogen or Hydrogen Autotransfer. *Chem. Rev*. **2019**, *119*, 2524-2549. (b) Das, K.; Barman, M. K.; Maji, B. Advancements in Multifunctional Manganese

Complexes for Catalytic Hydrogen Transfer Reactions. *Chem. Commun*. **2021**, *57*, 8534-8549.

(11) Bertini, F.; Glatz, M.; Gorgas, N.; Stoger, B.; Peruzzini, M.; Veiros, L. F.; Kirchner, K.; Gonsalvi, L. Carbon Dioxide Hydrogenation Catalysed by Well-Defined Mn(I) PNP Pincer Hydride Complexes. *Chem. Sci*. **2017**, *8*, 5024-5029.

(12) Das, U. K.; Kar, S.; Ben-David, Y.; Diskin-Posner, Y.; Milstein, D. Manganese Catalyzed Hydrogenation of Azo (N=N) Bonds to Amines. *Adv. Synth. Catal*. **2021**, *363*, 3744-3749.

(13) Sklyaruk, J.; Zubar, V.; Borghs, J. C.; Rueping, M. Methanol as the Hydrogen Source in the Selective Transfer Hydrogenation of Alkynes Enabled by a Manganese Pincer Complex. *Org. Lett*. **2020**, *22*, 6067-6071.

(14) Chatterjee, B.; Gunanathan, C. *Pincer Compounds: Chemistry and Applications.* Elsevier. Amsterdam (2018) pp. 519-538.

(15) (a) Chatterjee, B.; Gunanathan, C. Ruthenium Catalyzed Selective α-and α,β-Deuteration of Alcohols Using D_2O. *Org. Lett.*, **2015**, *17*, 4794-4797. (b) Chatterjee, B.; Gunanathan, C. The Ruthenium-Catalyzed Selective Synthesis of mono-Deuterated Terminal Alkynes. *Chem. Commun.* **2016**, *52*, 4509-4512. (c) Krishnakumar, V.; Gunanathan, C. Ruthenium-Catalyzed Selective α-Deuteration of Aliphatic Nitriles Using D_2O. *Chem. Commun.* **2018**, *54*, 8705-8708.

(16) Kar, S.; Goeppert, A.; Sen, R.; Kothandaraman, J.; Prakash, G. K. S. Regioselective Deuteration of Alcohols in D_2O Catalysed by Homogeneous Manganese and Iron Pincer Complexes. *Green Chem*., **2018**, *20*, 2706-2710.

(17) Zhou, Q.-Q.; Zou, Y.-Q.; Kar, S.; Diskin-Posner, Y.; Ben-David, Y.; Milstein, D. Manganese-Pincer-Catalyzed Nitrile Hydration, α-Deuteration, and α-Deuterated Amide Formation via Metal Ligand Cooperation. *ACS Catal*. **2021**, *11*, 10239-10245.

(18) Fertig, R.; Irrgang, T.; Freitag, F.; Zander, J.; Kempe, R. Manganese-Catalyzed and Base-Switchable Synthesis of Amines or Imines via Borrowing Hydrogen or Dehydrogenative Condensation. *ACS Catal*. **2018**, *8*, 8525-8530.

(19) Fu, S.; Shao, Z.; Wang, Y.; Liu, Q. Manganese-Catalyzed Upgrading of Ethanol into 1-Butanol. *J. Am. Chem. Soc*. **2017**, *139*, 11941-11948.

(20) Gawali, S. S.; Pandia, B. K.; Pal, S.; Gunanathan, C. Manganese(I)-Catalyzed Cross-Coupling of Ketones and Secondary Alcohols with Primary Alcohols. *ACS Omega* **2019**, *4*, 10741-10754.

(21) Gawali, S. S.; Pandia, B. K.; Gunanathan, C. Manganese(I)-Catalyzed α-Alkenylation of Ketones Using Primary Alcohols. *Org. Lett*. **2019**, *21*, 3842-3847.

(22) Chakraborty, S.; Das, U. K.; Ben-David, Y.; Milstein, D. Manganese Catalyzed α-Olefination of Nitriles by Primary Alcohols. *J. Am. Chem. Soc*. **2017**, *139*, 11710-11713.

(23) Yadav, V.; Landge, V. G.; Subaramanian, M.; Balaraman, E. Manganese-Catalyzed α-Olefination of Nitriles with Secondary Alcohols. *ACS Catal*. **2020**, *10*, 947-954.

(24) Zhang, G.; Irrgang, T.; Dietel, T.; Kallmeier, F.; Kempe, R. Manganese-Catalyzed Dehydrogenative Alkylation or α-Olefination of Alkyl-Substituted N-Heteroarenes with Alcohols. *Angew. Chem., Int. Ed*. **2018**, *57*, 9131-9135.

CHAPTER 2

Manganese(I) Catalyzed α-Alkenylation of Amides Using Alcohols with Liberation of Hydrogen and Water

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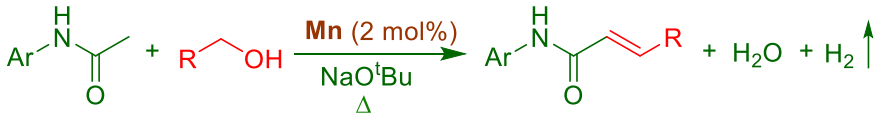
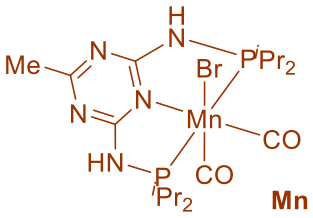
2.1 ABSTRACT



- direct olefination of amides
- alcohols as olefination reagents
- abundant base metal Mn catalyst
- only byproducts: H_2O & H_2
- sustainable catalysis



Herein, unprecedented manganese-catalyzed direct α-alkenylation of amides using alcohols is reported. Aryl amides are reacted with diverse primary alcohols, which provided the α,β-unsaturated amides in moderate to good yields with excellent selectivity. Mechanistic studies indicate that Mn(I) catalyst oxidizes the alcohols to their corresponding aldehydes and also plays an important role in efficient C=C bond formation through aldol condensation. This selective olefination is facilitated by metal-ligand cooperation by the aromatization-dearomatization process operating in the catalytic system. Alcohols are used as alkenylation reagents for the challenging α-alkenylation of amides with the highly abundant base metal manganese as a catalyst, which results in water and dihydrogen as the only byproduct, making this catalytic transformation attractive, sustainable, and environmentally benign.

2.2 INTRODUCTION

Alkenylation reactions leading to the construction of a new C=C bond are an important transformation in organic synthesis. A plethora of strategies is developed to introduce alkene functionality in an intramolecular fashion.[1] On the contrary, classical methods to construct

intermolecular C=C bonds remain limited to Wittig, Horner-Wadsworth-Emmons, Peterson olefination and few other reactions, which all suffer from the requirement of extensive prefunctionalization and excessive toxic reagents. Carbonyl coupling reactions suffer from the drawbacks such as multiple product formation, aerial oxidation and cost effectiveness.[2] Further, due to acidic hydrogen (N−H), amides are not compatible in these classical olefination reactions that require basic conditions.[2-4] There are only a few general catalytic protocols, such as alkene metathesis and diazo coupling reactions, known for the intermolecular olefination.[5]

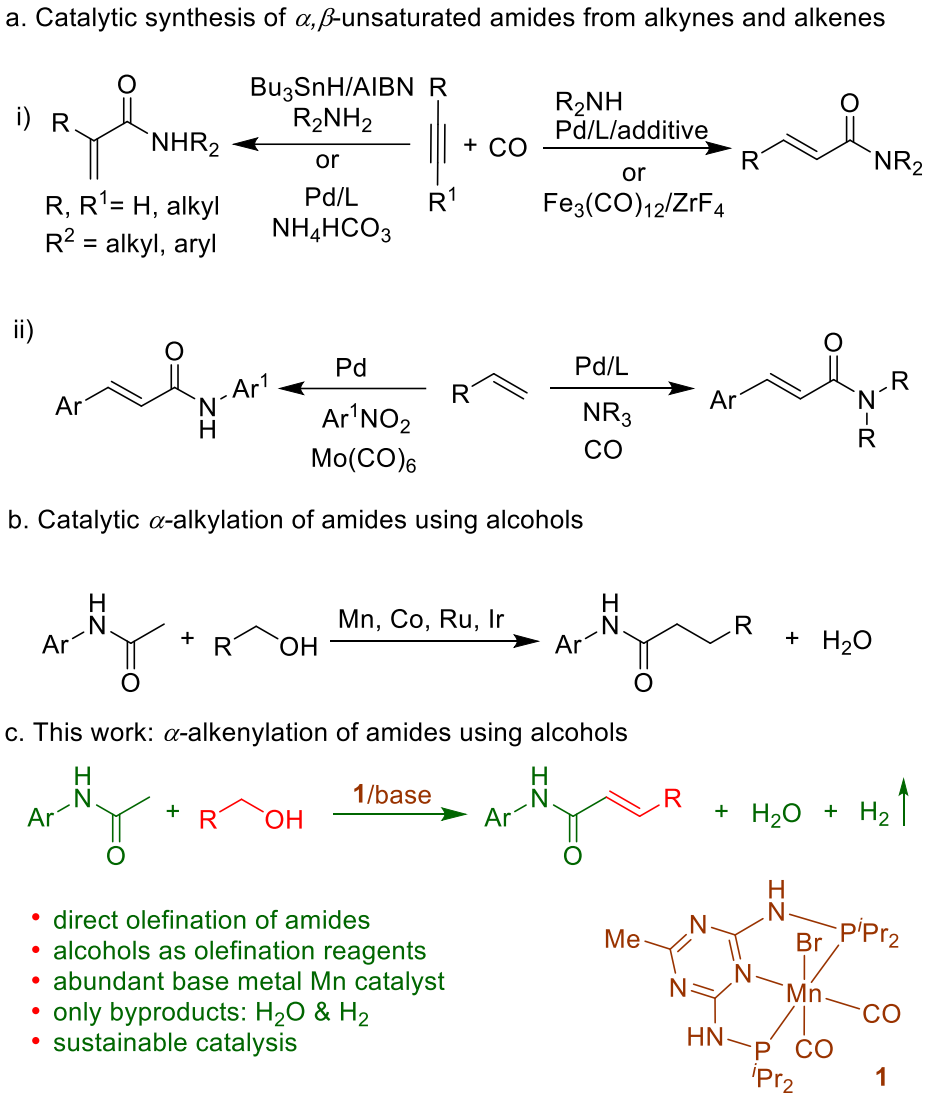
α,β-Unsaturated amides are a valuable class of compounds in organic chemistry. The unsaturated amide functionality is a core motif in various natural products, biologically active compounds, polymeric materials, and pharmaceuticals.[4] For example, avenanthramide exhibits anti-inflammatory and antioxidant properties and is used as a nutrition additive, whereas naturally abundant caffeic acid amides are known to have antitumor, antiviral, and other biological activities.[6,7] Moreover, *α,β*-unsaturated amides are key synthons in organic synthesis, are reactive in nucleophilic additions and pericyclic reactions, and also serve as raw materials for the synthesis of valuable polyamides.[8,9]

Conventional synthesis of *α,β*-unsaturated amides employs the nucleophilic substitution reaction of *α,β*-unsaturated carboxylic acids and amines together with excess coupling reagents, which results in undesired waste formation. Another conventional method involves controlled hydrolysis of acrylonitriles to acrylamides. However, both the methods also suffer from the limited availability of functionalized starting materials.[10] Owing to such multifaceted utilities, the development of efficient catalytic protocols for *α,β*-unsaturated amides has drawn considerable interest in recent years.[4a,10,11]

In general, two pathways are developed for the catalytic synthesis of *α,β*-unsaturated amides involving hydroaminocarbonylation of alkynes[12-15] and aminocarbonylation of alkenes (**Scheme 2.1a**).[16,17] Ryu and co-workers reported the radical mediated

hydroaminocarbonylation of alkynes with primary or secondary amines, which provided branched α,β-unsaturated amides.[12] Using NH_4HCO_3 as an ammonia surrogate, a palladium-

Scheme 2.1. Advances in Catalytic Synthesis of α,β-Unsaturated Amides



catalyzed hydroaminocarbonylation resulted in branched primary amides.[13] Alper developed a highly selective palladium catalyzed method for the synthesis of both linear and branched α,β-unsaturated amides in which the product selectivity is remarkably controlled by the use of different ligands and additives.[14] Iron catalyzed hydroaminocarbonylation of alkynes with primary and secondary amines to exclusive formation of linear amides has also been reported recently.[15] Beller and Lei reported the Pd/Cu catalyzed aminocarbonylation of alkenes to linear

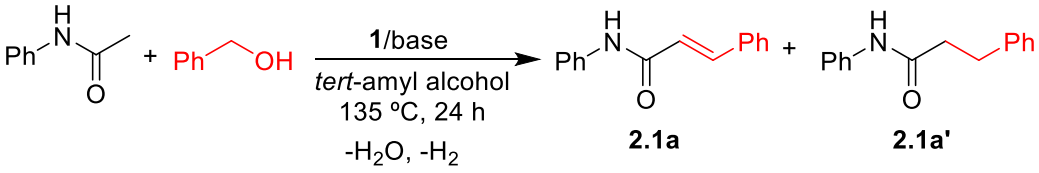
α,β-unsaturated amides, and the reactions proceeded via aerobic oxidative dealkylation of tertamines.[16] Palladium-catalyzed synthesis of linear *α,β*-unsaturated amides was also attained using $Mo(CO)_6$ as a carbonyl surrogate and nitroarene via aminocarbonylation of alkenes.[17] Synthetic methods for the *α,β*-desaturation or dehydrogenation of saturated alkyl amides to *α,β*-unsaturated amides were also developed.[18] Further, many methods are known for the synthesis of such unsaturated amides.[3,19] However, these protocols suffer from the requirement of complicated starting materials, elongated synthetic steps, toxic CO, additives, and activating reagents.[17-20] Thus, the development of a simple, selective, and direct synthesis of *α,β*-unsaturated amides is highly desirable.

Using biorenewable and abundant feedstock chemicals such as alcohols, an assortment of sustainable organic transformations have been developed through an acceptorless dehydrogenative coupling (ADC) strategy.[21] However, thus far, only a few examples of direct alkenylation using ADC of alcohols have been reported. Direct alkenylation of nitriles using alcohols was established by other research groups and us.[22] Using the manganese pincer 1 developed by Kempe, we have reported catalytic alkenylation of ketones by alcohols via ADC.[23,24] Manganese-catalyzed alkenylation of the heteroaryl methyl group[25] and aryl sulfone compounds[26] have been reported using alcohols. Achieving ADC in particular with carbon nucleophile is highly challenging, primarily because of the competing "borrowing hydrogen" reaction,[27] which leads to the hydrogenation of in situ formed *α,β*-unsaturated compounds.[28-30] Accordingly, the alkylation of amides using alcohols is well established (**Scheme 2.1b**).[29] On the contrary, alkenylation of amides using ADC of alcohol is unknown. Herein, we report the manganese pincer catalyzed direct alkenylation of amides using alcohols, in which selective synthesis of linear *α,β*-unsaturated amides with the liberation of molecular hydrogen and water is attained (**Scheme 2.1c**).

2.3 RESULTS AND DISCUSSIONS

We commenced our investigation with the reaction of acetanilide (0.5 mmol), benzyl alcohol (0.6 mmol), catalyst **1** (2 mol %), and cesium carbonate (30 mol %) in *tert*-amyl alcohol at 135 °C. Upon completion and workup, analysis of ^{1}H NMR spectra of the reaction mixture revealed

Table 2.1 Optimization for Catalytic *α*-Alkenylation of Amides Using Benzyl Alcohols[a]



Entry	cat. **1** (mol %)	base (mol %)	conv. (%)[b]	ratio[c] (**2.1a:2.1a'**)
1	2	Cs_2CO_3 (30)	87	85:4
2	5	Cs_2CO_3 (30)	99	60:10
3	2	Cs_2CO_3 (50)	77	76:5
4	2	Cs_2CO_3(100)	79	72:4
5	1	KO^{t}Bu (20)	71	74:5
6	2	NaO^{t}Bu (50)	87	76:5
7	2	NaO^{t}Bu (70)	96	83:4
8	2	NaO^{t}Bu (100)	89	>98:2
9	-	NaO^{t}Bu (100)	-	-
10	-	-	-	-
11[d]	2	NaO^{t}Bu (100)	91	>98:2
12[e]	2	NaO^{t}Bu (100)	-	-

[a] Reaction conditions: acetanilide (0.5 mmol), benzyl alcohol (0.6 mmol), tert-amyl alcohol (2 mL), catalyst **1**, and base were heated at 135 °C under nitrogen flow. [b] Conversion of acetanilide was determined by ^{1}H NMR analysis using methyl benzoate (0.25 mmol) as an internal

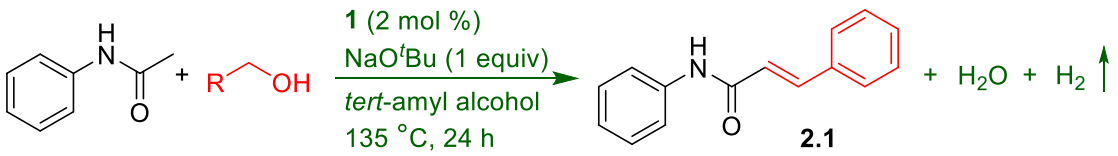
standard. [c] Ratio of products was calculated from ^{1}H NMR spectral analysis of reaction mixture. [d] Reaction performed at 150 °C, and product **2.1a** was isolated in 79% yield. [e] Reaction performed at 100 °C with molecular sieves (4 Å).

87% conversion of acetanilide with alkenylated (**2.1a**) and alkylated (**2.1a′**) amide products in an 85:4 ratio (entry 1, **Table 2.1**). Increasing the catalyst load to 5 mol % resulted in complete conversion of acetanilide, however with lower selectivity of the 60:10 (**2.1a**: **2.1a′**) α-alkenylated product (entry 2, **Table 2.1**). At 2 mol % of catalyst load, increasing the amount of base (50 mol %) decreased the conversion of acetanilide to 77% with 76:5 (**2.1a**: **2.1a′**) product selectivity (entry 3, **Table 2.1**). A similar outcome was observed when 1 equiv of cesium carbonate was used (entry 4, **Table 2.1**). In order to achieve better conversion and selectivity, the reaction was screened with 20 mol % of KO^{t}Bu and 1 mol % of catalyst, which resulted in 71% conversion with a selectivity of 74:5 (**2.1a**: **2.1a′**, entry 5, **Table 2.1**). Use of NaO^{t}Bu (50 mol %) base with 2 mol % of the catalyst under similar reaction conditions resulted in the selectivity of 76:5 (**2.1a**: **2.1a′**) with 87% conversion of acetanilide (entry 6, **Table 2.1**). Upon using 70 mol % NaO^{t}Bu, 96% conversion was observed with a selectivity of 83:4 (**2.1a**: **2.1a′**, entry 7, **Table 2.1**). Further, the use of 1 equiv of base, NaO^{t}Bu, provided the optimal reaction condition with complete selectivity for the α-alkenyl trans-product **2.1a** (entry 8, **Table 2.1**). As amide carbonyl is involved in amide-iminol tautomerization, which makes the protons on α-methylcarbon less acidic. As a result, stoichiometric base is required as the prior deprotonation might occur on N-H functionality of amide before the deprotonation on α-methylcarbon of amides. Hence, this reaction requires stoichiometric base. As a result, one equivalent of *tert*-butyl alcohol and partial formation of NaBr and NaOH will occur in situ reactions. No product formation was observed in control experiments performed by employing only base, and without catalyst and base, indicating that catalyst and base are essential (entries

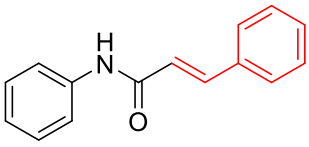
9, 10, **Table 2.1**). While the use of higher temperature has not much influence on the product yield, the reaction performed using dehydrants such as molecular sieves failed (entries 11, 12, **Table 2.1**).

With optimal reaction conditions in hand, a wide range of primary alcohols was subjected to the manganese-catalyzed α-alkenylation of acetanilide (**Scheme 2.2**). With benzyl alcohol, the corresponding α,β-unsaturated amide with complete selectivity for *E*-alkene formation was observed, and product **2.1a** was isolated in 83% yield. In general, benzyl alcohols bearing electron-donating substituents afforded the corresponding *E*-alkene products in moderate to good yields. A methyl group at the ortho and para positions produced the unsaturated amides

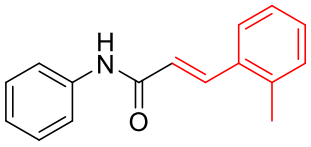
Scheme 2.2. Manganese Catalyzed α-Alkenylation of Acetanilide Using Alcohols[a]



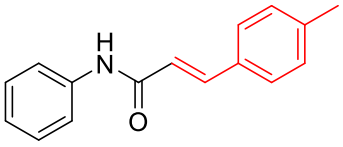
2.1



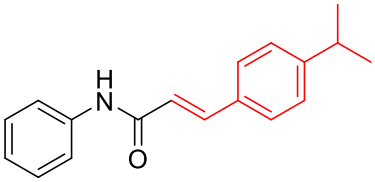
2.1a, 83% (89%)
77% (88%)[b]



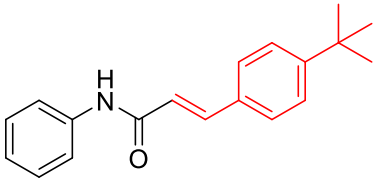
2.1b, 57%



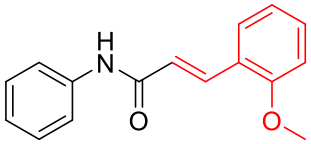
2.1c, 60% (77%)



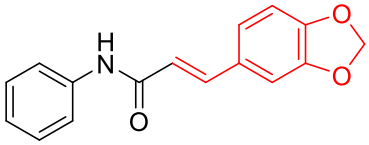
2.1d, 57% (84%)



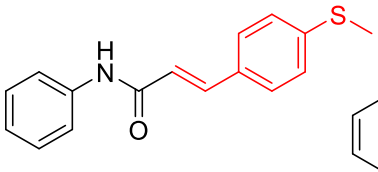
2.1e, 42% (>99%)



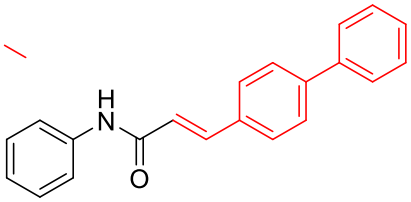
2.1f, 67%



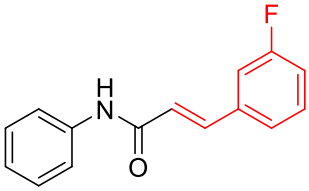
2.1g, 52% (65%)



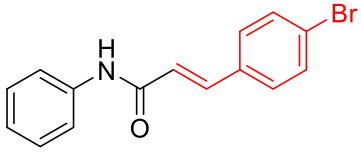
2.1h, 57% (84%)



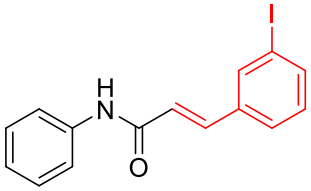
2.1i, 62% (79%)



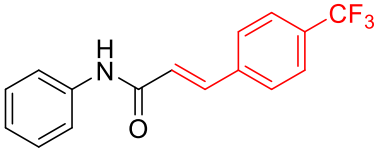
2.1j, 56% (70%)



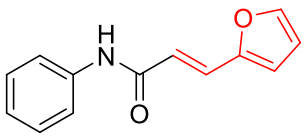
2.1k, 68% (89%)



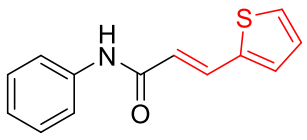
2.1l, 42% (66%)



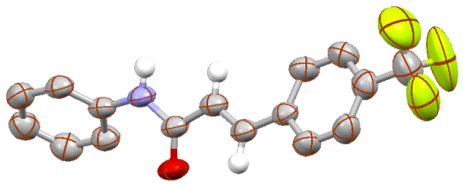
2.1m, 65% (86%)



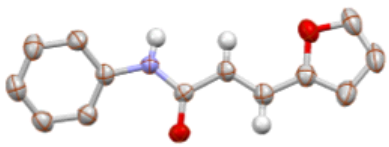
2.1n, 82%, 92%[c]



2.1o, 89%, 93%[c]



2.1m



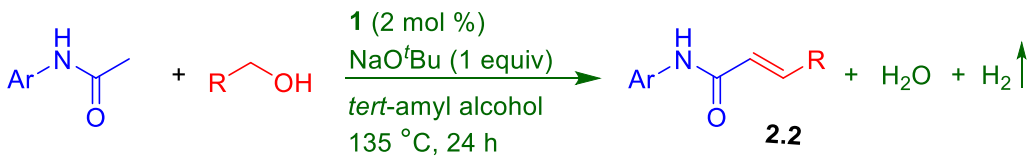
2.1n

[a] Reaction conditions: arylamide (acetanilide, 0.5 mmol), alcohol (0.6 mmol), *tert*-amyl alcohol (2 mL), catalyst 1 (2 mol %), and NaO^{t}Bu (1 equiv) were heated at 135 °C under nitrogen flow. Conversion of acetanilide was determined from ^{1}H NMR analysis of the reaction mixture using methyl benzoate (0.25 mmol) as an internal standard and given within the parentheses. [b] Yield of the 0.5 g scale reaction, performed for 36 h. [c]Yield obtained when the reaction was carried out using Cs_2CO_3 as a base; 5-8% of alkylation product was also present.

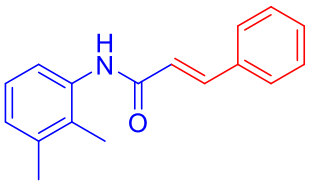
2.1b-**2.1c** in moderate yields. The *α*-alkenylation of acetanilide with 4-isopropyl and 4-tert-butyl benzyl alcohols afforded the corresponding products **2.1d**-**2.1e** in 57% and 42% yields, respectively. Reaction with 2-methoxybenzyl alcohol and piperonyl alcohol afforded the corresponding products **2.1f**-**2.1g** in 67% and 52% yields, respectively. Reaction with 4-thiomethylbenzyl alcohol provided the *α,β*-unsaturated amide **2.1h** in 57% yield. Screening benzyl alcohols containing electron-withdrawing substituents afforded products in moderate yields. With 4-phenylbenzyl alcohol, 79% conversion of acetanilide occurred, and product **2.1i** was isolated in 62% yield. With halogenated compounds such as 3-fluoro-, 4-bromo-, and 3-iodobenzyl alcohols, the corresponding alkene products **2.1j**-**2.1l** were obtained in 56%, 68%, and 42% yields, respectively. The reaction of acetanilide with 4-trifluoromethylbenzyl alcohol produced the *α,β*-unsaturated amide **2.1m** in 65% yield. Notably, heteroaryl alcohols such as furfuryl alcohol and 2-thiophenemethanol provided the corresponding products **2.1n**-**2.1o** in good yields. However, an aliphatic alcohol, such as 1-hexanol, resulted in complete alkylation of amide. Secondary alcohols such as 1-phenylethanol failed to react under this catalytic condition. Single-crystal X-ray analyses of products **2.1m** and **2.1n** unequivocally confirmed the trans geometry of alkene in these *α,β*-unsaturated amides (**Scheme 2.2**).

Encouraged by the versatility of this method, the scope of various amides with benzyl alcohols was explored (**Scheme 2.3**). The reaction of 2,3-dimethyl acetanilide with benzyl alcohol under

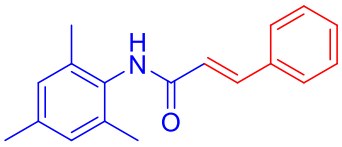
Scheme 2.3. Manganese Catalyzed *α*-Alkenylation of Amides Using Alcohols with H_2 Liberation[a]



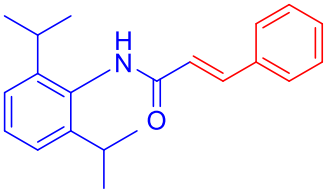
2.2



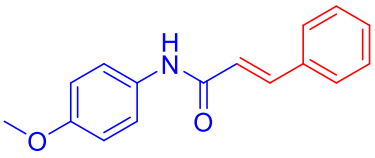
2.2a, 66%



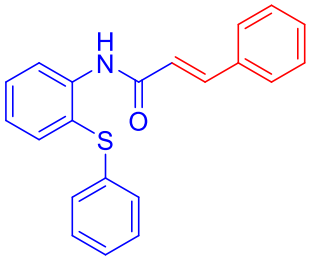
2.2b, 68%



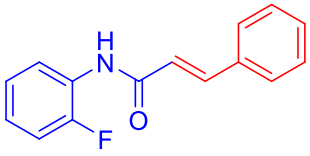
2.2c, 52%



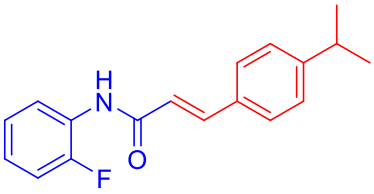
2.2d, 63% (86%)



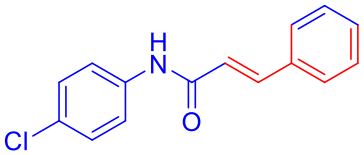
2.2e, 20% (98%)



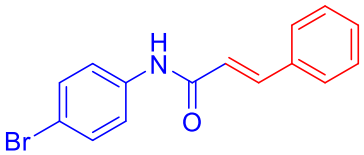
2.2f, 60% (88%)



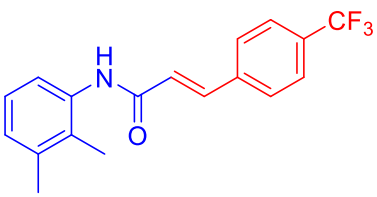
2.2g, 64%



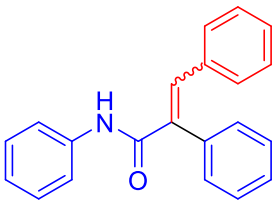
2.2h, 36%



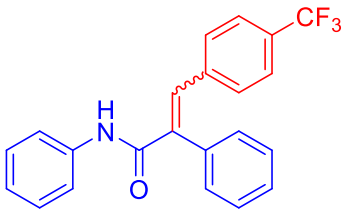
2.2i, 60% (91%)[b]



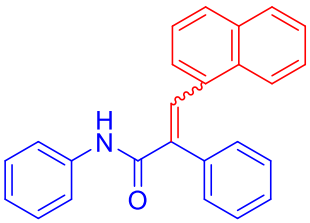
2.2j, 71%c



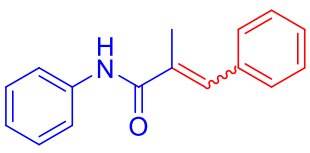
2.2k, 43%[c]



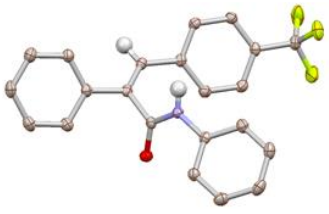
2.2l, 41%[c]



2.2m, 43%[c,d]



2.2n, 25%



Z-**2.2l**

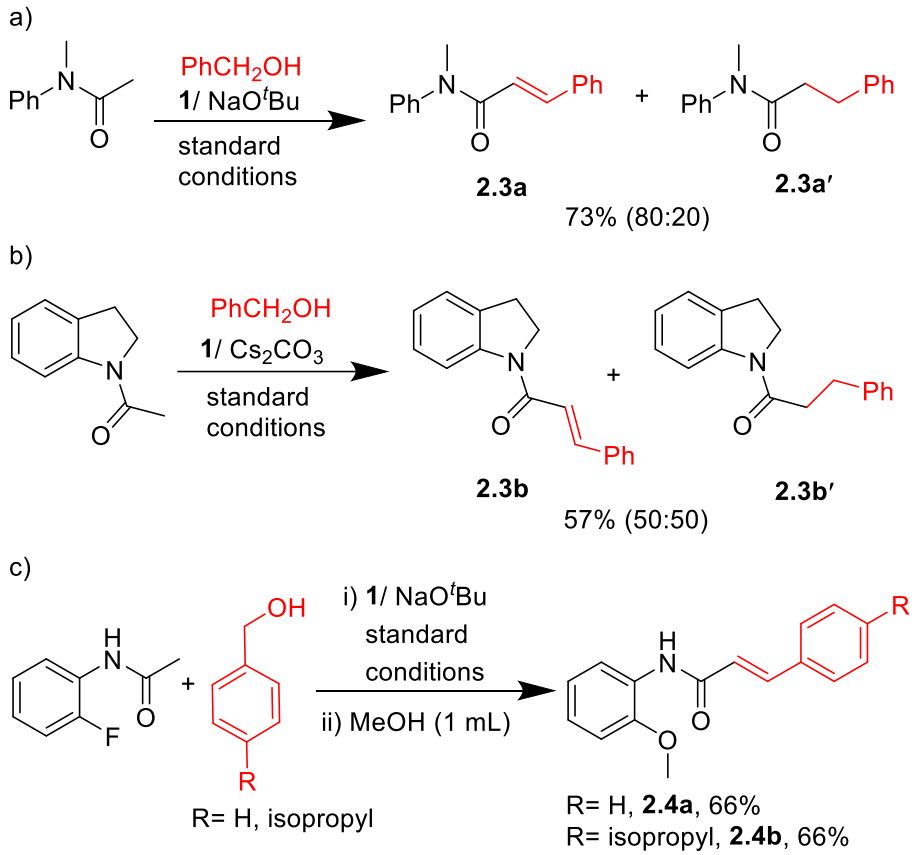
[a] Reaction conditions: same as that of footnote in Scheme **2.2**. [b]10% of alkylation product was also present. [c] KO^{t}Bu (1 equiv) was used as a base, the product isolated as *E*/*Z* mixture, and the ratio is not determined. [d] Catalyst **1** was used in 5 mol %.

---

standard conditions provided the corresponding *α,β*-unsaturated amide **2.2a** in 66% yield. Similarly, 2,4,6-trimethyl acetanilide afforded the product **2.2b** in 68% yield. High steric hindrance present in 2,6-diisopropyl acetanilide resulted in 52% of the product **2.2c**, and 4-methoxy substituted acetanilide produced the alkenylation product **2.2d** in 63% yield. When 2-thiophenylacetanilide was subjected to *α*-alkenylation with benzyl alcohol, only 20% product **2.2e** was obtained, and the majority of the starting amide was observed to undergo deacylation to result in the corresponding aniline. Amides containing electron-withdrawing groups such as 2-fluoro-, 4-chloro-, and 4-bromo- substitutions on arene resulted in products **2.2f**-**2.2i** in moderate to good yields. The reaction of 2,3-dimethyl acetanilide with 4-trifluorobenzyl alcohol afforded the *α*-alkenylation product **2.2j** in 71% yield. To explore the generality of the reaction, N,2-diphenylacetamide was reacted with benzyl alcohol to afford the corresponding *α,β*-unsaturated product **2.2k** in 43% yield in which the alkene formation occurred on internal carbon and both *E* and *Z* isomers were formed in the reaction. Further, N,2-diphenylacetamide was reacted with 4-trifluoromethylbenzyl alcohol and 1-napthalenemethanol, which provided products **2.2l** and **2.2m** in 41% and 43% yields, respectively, as an *E*/*Z* mixture. Upon crystallization of the *E*/*Z* mixture of **2.2l**, single-crystal X-ray structure of the cis-product, *Z*-**2.2l** was obtained (**Scheme 2.3**). When N-phenylpropionamide was subjected to alkenylation with benzyl alcohol, 24% of unsaturated amide **2.2n** was isolated.

To further test the scope of this catalytic method, tertiary amide such as N-methyl acetanilide was subjected to alkenylation with benzyl alcohol, which afforded 73% yield of **2.3a** as a mixture of alkenylation and alkylation products in an 80:20 ratio (**Scheme 2.4a**). The reaction

Scheme 2.4. *α*-Alkenylation of Tertiary Amides Using Primary Alcohols and Derivatization of *α*-Alkenyl-2-Fluoroacetanilide

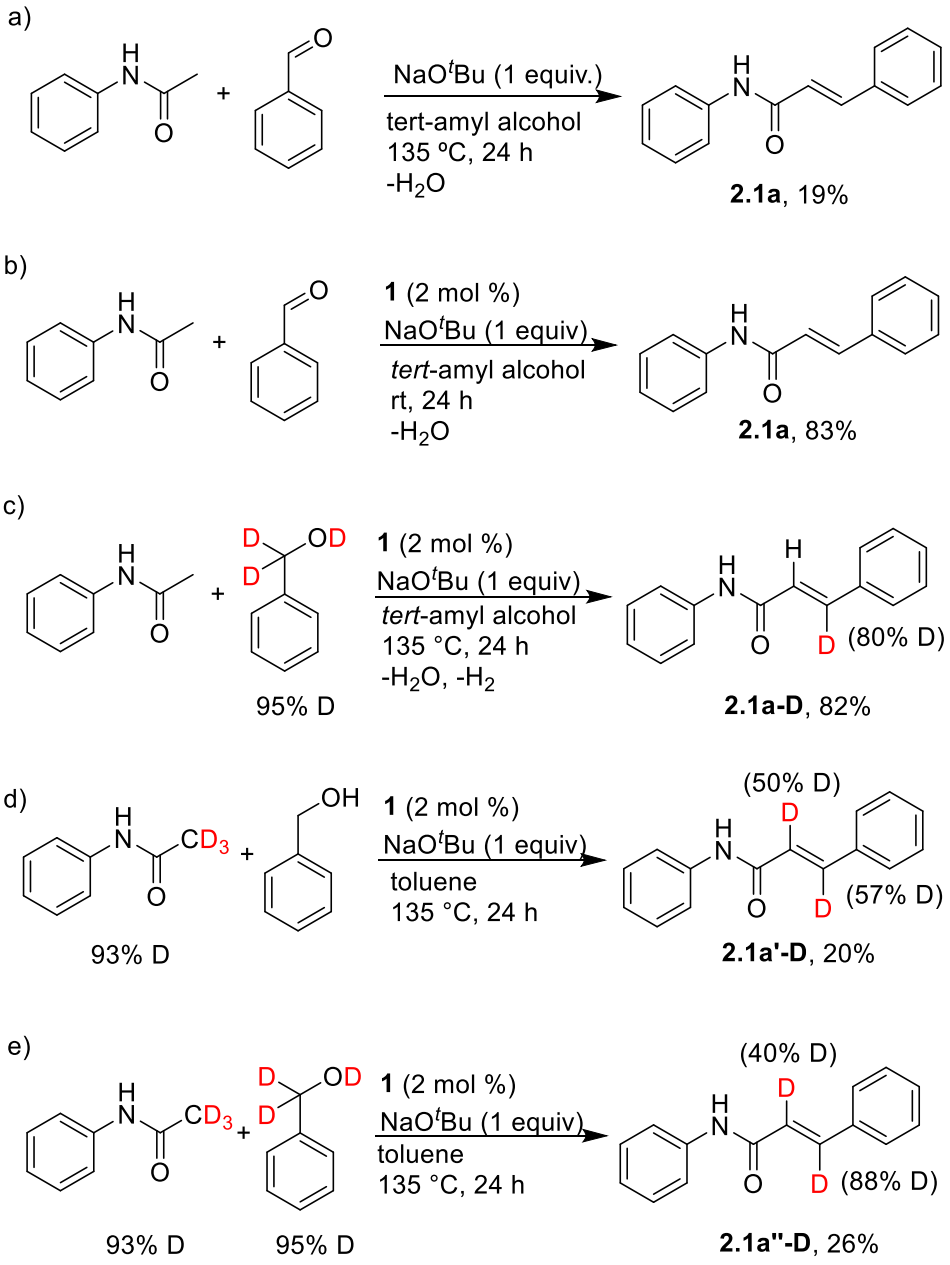


of N-acetyl indoline under standard condition using NaO^{t}Bu resulted in diacylation reaction, and thus, when the reaction was performed using Cs_2CO_3, 57% of products **2.3b** and **2.3b′** in 50:50 ratio were obtained (**Scheme 2.4b**). Further, the reaction of N-(2-fluorophenyl)acetamide with benzyl alcohols leads to the formation of N-(2-fluorophenyl)cinnamamide products (**2.2f** and **2.2g**), and when the reaction mixtures were further treated with methanol, the corresponding methoxy products **2.4a** and **2.4b** were obtained in 66% yields, which resulted from the S_NAr pathway (**Scheme 2.4c**).

Mechanistic Studies. To gain insights into the mechanism, the reaction of benzaldehyde with acetanilide was performed in both the absence and the presence of manganese catalyst, which

provided product **2.1a** in 19% and 83% yields, respectively (**Scheme 2.5a and b**). These experiments revealed that catalyst **1** plays a significant role in the C=C bond formation via the

Scheme 2.5. Mechanistic Studies for *α*-Alkenylation of Amides Using Primary Alcohols



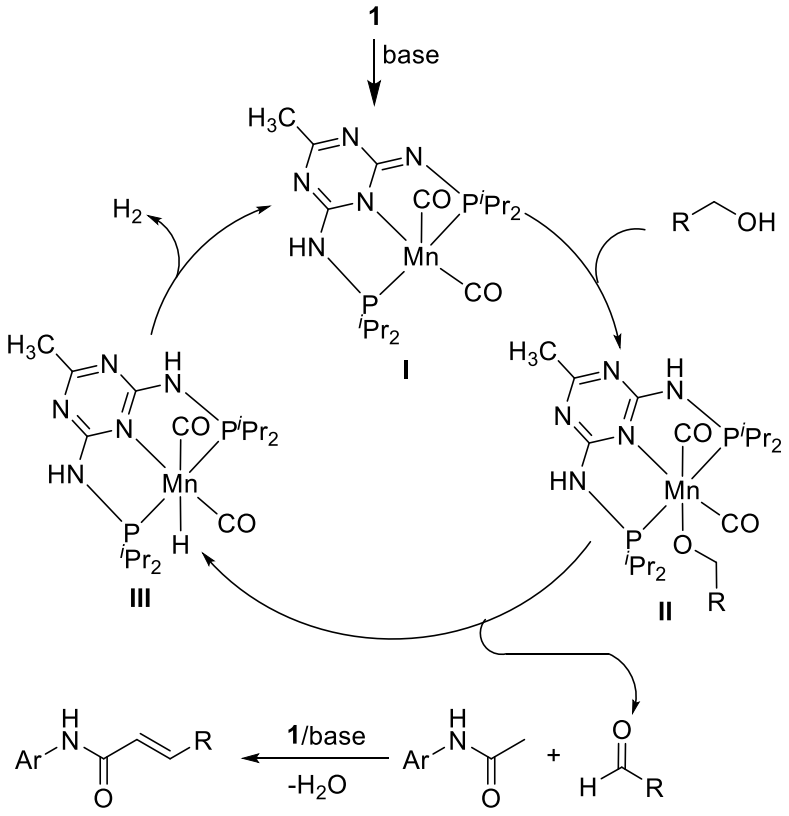
aldol reaction. Further, deuterium-labeling experiments were carried out. Upon reaction with *α*-deuterated benzyl alcohol-d_3, 80% deuterium incorporation was observed exclusively at the *β*-position of the *α,β*-unsaturated amide **2.1a**-D (**Scheme 2.5c**). When deuterated acetanilide-

d_3 was reacted with benzyl alcohol, 50% and 57% deuterium incorporation occurred at α- and β-positions of **2.1a′**-D due to deuterium scrambling (**Scheme 2.5d**). When both amide and alcohol were deuterated, α- and β-positions of product **2.1a′′**-D displayed 40% and 88% deuterium incorporation, respectively (**Scheme 2.5e**). These observations indicate that only when amide is deuterated, the deuterium scrambling takes place and confirms the aldol condensation.

On the basis of the experimental observations and mechanistic studies performed, a reaction mechanism for the manganese-catalyzed α-alkenylation of amides with alcohols is proposed in **Scheme 2.6**. Complex **1** reacts with a base to provide the dearomatized intermediate **I**. The coordinatively unsaturated intermediate **I** reacts with alcohol via O-H activation to provide alkoxy-ligated intermediate **II**. The research groups of Milstein, Kempe, Yu, and Liu have characterized such manganese alkoxy pincer complexes.[25c,31-33] β-Hydride elimination from intermediate **II** results in the formation of the corresponding aldehyde and Mn-hydride complex **III**. Intermediate **I** is regenerated in the catalytic cycle upon H_2 liberation from saturated intermediate **III**. All manganese intermediates in the catalytic cycle maintain a +1 oxidation state due to the aromatization and dearomatization metal-ligand cooperation operative in the catalytic system, facilitating this transformation. The liberated aldehyde then undergoes aldol condensation with amide under the catalytic conditions to provide the α-alkenyl amide product and water. As observed experimentally (**Scheme 2.5b**), the catalyst also plays an important role in aldol condensation, which leads to the efficient C=C bond formation in α-alkenylation of amides using alcohols as alkenylation reagents. Combination of careful catalyst selection and optimized experimental conditions are crucial for the selective synthesis of alkenyl amides. Catalyst **1** with methyl substitution on the pincer backbone favors the alkenyl products.[23] Similar manganese catalyst with phenyl substituent on the pincer backbone

favored the alkylation of ketones and secondary alcohols when reacted with primary alcohols.[28a]

Scheme 2.6. Proposed Mechanism for Manganese Pincer Catalyzed *α*-Alkenylation of Amides Using Alcohols



2.4 CONCLUSION

In summary, this work demonstrated a strategy for *α*-alkenylation of amides that uses highly abundant base metal manganese as a catalyst and cheap industrial feedstock alcohols as direct alkenylation reagents. Remarkably, water and molecular hydrogen are the only byproducts of these direct alkenylation reactions. The diverse substrate scope of both amides and alcohols is demonstrated. Tertiary amides were also amenable in this catalytic reaction, albeit providing a mixture of alkenylation and alkylation products. Mechanistic studies indicate that the manganese pincer catalyst oxidizes alcohols to aldehydes and plays an important role in efficient C=C bond formation through aldol condensation, which operates through

metal−ligand cooperation by the aromatization-dearomatization process. Deuterium-labeling experiments displayed that scrambling occurs only with the amidemethyl protons confirming the involvement of aldol condensation. Overall, this simple, attractive, and catalytic protocol advances the alkenylation reactions in chemical synthesis and can further develop sustainable transformations.

2.5 EXPERIMENTAL SECTION

General Information. All catalytic reactions were performed under inert atmosphere using standard Schlenk techniques. All stoichiometric reactions were performed in nitrogen atmosphere MBRAUN glovebox. Chemicals were purchased from Acros, Sigma-Aldrich, Alfa-aesar, and Himedia Chemicals and used without further purification. Dry solvents were prepared according to standard procedures. Infrared (IR) spectra were recorded in PerkinElmer FTIR and Thermo-Nicolet FT-IR spectrophotometers. High-resolution mass spectra (HRMS) were obtained on Bruker micrOTOF-Q II Spectrometer and are reported as m/z (relative intensity). Accurate masses are reported for the molecular ion $[M + Na]^+$, $[M+ H]^+$, and $[M]^+$. Nuclear magnetic resonance spectra (^{1}H NMR and ^{13}C NMR) were recorded at Bruker AV-700 (^{1}H at 700 MHz and ^{13}C at 175 MHz) and Bruker AV-400 (^{1}H at 400 MHz and ^{13}C at 100.6 MHz). ^{1}H NMR chemical shifts are referenced in parts per million (ppm) with respect to tetramethyl silane (TMS, δ 0.00 ppm), and ^{13}C{^{1}H} NMR chemical shifts are referenced in parts per million (ppm) with respect to $CDCl_3$ (δ 77.160 ppm). Coupling constants are reported in Hertz (Hz). ^{1}H NMR spectroscopy abbreviations: s, singlet; d, doublet; t, triplet; q, quartet; dd, doublet of doublets; dt, doublet of triplets; dq, doublet of quartets; td, triplet of doublets; qd, quartets of doublets; ddd, doublets of doublets of doublets; m, multiplet; br, broad. Assignment of spectra was done based on one-dimensional (dept-135) NMR techniques. The catalyst **1** was prepared following the literature procedure reported by Kempe.[31]

General Procedure for Synthesis of Amides. To a solution of aniline (5 mmol) and dichloromethane (DCM, 5 mL), trimethylamine (2 equiv, 10 mmol) was added under ice-cold conditions. The mixture was allowed to stir for 10 min. Then, a solution of acetyl chloride (10 mmol) in DCM was added dropwise over a period of 15 min. The reaction mixture was allowed to stir for 2 h. The completion of the reaction was monitored by TLC. After completion, the reaction mixture was quenched by the addition of water. The organic layer was extracted using DCM, washed with brine solution, and dried using anhydrous sodium sulfate. Solvents are removed under reduced pressure using a rotavapor, and the resulted residue was purified by column chromatography. The following amides were prepared and characterized by NMR analyses and data compared with the reported literature: N-(2,3-dimethylphenyl)acetamide,[34] N-mesitylacetamide,[35] N-(2,6-diisopropylphenyl) acetamide,36 N-(4-methoxyphenyl) acetamide,[37] N-(2-(phenylthio)phenyl) acetamide,[38] N-(2-fluorophenyl)acetamide,[39] N-(4-chlorophenyl)acetamide,[40] N-(4-bromophenyl)-acetamide, N-phenylpropanamide,[41] and N,2-diphenylacetamide.[42]

General Procedure for Optimization of *α*-Alkenylation of Amides Using Alcohols. To a Schlenk flask (25 mL) equipped with a stir bar, catalyst 1 (2 mol %), NaO^{t}Bu (1 equiv), acetanilide (0.5 mmol), benzyl alcohol (0.6 mmol), and tert-amyl alcohol (2 mL) were added under nitrogen atmosphere in a glovebox. The reaction mixture was taken out of the glovebox, equipped with a condenser, and the solution was heated at 135 °C (oil bath temperature) with stirring in an open system under nitrogen flow for 24 h. After cooling, the reaction mixture was transferred to an RB flask, and the solvent was evaporated under reduced pressure. The resultant residue was dissolved in chloroform, washed with water and brine. The collected organic layer was dried over anhydrous sodium sulfate and concentrated in a vacuum. Further, methyl benzoate (0.25 mmol) was added (as an internal standard) to the mixture, dissolved in $CDCl_3$ (1 mL), and subjected to ^{1}H NMR analysis from which the conversion was calculated.

General Procedure for *α*-Alkenylation of Amides Using Alcohols. To a Schlenk flask (25 mL) equipped with a stir bar, catalyst **1** (2 mol %), NaO^{t}Bu (1 equiv), amide (0.5 mmol), alcohol (0.6 mmol), and tert-amyl alcohol were added under nitrogen atmosphere in a glovebox. The reaction mixture was taken out of the glovebox, equipped with a condenser, and the solution was heated at 135 °C (oil bath temperature) with stirring in an open system under nitrogen flow for 24 h. After cooling, the reaction mixture was transferred to an RB flask. The solvent was removed under reduced pressure; the reaction mixture was dissolved in chloroform and washed with water and brine. The collected organic layer was dried over anhydrous sodium sulfate and concentrated in a vacuum. Further, methyl benzoate (0.25 mmol) was added (as an internal standard), the mixture was dissolved in $CDCl_3$ or CD_3OD (1 mL) and subjected to ^1H NMR analysis from which the conversion was calculated. $CDCl_3$ was removed in vacuo, and the residue was purified by silica gel (100-200 mesh) column chromatography using ethyl acetate/hexane mixture as eluent. Yields were calculated for isolated products.

Spectral Data of *α*-Alkenyl Amide Products

N-Phenylcinnamamide (2.1a).[43] This was purified by silica-gel column chromatography using ethyl acetate/hexane (10:90) mixture as an eluent. White solid. Yield (92 mg, 83%; 635 mg, 77% for the 0.5 g scale reaction). MP 155-157 °C. IR (DCM): 3060, 3028, 1661, 1626, 1596, 1578, 1539, 1495, 1351, 1248, 904, 704 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.67 (d, J = 15.5 Hz, 1H), 7.59-7.45 (m, 3H), 7.42 (dd, J_1 = 6.5 Hz, J_2 = 3.0 Hz, 2H), 7.30-7.26 (m, 3H), 7.24-7.17 (m, 2H), 7.04 (t, J = 7.4 Hz, 1H), 6.49 (d, J = 15.5 Hz, 1H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 164.5, 142.2, 138.1, 134.5, 129.8, 129.0, 128.8, 127.9, 124.4, 120.9, 120.2. HRMS (ESI) m/z calcd for $C_{15}H_{13}NONa$ $(M+Na)^+$: 246.0889, found: 246.0885.

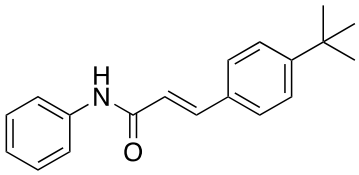
(*E*)-N-Phenyl-3-(o-tolyl)acrylamide (**2.1b**).[44] This was purified by silica-gel column chromatography using ethyl acetate/hexane (10:90) mixture as an eluent. White solid. Yield (68 mg, 57%). MP 159−161 °C IR (DCM): 3063, 2944, 2844, 1668, 1603, 1542, 1482, 1313, 1247, 1156, 951, 705 cm^{-1}. ^{1}H (400 MHz, CD_3OD): δ 8.21 (d, *J* = 15.6 Hz, 1H), 7.89 (d, *J* = 7.8 Hz, 2H), 7.84 (d, *J* = 7.5 Hz, 1H), 7.59-7.51 (m, 2H), 7.51-7.40 (m, 3H), 7.33 (t, *J* = 7.4 Hz, 1H), 6.92 (d, *J* = 15.6 Hz, 1H), 2.66 (s, 3H). $^{13}C\{^{1}H\}$ NMR (101 MHz, CD_3OD): δ 165.3, 139.0, 138.6, 137.3, 133.5, 130.4, 129.4, 128.4, 126.0, 125.8, 123.9, 121.8, 119.8, 18.4. HRMS (ESI) m/z calcd for $C_{16}H_{16}NO$ $(M+H)^+$: 238.1226, found: 238.1222.

(*E*)-N-Phenyl-3-(p-tolyl)acrylamide (**2.1c**). This was purified by silica-gel column chromatography using ethyl acetate/hexane (10:90) mixture as an eluent. White solid. Yield (69 mg, 60%). MP 184-186 °C. IR (DCM): 3038, 2922, 2853, 1653, 1623, 1550, 1498, 1336, 810, 689 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.67-7.63 (m, 2H), 7.56 (d, *J* = 5.8 Hz, 2H), 7.31 (d, *J* = 7.8 Hz, 2H), 7.25 (t, *J* = 7.8 Hz, 2H), 7.05 (dd, J_1 = 17.0 Hz, J_2 = 7.4 Hz, 3H), 6.48 (d, *J* = 15.5 Hz, 1H), 2.28 (s, 3H). $^{13}C\{^{1}H\}$ NMR (101 MHz, CD_3OD): δ 165.5, 141.4, 140.1, 138.6, 132.0, 129.2, 128.4, 127.5, 123.8, 119.8, 119.7, 20.0. HRMS (ESI) m/z calcd for $C_{16}H_{16}NO$ $(M+H)^+$: 238.1226, found: 238.1231.

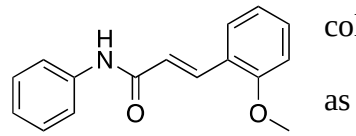
(*E*)-3-(4-Isopropylphenyl)-N-phenylacrylamide (**2.2d**). This was purified by silica-gel column chromatography using ethyl acetate/hexane (10:90) mixture as an eluent. White solid. Yield (75 mg, 57%). MP 122-124 °C IR (DCM): 3063, 2944, 2844, 1668, 1603, 1542, 1482, 1313, 1247, 951, 705 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.77 (s, 1H), 7.65 (d, *J* = 15.5 Hz, 1H), 7.56 (d, *J* = 7.2 Hz, 2H), 7.33 (d, *J* = 8.1 Hz, 2H), 7.24 (t, *J* = 7.9 Hz, 2H), 7.11 (d, *J* = 8.1 Hz, 2H), 7.03 (t, *J* = 7.3 Hz, 1H), 6.50 (d, *J* = 15.5 Hz, 1H), 2.82 (dt, J_1 = 13.8, J_2 = 6.9 Hz,

1H), 1.16 (d, *J* = 6.9 Hz, 6H). $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$): δ 164.5, 151.2, 142.3, 138.2, 132.2, 129.0, 128.1, 127.2, 126.9, 124.3, 120.0, 34.0, 23.8. HRMS (ESI) m/z calcd for $C_{18}H_{19}NONa$ $(M+Na)^+$: 288.1359, found: 288.1353.

(*E*)-3-(4-(tert-Butyl)phenyl)-N-phenylacrylamide (**2.2e**). This was purified by silica-gel column chromatography using ethyl acetate/ hexane (10:90) mixture as an eluent. White solid. Yield (58 mg, 42%). MP 141-143 °C. IR (DCM): 3299, 3058, 2961, 2867, 1661, 1622, 1537, 1497, 1343, 980, 715 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.60 (d, *J* = 15.5 Hz, 1H), 7.49 (s, 3H), 7.31 (d, *J* = 7.7 Hz, 2H), 7.27-7.17 (m, 4H), 6.98 (t, *J* = 7.2 Hz, 1H), 6.42 (d, *J* = 15.5 Hz, 1H), 1.18 (s, 9H). $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$): δ 165.0, 153.2, 141.9, 138.2, 131.8, 128.9, 127.7, 126.9, 125.7, 125.4, 124.2, 120.3, 34.7, 31.3, 31.1. HRMS (ESI) m/z calcd for $C_{19}H_{21}NONa$ $(M+Na)^+$: 302.1515, found: 302.1491.



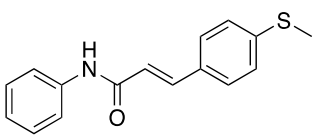
(*E*)-3-(2-Methoxyphenyl)-N-phenylacrylamide (**2.2f**). This was purified by silica-gel column chromatography using ethyl acetate/hexane (15:85) mixture as an eluent. White solid. Yield (84 mg, 67%). MP 160-162 °C. IR (DCM): 3438, 2935, 2837, 1657, 1623, 1598, 1488, 1343, 1180, 752 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.81 (d, *J* = 15.7 Hz, 1H), 7.49-7.44 (m, 3H), 7.26 (d, *J* = 7.5 Hz, 1H), 7.12 (t, *J* = 7.5 Hz, 3H), 6.90 (t, *J* = 7.1 Hz, 1H), 6.71 (t, *J* = 9.7 Hz, 2H), 6.52 (d, *J* = 15.7 Hz, 1H), 3.65 (s, 3H). $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$): δ 165.2, 158.2, 138.4, 137.4, 130.9, 128.9, 128.9, 124.0, 123.5, 121.7, 120.5, 120.0, 110.9, 55.2. HRMS (ESI) m/z calcd for $C_{16}H_{15}NO_2Na$ $(M+Na)^+$: 276.0995, found: 276.0995.



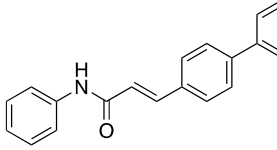
(*E*)-3-(Benzo[d][1,3]dioxol-5-yl)-N-phenylacrylamide (**2.2g**). This was purified by silica-gel column chromatography using ethyl acetate/hexane (20:80) mixture as an eluent. White solid. Yield (69 mg, 52%). MP 157-159 °C. IR (DCM): 3063, 3021, 2944, 2844, 1668, 1603, 1551,

1482, 1313, 951, 705 cm^{-1}. 1H NMR (400 MHz, $CDCl_3$): δ 7.92 (s, 1H), 7.62-7.50 (m, 3H), 7.23 (t, *J* = 7.8 Hz, 2H), 7.02 (t, *J* = 7.3 Hz, 1H), 6.89-6.81 (m, 2H), 6.66 (d, *J* = 8.0 Hz, 1H), 6.36 (d, *J* = 15.4 Hz, 1H), 5.89 (s, 2H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 164.5, 149.2, 148.2, 142.0, 138.2, 129.0, 124.3, 124.2, 120.1, 118.9, 108.5, 106.4, 101.4. HRMS (ESI) m/z calcd for $C_{16}H_{13}NO_3Na$ $(M+Na)^+$: 290.0788, found: 290.0770.

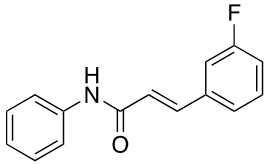
(*E*)-3-(4-(Methylthio)phenyl)-N-phenylacrylamide (**2.2h**). This was purified by silica-gel column chromatography using ethyl acetate/hexane (10:90) mixture as an eluent. White solid. Yield (85 mg, 57%). MP 310-312 °C. IR (DCM): 3302, 2922, 2852, 1664, 1622, 1598, 1546, 1498, 1318, 1093, 754 cm^{-1}. ^1H NMR (700 MHz, $CDCl_3$): δ 7.63 (d, J = 15.7 Hz, 1H), 7.55 (s, 2H), 7.38-7.27 (m, 5H), 7.19-7.14 (m, 2H), 7.05 (s, 1H), 6.43 (d, *J* = 15.7 Hz, 1H), 2.43 (s, 3H). $^{13}C\{^1H\}$ NMR (176 MHz, $CDCl_3$): δ 164.1, 141.8, 141.5, 138.1, 131.2, 129.1, 128.3, 126.1, 124.4, 119.9, 15.2. HRMS (ESI) m/z calcd for $C_{16}H_{16}NOS$ $(M+H)^+$: 270.0947, found: 270.0953.



(*E*)-3-([1,1′-Biphenyl]-4-yl)-N-phenylacrylamide (**2.2i**). This was purified by silica-gel column chromatography using ethyl acetate/hexane (10:90) mixture as an eluent. White solid. Yield (97 mg, 62%). MP 205-207 °C. IR (DCM): 3063, 2944, 2844, 1668, 1603, 1540, 1482, 1313, 951, 705 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.72 (d, *J* = 15.5 Hz, 1H), 7.52 (s, 8H), 7.37 (t, *J* = 6.9 Hz, 3H), 7.29-7.25 (m, 3H), 7.06 (t, *J* = 8 Hz, 1H), 6.52 (d, *J* = 15.5 Hz, 1H). $^{13}C\{^1H\}$ NMR (101 MHz, CD_3OD): δ 165.3, 142.6, 140.9, 140.1, 138.6, 133.8, 128.5, 128.4, 128.1, 127.4, 127.0, 126.5, 123.9, 120.7, 119.8. HRMS (ESI) m/z calcd for $C_{21}H_{17}NONa$ $(M+Na)^+$: 322.1202, found: 322.1194.

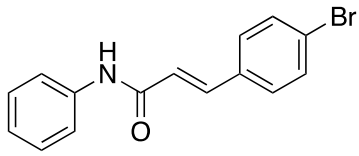


(*E*)-3-(3-Fluorophenyl)-N-phenylacrylamide (**2.2j**). This was purified by silica-gel column chromatography using ethyl acetate/hexane (10:90) mixture as an eluent. White solid. Yield (67 mg, 56%). MP 144-146 °C. IR (DCM):

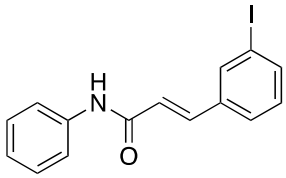


3437, 3029, 2848, 1662, 1628, 1583, 1499, 1443, 1250, 670 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.09 (s, 1H), 7.59 (d, *J* = 15.6 Hz, 3H), 7.23 (t, *J* = 7.9 Hz, 2H), 7.17 (dd, J_1 = 7.8, J_2 = 6.0 Hz, 1H), 7.09 (d, *J* = 7.7 Hz, 1H), 7.03 (dd, J_1 = 6.8, J_2 = 5.1 Hz, 2H), 6.94 (td, J_1 = 8.3, J_2 = 2.1 Hz, 1H), 6.55 (d, *J* = 15.5 Hz, 1H). $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$): δ 164.0, 162.9 (d, *J* = 245 Hz), 140.9, 137.9, 136.8 (d, *J* = 7.7 Hz), 130.3 (d, *J* = 8.3 Hz), 129.1, 124.6, 124.0 (d, *J* = 2.8 Hz), 122.4, 120.2, 116.7 (d, *J* = 21.4 Hz), 114.0 (d, *J* = 21.9 Hz). ^{19}F NMR (377 MHz, $CDCl_3$): δ -131.0. HRMS (ESI) m/z calcd for $C_{15}H_{13}FNO$ $(M+H)^+$: 242.0976, found: 242.0966.

(*E*)-3-(4-Bromophenyl)-N-phenylacrylamide (2.2k).[46] This was purified by silica-gel column chromatography using ethyl acetate/hexane (15:85) mixture as an eluent. White solid. Yield (103 mg, 68%). MP 184-186 °C. IR (DCM): 3033, 2838, 1652, 1558, 1506, 1485, 1326, 972, 743 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.63 (d, *J* = 15.7 Hz, 1H), 7.56 (d, *J* = 6.1 Hz, 1H), 7.45-7.41 (m, 3H), 7.33-7.28 (m, 4H), 7.21 (s, 1H), 7.09 (t, *J* = 7.4 Hz, 1H), 6.49 (d, *J* = 15.7 Hz, 1H). $^{13}C\{^{1}H\}$ NMR (101 MHz, CD_3OD): δ 164.9, 139.9, 138.5, 134.0, 131.8, 129.2, 128.5, 124.0, 123.5, 121.8, 119.8. HRMS (ESI) m/z calcd for $C_{15}H_{13}BrNO$ $(M+H)^+$: 302.0175, found: 302.0164.



(*E*)-3-(3-Iodophenyl)-N-phenylacrylamide (**2.2l**). This was purified by silica-gel column chromatography using ethyl acetate/hexane (15:85) mixture as an eluent. White solid. Yield (71 mg, 42%). MP 124-126 °C. IR (DCM): 3071, 3023, 2952, 2790, 1666, 1599, 1481,1318, 952, 699 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.81 (s, 1H), 7.66-7.43 (m, 4H), 7.39 (d, *J* = 5.3 Hz, 1H), 7.28 (dd, J_1 = 16.4, J_2 = 8.6 Hz, 2H), 7.20 (s, 1H), 7.06 (dt, J_1 = 7.6, J_2 = 6.7 Hz, 2H), 6.49 (d, *J* = 15.5 Hz, 1H). $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$): δ 163.5, 140.7, 138.7, 136.8, 136.4, 130.5, 129.1, 127.4, 124.6, 122.2, 120.0, 94.7. HRMS (ESI) m/z calcd for $C_{15}H_{12}INONa$ $(M+Na)^+$: 371.9856, found: 371.9877.



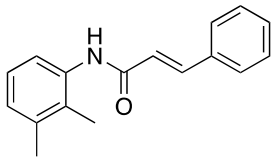
(*E*)-N-Phenyl-3-(4-(trifluoromethyl)phenyl) acrylamide (**2.2m**). This was purified by silica-gel column chromatography using ethyl acetate/hexane (20:80) mixture as an eluent. White solid. Yield (94 mg, 65%). MP 176-178 °C. IR (DCM): 3420, 2926, 2852, 1652, 1595, 1498, 1324, 895, 756 cm^{-1}. ^{1}H NMR (400 MHz, CD_3OD): δ 7.65 (d, J = 8.2 Hz, 2H), 7.58 (dd, J_1 = 15.3 Hz, J_2 = 7.2 Hz, 5H), 7.22 (t, J = 7.9 Hz, 2H), 7.01 (t, J = 7.4 Hz, 1H), 6.79 (d, J = 15.7 Hz, 1H). $^{13}C\{^{1}H\}$ NMR (101 MHz, CD_3OD): δ 164.5, 139.4, 138.6, 138.4, 131.0, 128.5, 127.9, 125.4, 125.4, 124.1, 123.7, 119.8. ^{19}F NMR (377 MHz, $CDCl_3$): δ −62.8. HRMS (ESI) m/z calcd for $C_{16}H_{12}F_3NONa$ $(M+Na)^+$: 314.0763, found: 314.0764.

(*E*)-3-(Furan-2-yl)-N-phenylacrylamide (**2.2n**). This was purified by silica-gel column chromatography using ethyl acetate/hexane (10:90) mixture as an eluent. Yellow solid. Yield (87 mg, 82% (using NaO^tBu as a base), 98 mg, 92% (using Cs_2CO_3 as a base)). MP 123-125 °C. IR (DCM): 3304, 3131, 2923, 2553, 2089, 1667, 1633, 1561, 1387, 883, 748 cm^{-1}. ^{1}H NMR (700 MHz, $CDCl_3$): δ 7.99 (s, 1H), 7.65 (d, J = 5.3 Hz, 2H), 7.53 (d, J = 15.2 Hz, 1H), 7.42 (s, 1H), 7.32 (t, J = 7.8 Hz, 2H), 7.12 (t, J = 7.0 Hz, 1H), 6.57 (d, J = 15.2 Hz, 1H), 6.53 (d, J = 3.2 Hz, 1H), 6.45 (dd, J_1 = 3.3, J_2 = 1.8 Hz, 1H). $^{13}C\{^{1}H\}$ NMR (176 MHz, $CDCl_3$): δ 164.3, 151.2, 144.2, 138.1, 129.0, 128.9, 124.3, 120.1, 118.7, 114.3, 112.2. HRMS (ESI) m/z calcd for $C_{13}H_{11}NO_2$ $(M+H)^+$: 214.0863, found: 214.0865.

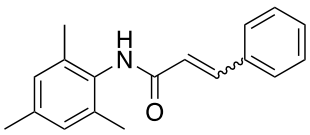
(*E*)-N-Phenyl-3-(thiophen-2-yl)acrylamide (**2.2o**). This was purified by silica-gel column chromatography using ethyl acetate/hexane (10:90) mixture as an eluent. White solid. Alkylated product is observed in 5%. Yield (105 mg, 93%). MP 148-150 °C. IR (DCM): 3413, 3054, 2853, 2790, 1654, 1598, 1543, 1498, 1332, 858, 754 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.57 (s, 1H), 7.72 (d, J = 15.3 Hz, 1H), 7.56 (d, J = 8.0 Hz, 2H), 7.18-7.11 (m, 4H), 6.98-6.93 (m, 2H), 6.83 (dd, J_1 = 5.1 Hz, J_2 = 3.6

Hz, 1H), 6.43 (d, *J* = 15.3 Hz, 1H). $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$): δ 164.6, 139.9, 138.2, 134.7, 130.6, 129.0, 128.0, 127.7, 124.4, 120.4, 120.1. HRMS (ESI) m/z calcd for $C_{13}H_{11}NOSNa$ $(M+Na)^+$: 252.0454, found: 252.0450.

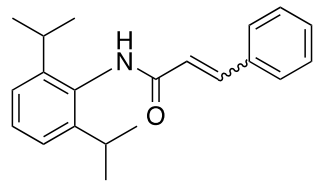
N-(2,3-Dimethylphenyl)cinnamamide (**2.3a**). This was purified by silica-gel column chromatography using ethyl acetate/hexane (10:90) mixture as an eluent. White solid. Yield (83 mg, 66%). MP 186-188 °C. IR (DCM): 3437, 2956, 1655, 1619, 1519, 1446, 1343, 992, 708 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.66 (d, *J* = 15.5 Hz, 1H), 7.42 (s, 3H), 7.28 (s, 4H), 7.02 (t, *J* = 7.6 Hz, 1H), 6.95 (s, 1H), 6.54 (d, *J* = 15.5 Hz, 1H), 2.21 (s, 3H), 2.10 (s, 3H). $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$): δ 164.3, 142.1, 137.4, 135.3, 134.7, 129.8, 128.8, 127.9, 127.6, 125.9, 122.3, 120.8, 20.6, 13.9. HRMS (ESI) m/z calcd for $C_{17}H_{17}NONa$ $(M+Na)^+$: 274.1202, found: 274.1206.



N-Mesitylcinnamamide (**2.3b**). This was purified by silica-gel column chromatography using ethyl acetate/hexane (10:90) mixture as an eluent. White solid. Yield (90 mg, 68%). MP 202-204 °C. IR (DCM): 3442, 2919, 1653, 1623, 1577, 1521, 1457, 1339, 849, 710 cm^{-1}. The ^{1}H and ^{13}C NMR spectra of this compound display two set of signals for alkenyl protons and carbons, respectively, despite the presence of only the *E* product. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.70 (d, *J* = 15.6 Hz, 1H), 7.57 (d, *J* = 15.7 Hz, 1H), 7.48 (s, 1H), 7.36 (dd, J_1 = 6.5, J_2 = 2.8 Hz, 2H), 7.31-7.19 (m, 5H), 6.87 (s, 1H), 6.74 (s, 2H), 6.62 (d, *J* = 15.7 Hz, 1H), 6.10 (d, *J* = 15.6 Hz, 1H), 2.19-2.08 (m, 11H). $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$): δ 164.8, 143.9, 141.6, 136.7, 136.4, 135.1, 134.8, 131.3, 129.9, 129.6, 129.2, 128.8, 128.7, 128.0, 127.9, 120.5, 115.9, 20.9, 18.5, 18.3. HRMS (ESI) m/z calcd for $C_{18}H_{19}NONa$ $(M+Na)^+$: 288.1359, found: 288.1356.

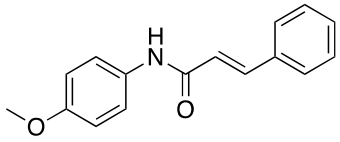


N-(2,6-Diisopropylphenyl)cinnamamide (**2.3c**). This was purified by silica-gel column chromatography using ethyl acetate/hexane (10:90) mixture as an eluent. White solid. Yield



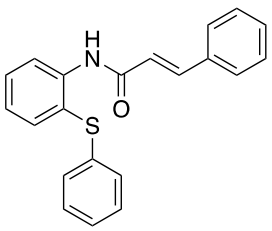
(80 mg, 52%). MP 254-256 °C. IR (DCM): 3445, 3024, 2963, 1659, 1623, 1578, 1528, 1465, 1447, 1360, 987, 725 cm^{-1}. The ^{1}H and ^{13}C NMR spectra of this compound display two set of signals for alkenyl protons and carbons, respectively despite the presence of only *E* product. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.68 (d, *J* = 15.6 Hz, 1H), 7.55 (d, *J* = 15.7 Hz, 1H), 7.48 (d, *J* = 20.8 Hz, 1H), 7.31 (t, *J* = 7.4 Hz, 2H), 7.25 (dd, J_1 = 8.8 Hz, J_2 = 5.1 Hz, 4H), 7.21-7.08 (m, 5H), 6.64 (d, *J* = 15.7 Hz, 1H), 6.10 (d, *J* = 15.7 Hz, 1H), 3.15 (dt, J_1 = 13.7, J_2 = 6.8 Hz, 1H), 3.06 (dt, J_1 = 13.7, J_2 = 6.8 Hz, 2H), 1.11 (s, 6H), 1.11-1.06 (m, 12H). $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$): δ 168.2, 165.6, 147.2, 146.4, 143.8, 141.9, 134.7, 131.3, 131.3, 131.2, 129.9, 129.7, 129.1, 128.7, 128.3, 128.0, 127.9, 123.9, 123.4, 120.2, 116.1, 28.8, 28.5, 24.0, 23.6, 23.0. HRMS (ESI) m/z calcd for $C_{21}H_{25}NONa$ $(M+Na)^{+}$: 330.1828, found: 330.1832.

N-(4-Methoxyphenyl)cinnamamide (**2.3d**). This was purified by silica-gel column



chromatography using ethyl acetate/hexane (15:85) mixture as an eluent. White solid. Yield (80 mg, 63%). MP 139-141 °C. IR (DCM): 3438, 2948, 2830, 1657, 1624, 1549, 1509, 1457, 1360, 830, 779 cm^{-1}. ^{1}H NMR (400 MHz, CD_3OD): δ 7.52 (d, *J* = 15.7 Hz, 1H), 7.46 (dd, J_1 = 7.3 Hz, J_2 = 5.1 Hz, 3H), 7.27 (m, 2H), 6.78 (d, *J* = 9.0 Hz, 2H), 6.65 (d, *J* = 15.7 Hz, 1H), 6.60 (s, 2H), 3.66 (s, 3H). $^{13}C\{^{1}H\}$ NMR (101 MHz, CD_3OD): δ 165.1, 156.8, 140.9, 134.8, 131.5, 129.5, 128.6, 127.5, 121.4, 116.8, 113.6, 54.4. HRMS (ESI) m/z calcd for $C_{16}H_{15}NO_2$ $(M+Na)^{+}$: 276.0995, found: 276.0989.

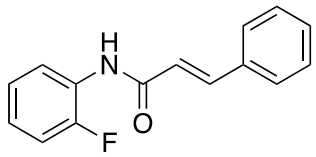
N-(2-(Phenylthio)phenyl)cinnamamide (**2.3e**). This was purified by silica-gel column



chromatography using ethyl acetate/hexane (10:90) mixture as an eluent. Viscous liquid. Yield (33 mg, 20%). IR (DCM): 3350, 3057, 2924, 2849, 2303, 1682, 1629, 1578, 1510, 1477, 1288, 923, 705 cm^{-1}. ^{1}H NMR (700 MHz, $CDCl_3$): δ 8.63-8.38 (m, 3H), 7.56-7.51 (m, 2H), 7.48-7.41 (m, 3H), 7.34-

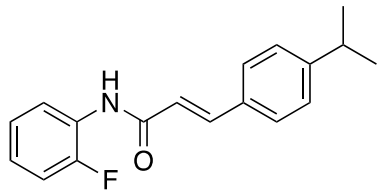
7.27 (m, 3H), 7.20-7.18 (m, 2H), 7.10-7.04 (m, 3H), 6.34 (d, *J* = 15.5 Hz, 1H). $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$): δ 163.9, 142.3, 140.2, 136.6, 135.7, 134.5, 131.1, 130.0, 129.4, 128.8, 128.0, 127.2, 126.4, 124.5, 121.0, 120.9. HRMS (ESI) m/z calcd for $C_{21}H_{17}NOSNa$ $(M+Na)^+$: 354.0923, found: 354.0923.

N-(2-Fluorophenyl)cinnamamide (**2.3f**). This was purified by silicagel column



chromatography using ethyl acetate/hexane (10:90) mixture as an eluent. White solid. Yield (72 mg, 60%). MP 135-137 °C. IR (DCM): 3350, 3048, 2946, 2830, 1664, 1629, 1549, 1501, 1448, 1288, 910, 705 cm^{-1}. ^{1}H NMR (400 MHz, CD_3OD): δ 7.96 (s, 1H), 7.57 (d, *J* = 15.7 Hz, 1H), 7.53-7.42 (m, 2H), 7.33-7.19 (m, 3H), 7.04 (dd, J_1 = 5.7 Hz, J_2 = 2.1 Hz, 3H), 6.81 (d, *J* = 15.7 Hz, 1H). $^{13}C\{^{1}H\}$ NMR (101 MHz, CD_3OD): δ 165.6, 155.1, 142.0, 134.7, 129.7, 128.6, 127.6, 126.0, 125.9, 125.3, 124.0, 123.9, 120.3, 115.0, 114.8. ^{19}F NMR (377 MHz, $CDCl_3$): δ −132.1. HRMS (ESI) m/z calcd for $C_{15}H_{12}FNONa$ $(M+Na)^+$: 264.0795, found: 264.0795.

(*E*)-N-(2-Fluorophenyl)-3-(4-isopropylphenyl)acrylamide (**2.3g**).[45] This was purified by



silica-gel column chromatography using ethyl acetate/hexane (10:90) mixture as an eluent. White solid. Yield (91 mg, 64%). MP 98-100 °C. IR (DCM): 3051, 2948, 2830, 1663, 1624, 1509, 1235, 830, 710 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.39 (t, *J* = 7.5 Hz, 1H), 7.68 (d, *J* = 15.5 Hz, 1H), 7.50 (s, 1H), 7.41 (d, *J* = 8.2 Hz, 2H), 7.20-7.14 (m, 2H), 7.07 (dd, J_1 = 13.2, J_2 = 4.5 Hz, 1H), 7.04-6.94 (m, 2H), 6.48 (d, *J* = 15.5 Hz, 1H), 2.85 (dt, J_1 = 13.8, J_2 = 6.9 Hz, 1H), 1.18 (d, *J* = 6.9 Hz, 6H). $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$): δ 164.1, 151.5, 143.0, 132.1, 128.2, 127.0, 124.7, 124.6, 124.3, 124.2, 121.8, 119.4, 114.8, 114.6, 34.1, 23.8. ^{19}F NMR (377 MHz, $CDCl_3$): δ −131.7. HRMS (ESI) m/z calcd for $C_{18}H_{19}FNO$ $(M+H)^+$: 284.1445, found: 284.1426.

N-(4-Chlorophenyl)cinnamamide (**2.3h**). This was purified by silicagel column chromatography using ethyl acetate/hexane (15:85) mixture as an eluent. White solid. Yield (46 mg, 36%). MP 183-185 °C. IR (DCM): 3441, 3025, 2922, 1659, 1626, 1556, 1505, 1407, 1298, 922, 684 cm^{-1}. ^{1}H NMR (400 MHz, CD_3OD): δ 7.61 (s, 1H), 7.56 (d, *J* = 4.3 Hz, 2H), 7.50 (dd, J_1 = 7.5 Hz, J_2 = 1.8 Hz, 2H), 7.35-7.26 (m, 3H), 7.24-7.18 (m, 2H), 6.67 (d, *J* = 15.7 Hz, 1H). $^{13}C\{^{1}H\}$ NMR (101 MHz, CD_3OD): δ 165.2, 141.7, 137.4, 134.7, 129.7, 128.7, 128.6, 128.6, 128.4, 127.5, 121.0, 120.6. HRMS (ESI) m/z calcd for $C_{15}H_{12}ClNONa$ $(M+Na)^+$: 280.0500, found: 280.0489.

N-(4-Bromophenyl)cinnamamide (**2.3i**). This was purified by silicagel column chromatography using ethyl acetate/hexane (15:85) mixture as an eluent. Compound isolated was mixture of alkenyl (major) and alkylated (minor) products. White solid. Yield (90 mg, 60%). MP 195-197 °C. IR (DCM): 3419, 3023, 2921, 1674, 1645, 1520, 1489, 1418, 977, 710 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.67 (d, *J* = 15.5 Hz, 1H), 7.44 (s, 4H), 7.37 (d, *J* = 8.7 Hz, 2H), 7.31 (dd, J_1 = 8.0, J_2 = 5.0 Hz, 3H), 7.18 (s, 1H), 6.46 (d, *J* = 15.5 Hz, 1H), 2.97 (t, *J* = 7.5 Hz, 2H, alkylated), 2.58 (t, *J* = 7.5 Hz, 2H, alkylated). $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$): δ 164.0, 142.9, 137.1, 134.5, 132.1, 130.2, 128.9, 128.0, 125.0, 121.5, 120.4. HRMS (ESI) m/z calcd for $C_{15}H_{12}BrNONa$ $(M+Na)^+$: 323.9994, found: 323.9985.

(*E*)-N-(2,3-Dimethylphenyl)-3-(4-(trifluoromethyl) phenyl)-acrylamide (**2.3j**). This was purified by silica-gel column chromatography using ethyl acetate/hexane (20:80) mixture as an eluent. White solid. Yield (113 mg, 71%). MP 230-232 °C. IR (DCM): 3437, 2956, 2854, 1655, 1625, 1510, 1440, 1343, 991, 756 cm^{-1}. ^{1}H NMR (400 MHz, CD_3OD): δ 7.83 (d, *J* = 8.1 Hz, 2H), 7.75-7.71 (m, 3H), 7.23 (d, *J* = 6.7 Hz, 1H), 7.15-7.10 (m, 2H), 7.01 (d, *J* = 15.8 Hz, 1H), 2.34 (s, 3H), 2.21 (s, 3H). $^{13}C\{^{1}H\}$ NMR (101 MHz, CD_3OD): δ 165.3, 139.4, 138.7,

138.4, 137.4, 135.1, 131.7, 131.0, 130.7, 128.0, 127.8, 125.5, 125.4, 125.3, 123.5, 123.3, 19.1, 12.9. ^{19}F NMR (377 MHz, $CDCl_3$): δ −62.8. HRMS (ESI) m/z calcd for $C_{18}H_{16}F_3ON$ $(M+H)^+$: 320.1245, found: 320.1257.

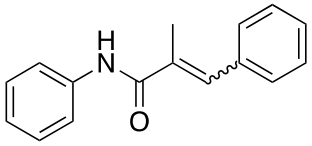
N,2,3-Triphenylacrylamide (**2.3k**). This was purified by silica-gel column chromatography using ethyl acetate/hexane (5:95) mixture as an eluent. White solid. Yield (65 mg, 43%). MP 142-144 °C. IR (DCM): 3420, 3047, 2926, 2852, 1652, 1598, 1510, 1324, 913, 712 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.90 (s, 1H), 7.47-7.40 (m, 3H), 7.37 (d, *J* = 7.8 Hz, 3H), 7.31-7.27 (m, 1H), 7.27-7.25 (m, 1H), 7.24-7.18 (m, 3H), 7.16-7.04 (m, 5H), 7.04-6.98 (m, 1H), 6.98-6.92 (m, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ 165.0, 138.2, 137.8, 135.8, 134.8, 134.6, 130.5, 130.0, 129.9, 129.0, 128.9, 128.8, 128.2, 124.4, 119.9. HRMS (ESI) m/z calcd for $C_{21}H_{17}NONa$ $(M+Na)^+$: 322.1202, found: 322.1190.

N,2-Diphenyl-3-(4-(trifluoromethyl)phenyl) acrylamide (**2.3l**). This was purified by silica-gel column chromatography using ethyl acetate/ hexane (5:95) mixture as an eluent. White solid. Yield (75 mg, 41%). MP 215-217 °C. IR (DCM): 3442, 2919, 1653, 1623, 1577, 1521, 1456, 1339, 892, 712 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.47-7.39 (m, 6H), 7.28-7.21 (m,5H), 7.16 (t, *J* = 7.9 Hz, 3H), 6.98 (t, *J* = 7.4 Hz, 1H), 6.90 (s, 1H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ 167.3, 140.2, 138.6, 137.3, 136.4, 129.1, 129.0, 128.9, 128.8, 127.6, 126.5, 125.6, 125.1, 120.2. ^{19}F NMR (377 MHz, $CDCl_3$): δ −62.7. HRMS (ESI) m/z calcd for $C_{22}H_{17}F_3NO$ $(M+H)^+$: 368.1257, found: 368.1271.

3-(Naphthalen-1-yl)-N,2-diphenylacrylamide (**2.3m**). This was purified by silica-gel column chromatography using ethyl acetate/ hexane (5:95) mixture as an eluent. White solid. Yield (68 mg, 43%). MP 172-174 °C. IR (DCM): 3063, 3021, 2944, 2844, 1668, 1603, 1547, 1482, 1313, 895, 707 cm^{-1}. ^{1}H

NMR (400 MHz, $CDCl_3$): δ 8.50 (s, 1H), 8.08 (d, *J* = 8.3 Hz, 1H), 7.79-7.67 (m, 1H), 7.59 (d, *J* = 8.2 Hz, 1H), 7.49-7.36 (m, 5H), 7.26-7.19 (m, 6H), 7.19-7.12 (m, 2H), 7.08-6.97 (m, 2H), 6.84 (d, *J* = 7.2 Hz, 1H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 165.1, 137.8, 137.5, 136.6, 135.4, 133.3, 132.5, 132.2, 130.3, 129.3, 129.0, 128.6, 128.6, 127.7, 126.5, 126.0, 125.0, 124.6, 124.4, 119.9. HRMS (ESI) m/z calcd for $C_{25}H_{19}NONa$ $(M+Na)^+$: 372.1359, found: 372.1366.

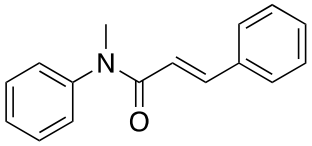
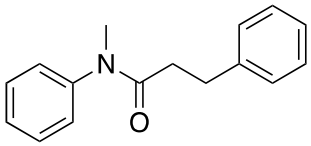
(*E*)-2-Methyl-N,3-diphenylacrylamide (**2.3n**). This was purified by silica-gel column chromatography using ethyl acetate/hexane (10:90) mixture as an eluent. Compound isolated was mixture of cis (minor) and trans (major) isomers. White solid. Yield (28 mg, 24%). MP 97-99 °C. IR (DCM): 3437, 2956, 2877, 1655, 1619, 1519, 1446, 1343, 910, 708 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.53 (d, *J* = 7.7 Hz, 3H), 7.35-7.31 (m, 5H), 7.29-7.21 (m, 4H), 7.19-7.14 (m, 1H), 7.06 (t, *J* = 7.4 Hz, 1H), 6.61 (s, 1H, cis isomer), 2.14 (s, 3H, trans isomer), 2.11 (s, 3H, cis isomer). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 167.8, 138.0, 135.8, 134.3, 132.9, 129.4, 129.1, 128.6, 128.4, 128.1, 127.0, 124.4, 120.3, 14.4. HRMS (ESI) m/z calcd for $C_{16}H_{16}NO$ $(M+H)^+$: 238.1226, found: 238.1230.



General Procedure for Derivatization of *α*-Alkenyl Amides. To a Schlenk flask (25 mL) equipped with a stir bar, catalyst **1** (2 mol %), NaO^tBu (1 equiv), 2-fluoro acetanilide (0.5 mmol), aryl alcohol (0.6 mmol), and tert-amyl alcohol were added under nitrogen atmosphere in a glovebox. The reaction mixture was taken out of the glovebox, equipped with a condenser, and the solution heated at 135 °C (oil bath temperature) with stirring in an open system under nitrogen flow for 24 h. Then, methanol was added to the reaction mixture under nitrogen flow and further stirred for 3 h. The reaction mixture was transferred to an RB flask, and the solvent was evaporated under reduced pressure. The solvent was removed under reduced pressure; the reaction mixture was dissolved in chloroform and washed with water and brine. The collected organic layer was dried over anhydrous sodium sulfate and concentrated in a vacuum. The

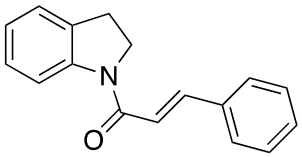
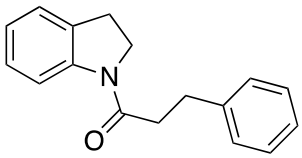
resultant residue was purified by silica gel (100−200 mesh) column chromatography using ethyl acetate/hexane mixture as eluent. Yields were calculated for isolated products.

N-Methyl-N-phenylcinnamamide (**2.3a**) and **N-methyl-N,3-diphenylpropanamide** (**2.3a′**).

These were purified by silica-gel column chromatography using ethyl acetate/hexane (10:90) mixture as an eluent. Viscous liquids. Yield (86 mg, 73%). IR (DCM): 2951, 2823, 1663, 1610, 1540, 1416, 1343, 895, 708 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.60 (d, *J* = 15.5 Hz, 1H), 7.41-7.32 (m, 2H), 7.34-7.23 (m, 3H), 7.21 (m, 6H), 7.16 (dd, J_1 = 7.2 Hz, J_2 = 2.1 Hz, 3H), 6.29 (d, *J* = 15.3 Hz, 1H), 3.34 (s, 3H), 3.17 (s, 3H, alkylated), 2.83 (t, *J* = 7.9 Hz, 2H, alkylated), 2.29 (t, *J* = 8.0 Hz, 2H, alkylated). $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$): δ 166.2, 143.6, 141.7, 135.2, 129.7, 129.6, 129.5, 128.7, 128.5, 128.4, 128.3, 127.8, 127.8, 127.6, 127.3, 127.0, 126.0, 118.8, 37.6, 36.0, 31.8. HRMS (ESI) m/z calcd for $C_{16}H_{15}NONa$ $(M+Na)^+$: 260.1046, found: 260.1039.

(*E*)-1-(Indolin-1-yl)-3-phenylprop-2-en-1-one (**2.3b**) and **1-(Indolin-1-yl)-3-phenylpropan-1-one** (**2.3b′**). These were purified by silicagel column chromatography using ethyl acetate/hexane (10:90) mixture as an eluent. White solids. Yield (70 mg, 57%). MP 107-109 °C. IR (DCM): 2977, 2856, 1651, 1607, 1590, 1479, 1351, 991, 910, 708 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.27 (s, 1H), 8.18 (d, *J* = 8.1 Hz, 1H), 7.73 (d, *J* = 15.4 Hz, 1H), 7.53-7.41 (m, 2H), 7.34-7.25 (m, 3H), 7.25-7.15 (m, 2H), 7.14-7.01 (m, 3H), 6.99-6.86 (m, 2H), 6.75 (d, *J* = 14.4 Hz, 1H), 4.14 (t, *J* = 8.5 Hz, 2H), 3.84 (t, *J* = 8.5 Hz, 1H), 3.14 (d, *J* = 22.3 Hz, 2H), 3.06-2.91 (m, 2H), 2.67-2.56 (m, 1H). $^{13}C\{^{1}H\}$ (101 MHz, $CDCl_3$): δ 170.3, 164.2, 143.2, 141.2, 135.0, 129.9, 128.8, 128.5, 128.4, 127.9, 127.5, 127.5, 126.1, 124.5, 123.8, 123.5, 118.9, 117.5, 116.9, 47.8, 37.8, 30.7, 27.9. HRMS (ESI) m/z calcd for $C_{17}H_{16}NO$ $(M+H)^+$: 250.1226, found: 250.1224.

N-(2-Methoxyphenyl)cinnamamide (**2.4a**). This was purified by silica-gel column chromatography using ethyl acetate/hexane (15:85) mixture as an eluent. White solid. Yield (76 mg, 66%). MP 135-137 °C. IR (DCM): 3441, 3025, 2922, 1659, 1626, 1505, 1407, 991, 698 cm^{-1}. ^{1}H NMR (700 MHz, $CDCl_3$): δ 8.44 (s, 1H), 7.66 (d, *J* = 15.5 Hz, 1H), 7.48 (d, *J* = 7.0 Hz, 2H), 7.30 (dd, J_1 = 15.3, J_2 = 7.7 Hz, 3H), 7.17 (s, 1H), 6.98 (t, *J* = 7.6 Hz, 1H), 6.91 (t, *J* = 7.6 Hz, 1H), 6.82 (d, *J* = 8.0 Hz, 1H), 6.50 (d, *J* = 15.5 Hz, 1H), 3.83 (s, 3H). $^{13}C\{^{1}H\}$ NMR (101 MHz, CD_3OD): δ 165.6, 149.9, 141.3, 135.3, 129.5, 128.6, 128.0, 127.6, 124.8, 121.7, 121.0, 120.1, 110.3, 54.8. HRMS (ESI) m/z calcd for $C_{16}H_{16}NO_2$ $(M+H)^+$: 254.1176, found: 254.1189.

(*E*)-3-(4-Isopropylphenyl)-N-(2-methoxyphenyl) acrylamide (**2.4b**). This was purified by silica-gel column chromatography using ethyl acetate/hexane (15:85) mixture as an eluent. White solid. Yield (97 mg, 66%). MP 122-124 °C. IR (DCM): 3443, 3028, 2934, 1662, 1618, 1510, 1399, 983, 704 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.47 (d, *J* = 7.2 Hz, 1H), 7.89 (s, 1H), 7.66 (d, *J* = 15.5 Hz, 1H), 7.43 (d, *J* = 8.2 Hz, 2H), 7.18 (d, *J* = 8.0 Hz, 2H), 6.96 (dtd, J_1 = 25.3 Hz, J_2 = 7.7 Hz, J_3 = 1.5 Hz, 2H), 6.83 (dd, J_1 = 8.0, J_2 = 1.3 Hz, 1H), 6.49 (d, *J* = 15.5 Hz, 1H), 3.85 (s, 3H), 2.87 (dt, J_1 = 13.8 Hz, J_2 = 6.9 Hz, 1H), 1.20 (d, *J* = 6.9 Hz, 6H). $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$): δ 163.9, 151.1, 147.8, 142.0, 132.4, 128.1, 127.9, 126.9, 123.7, 121.2, 120.3, 120.0, 109.9, 55.7, 34.0, 23.8. HRMS (ESI) m/z calcd for $C_{19}H_{21}NO_2$ $(M)^+$: 296.1645, found: 296.1658.

Procedure for Mechanistic Studies. Reaction of Acetanilide with Benzaldehyde without Catalyst 1. To a Schlenk flask (25 mL) equipped with a stir bar, NaO^{t}Bu (1 equiv), acetanilide (0.5 mmol), benzaldehyde (0.6 mmol), and tert-amyl alcohol (2 mL) were added under nitrogen atmosphere in a glovebox. The reaction mixture was taken out of the glovebox and heated at 135 °C for 24 h. The reaction mixture was transferred to an RB flask. The solvent was removed

under reduced pressure; the reaction mixture was dissolved in chloroform and washed with water and brine. The resultant residue was purified by silica gel (100−200 mesh) column chromatography using ethyl acetate/hexane mixture as eluent. Yield was calculated for the isolated product.

Reaction of Acetanilide with Benzaldehyde with Catalyst 1. To a Schlenk flask (25 mL) equipped with a stir bar, catalyst **1** (2 mol %), NaO^{t}Bu (1 equiv), acetanilide (0.5 mmol), benzaldehyde (0.6 mmol), and tert-amyl alcohol (2 mL) were added under nitrogen atmosphere in a glovebox. The reaction mixture was taken out of the glovebox, equipped with a condenser, and the solution heated at 135 °C (oil bath temperature) with stirring in an open system under nitrogen flow for 24 h. Further workup and isolation were carried out as per the general procedure.

Reaction of Acetanilide with Benzyl Alcohol-d3. To a Schlenk flask (25 mL) charged with a magnetic stir bar, catalyst **1** (2 mol %), NaO^{t}Bu (1 equiv), acetanilide (0.5 mmol), benzyl alcohol-d3 (0.6 mmol), and tert-amyl alcohol (2 mL) were added under nitrogen atmosphere in a glovebox. The reaction mixture was taken out of the glovebox, equipped with a condenser, and the solution heated at 135 °C (oil bath temperature) with stirring in an open system under nitrogen flow for 24 h. Further workup and isolation were carried out as per the general procedure.

Reaction of Acetanilide-d3 with Benzyl Alcohol. To a Schlenk flask (25 mL) charged with a magnetic stir bar, catalyst **1** (2 mol %), NaO^{t}Bu (1 equiv), acetanilide-d3 (0.5 mmol), benzyl alcohol (0.6 mmol), and toluene (2 mL) were added under nitrogen atmosphere in a glovebox. Toluene was chosen as a solvent as the deuterated acetanilide exhibited H/D exchange with tert-amyl alcohol. The reaction mixture was taken out of the glovebox, equipped with a condenser, and the solution heated at 135 °C (oil bath temperature) with stirring in an open

system under nitrogen flow for 24 h. Further workup and isolation were carried out as per the general procedure.

Reaction of Acetanilide-d3 with Benzyl Alcohol-d3. To a Schlenk flask (25 mL) charged with a magnetic stir bar, catalyst **1** (2 mol %), NaO^{t}Bu (1 equiv), acetanilide-d3 (0.5 mmol), benzyl alcohol-d3 (0.6 mmol), and toluene (2 mL) were added under nitrogen atmosphere in a glovebox. Toluene was chosen as a solvent as the deuterated acetanilide exhibited H/D exchange with tert-amyl alcohol. The reaction mixture was taken out of the glovebox, equipped with a condenser, and the solution heated at 135 °C (oil bath temperature) with stirring in an open system under nitrogen flow for 24 h. Further workup and isolation were carried out as per the general procedure.

X-ray Analysis of *α*-Alkenyl Amide Products 2.1m, 2.1n, and 2.2l. Crystals suited for single crystal X-ray diffraction measurements were mounted on a glass fiber. Geometry and intensity data were collected with a Rigaku Smartlab X-ray diffractometer equipped with graphitemonochromated Cu Kα radiation (λ = 1.54184 Å, multilayer optics). Intensities were integrated with SAINT+47 and corrected for absorption with SADABS.48 The structures were solved by direct methods and refined on F2 with SHELXL-9749 using Olex-250 software.

Crystal Data of *α*-Alkenyl Amide Product 2.1m. $C_{16}H_{12}F_3NO$, white solid, M = 291.27 g/mol, orthorhombic with space group $P2_12_12_1$, a = 16.9998(3) Å, b = 10.00910(10) Å, c = 8.18750(10) Å, α = 90°, β = 90°, γ = 90°, V = 1393.13 (3) Å^3, Z = 4, F(000) = 600, μ- (Cu Kα) = 0.981 mm^{-1}, $2\theta_{max}$ = 77.2200, ρ_{calcd} = 1.389 g/cm^3, T = 293(2) K, 9610 Reflections collected, 8986 unique, R_1 = 0.0479, WR_2 = 0.1422 (all data). The structure has been deposited at the CCDC data center and can be retrieved using the deposit number **CCDC 2038569**.

Crystal Data of *α*-Alkenyl Amide Product 2.1n. $C_{13}H_{11}NO_2$, white solid, M = 213.23 g/mol, orthorhombic with space group P121/n1, a = 10.6354(6) Å, b = 8.8279(6) Å, c = 24.4301(15) Å, α = 90°, β = 90°, γ = 90°, V = 2293.72 (2) Å^3, Z = 8, F(000) = 898.78, μ-(Cu Kα) = 0.683

mm^{-1}, $2\theta_{max}$ = 77.2200, ρ_{calcd} = 1.235 g/cm^3, T = 100.00(12) K, 1883 Reflections collected, 1484 unique, R_1 = 0.0634, WR_2 = 0.1654 (all data). The structure has been deposited at the CCDC data center and can be retrieved using the deposit number **CCDC 2038570**.

Crystal Data of *α*-Alkenyl Amide Product 2.2l. $C_{22}H_{16}F_3NO$, white solid, M = 367.36 g/mol, orthorhombic with space group P_{bca}, a = 8.62490(1) Å, b = 17.4341(2) Å, c = 23.5971(3) Å, α = 90°, β = 90°, γ = 90°, V = 3548.23 (7) $Å^3$, Z = 8, F(000) = 1520, μ-(Cu Kα) = 0.776 mm^{-1}, $2\theta_{max}$ = 79.4100, ρ_{calcd} = 1.375 g/cm^3, T = 100.00(12) K, 9610 Reflections collected, 15971 unique, R_1 = 0.0477, WR_2 = 0.1369 (all data). The structure has been deposited at the CCDC data center and can be retrieved using the deposit number **CCDC 2038571**.

2.6.NOTES AND REFERENCES

(1) (a) Takeda, T., Ed. *Modern Carbonyl Olefination: Methods and Applications*; Wiley-VCH, 2006. (b) Wang, J., Ed. *Stereoselective Alkene Synthesis*; Springer-Verlag: Berlin, 2012.

(2) (a) Blakemore, P. R.; Sephton, S. M.; Ciganek, E. The Julia- Kocienski Olefination. *Org. React*. **2018**, *95*, 1-422. (b) van Staden, L. F.; Gravestock, D.; Ager, D. J. New Developments in the Peterson Olefination Reaction. *Chem. Soc. Rev*. **2002**, *31*, 195-200. (c) Maryanoff, B. E.; Reitz, A. B. The Wittig Olefination Reaction and Modifications Involving Phosphoryl-Stabilized Carbanions. Stereochemistry, Mechanism, and Selected Synthetic Aspects. *Chem. Rev*. **1989**, *89*, 863-927. (d) McMurry, J. E. Carbonyl-Coupling Reactions Using Low-Valent Titanium. *Chem. Rev*. **1989**, *89*, 1513-1524.

(3) Mahrwald, R., Ed. *Modern Aldol Reactions*; Wiley-VCH: Weinheim, Germany, 2004.

(4) (a) Pattabiraman, V. J.; Bode, J. W. Rethinking Amide Bond Synthesis. *Nature* **2011**, *480*, 471−479. (b) Valeur, E.; Bradley, M. Amide Bond Formation: Beyond the Myth of Coupling Reagents. *Chem. Soc. Rev*. **2009**, *38*, 606-631. (c) Montalbetti, C. A. G.

N.; Falque, V. Amide Bond Formation and Peptide Coupling. *Tetrahedron* **2005**, *61*, 10827-10852. (d) Pearson, A. J.; Roush, W. R., Eds. *Handbook of Reagents for Organic Synthesis: Activating Agents and Protecting Groups*; Wiley-VCH: New York, 1999.

(5) (a) Hansen, J. H.; Parr, B. T.; Pelphrey, P.; Jin, Q.; Autschbach, J.; Davies, H. M. L. Rhodium(II)-Catalyzed Cross-Coupling of Diazo Compounds. *Angew. Chem., Int. Ed.* **2011**, *50*, 2544-2548. (b) Vougioukalakis, G. C.; Grubbs, R. H. Ruthenium-Based Heterocyclic Carbene-Coordinated Olefin Metathesis Catalysts. *Chem. Rev*. **2010**, *110*, 1746-1787. (c) Hoveyda, A. H.; Zhugralin, A. R. The Remarkable Metal-Catalysed Olefin Metathesis Reaction. *Nature* **2007**, *450*, 243-251.

(6) (a) Fu, P.; Johnson, M.; Chen, H.; Posner, B. A.; MacMillan, J. B. Carpatamides A-C, Cytotoxic Arylamine Derivatives from a Marine-Derived Streptomyces sp. *J. Nat. Prod*. **2014**, *77*, 1245-1248. (b) Mu, X.; Wu, T.; Wang, H.-Y.; Guo, Y.-L.; Liu, G. S. Palladium- Catalyzed Oxidative Aryltrifluoromethylation of Activated Alkenes at Room Temperature. *J. Am. Chem. Soc*. **2012**, *134*, 878-881. (c) Buchanan, M. S.; Carroll, A. R.; Addepalli, R.; Avery, V. M.; Hooper, J. N. A.; Quinn, R. J. Psammaplysenes C and D, Cytotoxic Alkaloids from Psammoclemma sp. *J. Nat. Prod.* **2007**, *70*, 1827-1829. (d) Viswanadhan, V. N.; Sun, Y. X.; Norman, M. H. Three-Dimensional Quantitative Structure-Activity Relationships and Activity Predictions of Human TRPV1 Channel Antagonists: Comparative Molecular Field Analysis and Comparative Molecular Similarity Index Analysis of Cinnamides. *J. Med. Chem*. **2007**, *50*, 5608-5619. (e) Greenberg, A.; Breneman, C. M.; Liebman, J. F., Eds.; *The Amide Linkage: Selected Structural Aspects in Chemistry, Biochemistry and Materials Science*; Wiley-VCH: New York, 2000. (f) Putt, K. S.; Nesterenko, V.; Dothager, R. S.; Hergenrother, P. J. The Compound 13-D Selectively Induces Apoptosis in White Blood Cancers versus Other Cancer Cell Types. *ChemBioChem* **2006**, *7*, 1916-1922.

(7) (a) Gehringer, M.; Laufer, S. A. Emerging and Re-Emerging Warheads for Targeted Covalent Inhibitors: Applications in Medicinal Chemistry and Chemical Biology. *J. Med. Chem.* **2019**, *62*, 5673-5724. (b) Avalos-Alanís, F.; Hernández-Fernández, E.; Carranza- Rosales, P.; López-Cortina, S.; Hernández-Fernández, J.; Ordóñez, M.; Guzmán-Delgado, N.; Morales-Vargas, A.; Velázquez-Moreno, V.; Santiago-Mauricio, M. Synthesis, Antimycobacterial and Cytotoxic Activity of α,β-Unsaturated Amides and 2,4-Disubstituted Oxazoline Derivatives. *Bioorg. Med. Chem. Lett*. **2017**, *27*, 821-825. (c) Shi, Z.- H.; Li, N.-G.; Shi, Q.-P.; Tang, H.; Tang, Y.-P.; Li, W.; Yin, L.; Yang, J.-P.; Duan, J.-A. Synthesis and Structure−Activity Relationship Analysis of Caffeic Acid Amides as Selective Matrix Metalloproteinase Inhibitors. *Bioorg. Med. Chem. Lett*. **2013**, *23*, 1206-1211. (d) Collins, F. W. In *Oats: Chemistry and Technology*, 2nd ed., Webster, F. H.; Wood, P. J., Eds.; AACC International: St. Paul, MN, 2011; pp 157-217. (e) Fu, J.; Cheng, K.; Zhang, Z.-M.; Fang, R.-Q.; Zhu, H.-L. Synthesis, Structure and Structure−Activity Relationship Analysis of Caffeic Acid Amides as Potential Antimicrobials. *Eur. J. Med. Chem*. **2010**, *45*, 2638-2643. (f) Bryngelsson, S.; Dimberg, L. H.; Kamal- Eldin, A. Effects of Commercial Processing on Levels of Antioxidants in Oats (Avena Sativa L.). *J. Agric. Food Chem*. **2002**, *50*, 1890-1896. (g) Collins, F. W. Oat Phenolics: Avenanthramides, Novel Substituted N-Cinnamoylanthranilate Alkaloids from Oat Groats and Hulls. *J. Agric. Food Chem*. **1989**, *37*, 60-66.

(8) (a) Liu, K.; Sui, L.-C.; Jin, Q.; Li, D.-Y.; Liu, P.-N. CuBr- Mediated Radical Cascade Difluoro acetamidation of Acrylamides using α,α-Difluoro-α-(TMS)-acetamides. *Org. Chem. Front*. **2017**, *4*, 1606-1610. (b) Zhang, M.; Kumagai, N.; Shibasaki, M. α,β - Unsaturated Amides as Dipolarophiles: Catalytic Asymmetric exo- Selective 1,3-Dipolar Cycloaddition with Nitrones. *Chem. - Eur. J*. **2017**, *23*, 12450-12455. (c)

Zhang, H.; Gu, Z.; Li, Z.; Pan, C.; Li, W.; Hu, H.; Zhu, C. Silver-Catalyzed Cascade Radical Cyclization: A Direct Approach to 3,4-Disubstituted Dihydroquinolin-2(1H)-ones through Activation of the P−H Bond and Functionalization of the C(sp2)−H Bond. *J. Org. Chem*. **2016**, *81*, 2122-2127. (d) Aihara, Y.; Chatani, N. Nickel Catalyzed Direct Alkylation of C-H Bonds in Benzamides and Acrylamides with Functionalized Alkyl Halides via Bidentate-Chelation Assistance. *J. Am. Chem. Soc*. **2013**, *135*, 5308-5311. (e) Ueda, S.; Okada, T.; Nagasawa, H. Oxindole Synthesis by Palladium-Catalysed Aromatic C-H Alkenylation. *Chem. Commun*. **2010**, *46*, 2462-2464. (f) Fan, J.-H.; Wei, W.-T.; Zhou, M.-B.; Song, R.-J.; Li, J.-H. Palladium-Catalyzed Oxidative Difunctionalization of Alkenes with α-Carbonyl Alkyl Bromides Initiated through a Hecktype Insertion: A Route to Indolin-2-ones. *Angew. Chem., Int. Ed*. **2014**, *53*, 6650-6654.

(9) (a) Caulfield, M. J.; Qiao, G. G.; Solomon, D. H. Some Aspects of the Properties and Degradation of Polyacrylamides. *Chem. Rev*. **2002**, *102*, 3067-3083. (b) Shiohara, K.; Habaue, S.; Okamoto, Y. Asymmetric Anionic Polymerization of Alkyl-Substituted N,NDiphenylacrylamide Derivatives. *Polym. J*. **1998**, *30*, 249-255.

(10) (a) Ojeda-Porras, A.; Gamba-Sańchez, D. Recent Developments in Amide Synthesis using Nonactivated Starting Materials. *J. Org. Chem*. **2016**, *81*, 11548-11555. (b) de Figueiredo, R. M.; Suppo, J.-S.; Campagne, J.-M. Nonclassical Routes for Amide Bond Formation. *Chem. Rev*. **2016**, *116*, 12029-12122. (c) Lundberg, H.; Tinnis, F.; Selander, N.; Adolfsson, H. Catalytic Amide Formation from Non- Activated Carboxylic Acids and Amines. *Chem. Soc. Rev*. **2014**, *43*, 2714-2742. (d) Bode, J. W. Reinventing Amide Bond Formation. *Top. Organomet. Chem*. **2012**, *44*, 13-34. (e) Allen, C. L.; Williams, J. M. Metal- Catalysed Approaches to Amide Bond Formation. *Chem. Soc. Rev*. **2011**, *40*, 3405-3415. (f) Valeur, E.; Bradley, M. Amide Bond Formation: Beyond the Myth of

Coupling Reagents. *Chem. Soc. Rev*. **2009**, *38*, 606-631. (g) Montalbetti, C. A. G. N.; Falque, V. Amide Bond Formation and Peptide Coupling. *Tetrahedron* **2005**, *61*, 10827-10852.

(11) (a) Jackson, P.; Widen, J. C.; Harki, D. A.; Brummond, K. M. Covalent Modifiers: A Chemical Perspective on the Reactivity of α,β- Unsaturated Carbonyls with Thiols via Hetero-Michael Addition Reactions. *J. Med. Chem*. **2017**, *60*, 839-885. (b) Concellon, J. M.; Rodriguez-Solla, H.; Diaz, P. Sequential Reactions Promoted by Manganese: Completely Stereoselective Synthesis of (E)-α,β -Unsaturated Amides, Ketones, Aldehydes, and Carboxylic Acids. *J. Org. Chem*. **2007**, *72*, 7974-7979. (c) Kojima, S.; Inai, H.; Hidaka, T.; Ohkata, K. Highly Z-Selective Synthesis of α,β-Unsaturated Amides with the Peterson Reaction between α-Silylamides and Aldehydes. *Chem. Commun*. **2000**, 1795-1796.

(12) Uenoyama, Y.; Fukuyama, T.; Nobuta, O.; Matsubara, H.; Ryu, I. Alkyne Carbonylation by Radicals: Tin-Radical-Catalyzed Synthesis of α-Methylene Amides from 1-Alkynes, Carbon Monoxide, and Amines. *Angew. Chem., Int. Ed*. **2005**, *44*, 1075-1078.

(13) Wang, D.; Guo, W.; Zhou, Q.; Liu, L.; Lu, Y.; Liu, Y. Hydroaminocarbonylation of Alkynes to Produce Primary α,β -Unsaturated Amides Using NH_4HCO_3 Dually as Ammonia Surrogate and Brønsted Acid Additive. *ChemCatChem* **2018**, *10*, 4264-4268.

(14) Sha, F.; Alper, H. Ligand- and Additive-Controlled Pd- Catalyzed Aminocarbonylation of Alkynes with Aminophenols: Highly Chemo- and Regioselective Synthesis of α,β-Unsaturated Amides. *ACS Catal*. **2017**, *7*, 2220-2229.

(15) Huang, Z.; Dong, Y.; Li, Y.; Makha, M.; Li, Y. Enhancing Ligand-Free Fe-Catalyzed Aminocarbonylation of Alkynes by ZrF_4. *ChemCatChem* **2019**, *11*, 5236-5240.

(16) Shi, R.; Zhang, H.; Lu, L.; Gan, P.; Sha, Y.; Zhang, H.; Liu, Q.; Beller, M.; Lei, A. (E)-α,β -Unsaturated Amides from Tertiary Amines, Olefins and CO via Pd/Cu-Catalyzed Aerobic Oxidative Ndealkylation. *Chem. Commun*. **2015**, *51*, 3247-3250.

(17) Peng, J.-B.; Geng, H.-Q.; Li, D.; Qi, X.; Ying, J.; Wu, X.-F. Palladium-Catalyzed Carbonylative Synthesis of α,β Unsaturated Amides from Styrenes and Nitroarenes. *Org. Lett*. **2018**, *20*, 4988-4993.

(18) (a) Chen, M.; Dong, G. Direct Catalytic Desaturation of Lactams Enabled by Soft Enolization. *J. Am. Chem. Soc*. **2017**, *139*, 7757-7760. (b) Teskey, C. J.; Adler, P.; Goncalves, C. R.; Maulide, N. Chemoselective α,β-Dehydrogenation of Saturated Amides. *Angew. Chem., Int. Ed*. **2019**, *58*, 447-451. (c) Chen, Y.; Turlik, A.; Newhouse, T. R. Amide α,β-Dehydrogenation Using Allyl-Palladium Catalysis and a Hindered Monodentate Anilide. *J. Am. Chem. Soc*. **2016**, *138*, 1166-1169.

(19) (a) Song, X.-R.; Song, B.; Qiu, Y.-F.; Han, Y.-P.; Qiu, Z.-H.; Hao, X.-H.; Liu, X.-Y.; Liang, Y.-M. TMSCl-Mediated Synthesis of α,β-Unsaturated Amides via C−C Bond Cleavage and C−N Bond Formation of Propargyl Alcohols with Trimethylsilyl Azide. *J. Org. Chem*. **2014**, *79*, 7616-7625. (b) Lu, M.; Lin, Z.; Chen, S.; Chen, H.; Huang, M.; Cai, S. Visible-Light-Enabled Oxidative Coupling of Alkenes with Dialkylformamides To Access Unsaturated Amides. *Org. Lett*. **2019**, *21*, 9929-9933.

(20) (a) Concelloń, J. M.; Rodríguez-Solla, H.; Concelloń, C.; Simal, C.; Alvaredo, N. Sequential Synthesis of (E)-α,β-Unsaturated Primary Amides with Complete Stereoselectivity. *J. Org. Chem*. **2010**, *75*, 3451-3453. (b) Hadden, M. K.; Blagg, B. S. J. Synthesis and Evaluation of Radamide Analogues, A Chimera of Radicicol and Geldanamycin. *J. Org. Chem*. **2009**, *74*, 4697-4704. (c) Feuillet, F. J. P.; Cheeseman, M.; Mahon, M. F.; Bull, S. D. Stereoselective Synthesis of (E)-Trisubstituted α,β-Unsaturated Amides and Acids. *Org. Biomol. Chem*. **2005**, *3*, 2976-2989. (d) Kim, S.;

Lim, C. J. Radical-Mediated γ-Functionalizations of α,β-Unsaturated Carboxylic Amides. *Angew. Chem., Int. Ed*. **2004**, *43*, 5378-5380. (e) Han, S.-Y.; Kim, Y.-A. Recent Development of Peptide Coupling Reagents in Organic Synthesis. *Tetrahedron* **2004**, *60*, 2447-2467. (f) Chiacchio, U.; Rescifina, A.; Chiacchio, M. A.; Romeo, G.; Romeo, R. New Rearrangement of 4-Isoxazoline System: Conversion of Ketones into α,β-Unsaturated Amides. *J. Org. Chem*. **2003**, *68*, 3718-3720. (g) Concelloń, J. M.; Bardales, E. Synthesis of Aromatic (E)- or (Z)-α,β-Unsaturated Amides with Total or Very High Selectivity from α,β-Epoxyamides and Samarium Diiodide. *J. Org. Chem*. **2003**, *68*, 9492-9495. (h) Concelloń, J. M.; Peré z-Andreś, J. A.; Rodríguez- Solla, H. Synthesis of (E)-α,β-Unsaturated Esters and Amides with Total Selectivity Using Samarium Diiodide. *Angew. Chem., Int. Ed*. **2000**, *39*, 2773-2775.

(21) (a) Crabtree, R. H. Homogeneous Transition Metal Catalysis of Acceptorless Dehydrogenative Alcohol Oxidation: Applications in Hydrogen Storage and to Heterocycle Synthesis. *Chem. Rev*. **2017**, *117*, 9228-9246. (b) Gunanathan, C.; Milstein, D. Applications of Acceptorless Dehydrogenation and Related Transformations in Chemical Synthesis. *Science* **2013**, *341*, 1229712.

(22) (a) Yadav, V.; Landge, V. G.; Subaramanian, M.; Balaraman, E. Manganese-Catalyzed α-Olefination of Nitriles with Secondary Alcohols. *ACS Catal*. **2020**, *10*, 947-954. (b) Thiyagarajan, S.; Gunanathan, C. Ruthenium-Catalyzed α-Olefination of Nitriles Using Secondary Alcohols. *ACS Catal*. **2018**, *8*, 2473-2478. (c) Chakraborty, S.; Das, U. K.; Ben-David, Y.; Milstein, D. Manganese Catalyzed α-Olefination of Nitriles by Primary Alcohols. *J. Am. Chem. Soc*. **2017**, *139*, 11710-11713.

(23) Gawali, S. S.; Pandia, B. K.; Gunanathan, C. Manganese(I)- Catalyzed α-Alkenylation of Ketones Using Primary Alcohols. *Org. Lett*. **2019**, *21*, 3842-3847.

(24) (a) Michlik, S.; Kempe, R. A Sustainable Catalytic Pyrrole Synthesis. *Nat. Chem*. **2013**, *5*, 140-144. (b) Deibl, N.; Kempe, R. Manganese-Catalyzed Multicomponent Synthesis of Pyrimidines from Alcohols and Amidines. *Angew. Chem., Int. Ed*. **2017**, *56*, 1663-1666. (c) Kallmeier, F.; Dudziec, B.; Irrang, T.; Kempe, R. Manganese- Catalyzed Sustainable Synthesis of Pyrroles from Alcohols and Amino Alcohols. *Angew. Chem., Int. Ed*. **2017**, *56*, 7261-7265. (d) Fertig, R.; Irrang, T.; Freitag, F.; Zander, J.; Kempe, R. Manganese-Catalyzed and Base-Switchable Synthesis of Amines or Imines via Borrowing Hydrogen or Dehydrogenative Condensation. *ACS Catal*. **2018**, *8*, 8525-8530. (e) Freitag, F.; Irrang, T.; Kempe, R. Mechanistic Studies of Hydride Transfer to Imines from a Highly Active and Chemoselective Manganate Catalyst. *J. Am. Chem. Soc*. **2019**, *141*, 11677-11685.

(25) (a) Das, J.; Vellakkaran, M.; Sk, M.; Banerjee, D. Iron- Catalyzed Coupling of Methyl N-Heteroarenes with Primary Alcohols: Direct Access to E-Selective Olefins. *Org. Lett*. **2019**, *21*, 7514-7518. (b) Ramalingam, B. M.; Ramakrishna, I.; Baidya, M. Nickel-Catalyzed Direct Alkenylation of Methyl Heteroarenes with Primary Alcohols. *J. Org. Chem*. **2019**, *84*, 9819-9825. (c) Zhang, G.; Irrgang, T.; Dietel, T.; Kallmeier, F.; Kempe, R. Manganese-Catalyzed Dehydrogenative Alkylation or α-Olefination of Alkyl-Substituted N-Heteroarenes with Alcohols. *Angew. Chem., Int. Ed*. **2018**, *57*, 9131- 9135. (d) Barman, M. K.; Waiba, S.; Maji, B. Manganese-Catalyzed Direct Olefination of Methyl-Substituted Heteroarenes with Primary Alcohols. *Angew. Chem., Int. Ed*. **2018**, *57*, 9126-9130.

(26) Waiba, S.; Barman, M. K.; Maji, B. Manganese-Catalyzed Acceptorless Dehydrogenative Coupling of Alcohols with Sulfones: A Tool to Access Highly Substituted Vinyl Sulfones. *J. Org. Chem*. **2019**, *84*, 973-982.

(27) For reviews, see: (a) Corma, A.; Navas, J.; Sabater, M. J. Advances in One-Pot Synthesis Through Borrowing Hydrogen Catalysis. *Chem. Rev*. **2018**, *118*, 1410-1459. (b) Faisca Phillips, A. M.; Pombeiro, A. J. L.; Kopylovich, M. N. Recent Advances in Cascade Reactions Initiated by Alcohol Oxidation. *ChemCatChem* **2017**, *9*, 217-246. (c) Crabtree, R. H. Homogeneous Transition Metal Catalysis of Acceptorless Dehydrogenative Alcohol Oxidation: Applications in Hydrogen Storage and to Heterocycle Synthesis. *Chem. Rev*. **2017**, *117*, 9228-9246. (d) Khusnutdinova, J. R.; Milstein, D. Metal-Ligand Cooperation. *Angew. Chem., Int. Ed*. **2015**, *54*, 12236-12273. (e) Gunanathan, C.; Milstein, D. Bond Activation and Catalysis by Ruthenium Pincer Complexes. *Chem. Rev*. **2014**, *114*, 12024-12087.

(28) (a) Gawali, S. S.; Pandia, B. K.; Pal, S.; Gunanathan, C. Manganese(I)-Catalyzed Cross-Coupling of Ketones and Secondary Alcohols with Primary Alcohols. *ACS Omega* **2019**, *4*, 10741-10754. (b) Thiyagarajan, S.; Gunanathan, C. Catalytic Cross-Coupling of Secondary Alcohols. *J. Am. Chem. Soc*. **2019**, *141*, 3822-3827. (c) Thiyagarajan, S.; Gunanathan, C. Ruthenium-Catalyzed Direct Cross-Coupling of Secondary Alcohols to β-Disubstituted Ketones. *Synlett* **2019**, *30*, 2027-2034. (d) Thiyagarajan, S.; Gunanathan, C. Facile Ruthenium(II)-Catalyzed α-Alkylation of Arylmethyl Nitriles Using Alcohols Enabled by Metal−Ligand Cooperation. *ACS Catal*. **2017**, *7*, 5483-5490.

(29) (a) Chakraborty, S.; Daw, P.; Ben-David, Y.; Milstein, D. Manganese-Catalyzed α-Alkylation of Ketones, Esters, and Amides Using Alcohols. *ACS Catal*. **2018**, *8*, 10300-10305. (b) Jang, Y. K.; Kruckel, T.; Rueping, M.; El-Sepelgy, O. Sustainable Alkylation of Unactivated Esters and Amides with Alcohols Enabled by Manganese Catalysis. *Org. Lett*. **2018**, *20*, 7779-7783. (c) Deibl, N.; Kempe, R. General and Mild Cobalt-Catalyzed C-Alkylation of Unactivated Amides and Esters with Alcohols. *J. Am. Chem. Soc*. **2016**, *138*, 10786-10789. (d) Chaudhari, M. B.; Bisht, G. S.; Kumari, P.; Gnanaprakasam, B.

Ruthenium-Catalyzed Direct α-Alkylation of Amides Using Alcohols. *Org. Biomol. Chem*. **2016**, *14*, 9215-9220. (e) Yao, W.; Mab, X.; Guo, L.; Jia, X.; Hua, A.; Huang, Z. A Highly Efficient Catalytic α-Alkylation of Unactivated Amides Using Primary Alcohols. *Tetrahedron Lett*. **2016**, *57*, 2919-2921. (f) Guo, L.; Liu, Y.; Yao, W.; Leng, X.; Huang, Z. Iridium-Catalyzed Selective α-Alkylation of Unactivated Amides with Primary Alcohols. *Org. Lett*. **2013**, *15*, 1144-1147.

(30) (a) Kaithal, A.; Bonn, P. v.; Holscher, M.; Leitner, W. Manganese(I)-Catalyzed β-Methylation of Alcohols Using Methanol as C1 Source. *Angew. Chem., Int. Ed*. **2020**, *59*, 215-220. (b) Kaithal, A.; Gracia, L.-L.; Camp, C.; Quadrelli, E. A.; Leitner, W. Direct Synthesis of Cycloalkanes from Diols and Secondary Alcohols or Ketones Using a Homogeneous Manganese Catalyst. *J. Am. Chem. Soc*. **2019**, *141*, 17487-17492. (c) Borghs, J. C.; Lebedev, Y.; Rueping, M.; El-Sepelgy, O. Sustainable Manganese-Catalyzed Solvent-Free Synthesis of Pyrroles from 1,4-Diols and Primary Amines. *Org. Lett*. **2019**, *21*, 70-74. (d) Peña-López, M.; Piehl, P.; Elangovan, S.; Neumann, H.; Beller, M. Manganese-Catalyzed Hydrogen-Autotransfer C−C Bond Formation: α-Alkylation of Ketones with Primary Alcohols. *Angew. Chem., Int. Ed*. **2016**, *55*, 14967-14971. (e) Elangovan, S.; Neumann, J.; Sortais, J.-B.; Junge, K.; Darcel, C.; Beller, M. Efficient and Selective N-Alkylation of Amines with Alcohols Catalysed by Manganese Pincer Complexes. *Nat. Commun*. **2016**, *7*, 12641. (f) Mukherjee, A.; Nerush, A.; Leitus, G.; Shimon, L. J. W.; Ben-David, Y.; Jalapa, N. A. E.; Milstein, D. Managanese-Catalyzed Environmentally Benign Dehydrogenative Coupling of Alcohols and Amines to Form Aldimines and H2: A Catalytic and Mechanistic Study. *J. Am. Chem. Soc*. **2016**, *138*, 4298- 4301.

(31) Kallmeier, F.; Irrgang, T.; Dietel, T.; Kempe, R. Highly Active and Selective Manganese C=O Bond Hydrogenation Catalysts: The Importance of the Multidentate

Ligand, the Ancillary Ligands, and the Oxidation State. *Angew. Chem., Int. Ed*. **2016**, *55*, 11806-11809.

(32) Das, U. K.; Ben-David, Y.; Diskin-Posner, Y.; Milstein, D. N Substituted Hydrazones by Manganese-Catalyzed Coupling of Alcohols with Hydrazine: Borrowing Hydrogen and Acceptorless Dehydrogenation in One System. *Angew. Chem., Int. Ed*. **2018**, *57*, 2179-2182.

(33) (a) Liu, T.; Wang, L.; Wu, K.; Yu, Z. Manganese-Catalyzed β- Alkylation of Secondary Alcohols with Primary Alcohols under Phosphine-Free Conditions. *ACS Catal*. **2018**, *8*, 7201−7207. (b) Fu, S.; Shao, Z.; Wang, Y.; Liu, Q. Manganese-Catalyzed Upgrading of Ethanol into 1-Butanol. *J. Am. Chem. Soc*. **2017**, *139*, 11941-11948.

(34) Havlík, M.; Král, V.; Kaplánek, R.; Dolenský, B. One-Pot Reaction as an Efficient Method for Rigid Molecular Tweezers. *Org. Lett*. **2008**, *10*, 4767-4769.

(35) van Dijk, T.; Rong, M. K.; Borger, J. E.; Nieger, M.; Slootweg, J. C.; Lammertsma, K. Bis(imino)phosphanes: Synthesis and Coordination Chemistry. *Organometallics* **2016**, *35*, 827-835.

(36) Patten, T. E.; Troeltzsch, C.; Olmstead, M. M. Copper(I) and -(II) Complexes of Neutral and Deprotonated N-(2,6-Diisopropylphenyl)- 3-[bis(2-pyridylmethyl)amino] propenamide. *Inorg. Chem*. **2005**, *44*, 9197-9206.

(37) Li, C.; Wang, M.; Lu, X.; Zhang, L.; Jiang, J.; Zhang, L. Reusable Brønsted Acidic Ionic Liquid Efficiently Catalyzed N Formylation and N-Acylation of Amines. *ACS Sustainable Chem. Eng*. **2020**, *8*, 4353-4361.

(38) Ma, W.; Weng, Z.; Rogge, T.; Gu, L.; Lin, J.; Peng, A.; Luo, X.; Gou, X.; Ackermann, L. Ruthenium(II)-Catalyzed C-H Chalcogenation of Anilides. *Adv. Synth. Catal*. **2018**, *360*, 704-710.

(39) Panini, P.; Chopra, D. Quantitative Insights into Energy Contributions of Intermolecular Interactions in Fluorine and Trifluoromethyl Substituted Isomeric N-phenylacetamides and Nmethylbenzamides. *CrystEngComm* **2013**, *15*, 3711-3733.

(40) Breising, V. M.; Kayser, J. M.; Kehl, A.; Schollmeyer, D.; Liermann, J. C.; Waldvogel, S. R. Electrochemical Formation of N,N -diarylhydrazines by Dehydrogenative N−N Homocoupling Reaction. *Chem. Commun*. **2020**, *56*, 4348-4351.

(41) Liu, J.; Zhang, C.; Zhang, Z.; Wen, X.; Dou, X.; Wei, J.; Qiu, X.; Song, S.; Jiao, N. Nitromethane as a Nitrogen Donor in Schmidt-type Formation of Amides and Nitriles. *Science* **2020**, *367*, 281-285.

(42) Yu, W.; Yang, S.; Xiong, F.; Fan, T.; Feng, Y.; Huang, Y.; Fu, J.; Wang, T. Palladium Catalyzed Carbonylation of Benzylic Ammonium Salts to Amides and Esters via C−N Bond Activation. *Org. Biomol. Chem*. **2018**, *16*, 3099-3103.

(43) Yi, X.; Lei, S.; Liu, W.; Che, F.; Yu, C.; Liu, X.; Wang, Z.; Zhou, X.; Zhang, Y. Copper-Catalyzed Radical N-Demethylation of Amides Using N-Fluorobenzenesulfonimide as an Oxidant. *Org. Lett*. **2020**, *22*, 4583-4587.

(44) Qiu, J.; Zhang, R. DDQ-Promoted Direct Transformation of Benzyl Hydrocarbons to Amides via Tandem Reaction of the CDC Reaction and Beckmann Rearrangement. *Org. Biomol. Chem*. **2013**, *11*, 6008-6012.

(45) Germain, A. R.; Carmody, L. C.; Nag, P. P.; Morgan, B.; verPlank, L.; Fernandez, C.; Donckele, E.; Feng, Y.; Perez, J. R.; Dandapani, S.; Palmer, M.; Lander, E. S.; Gupta, P. B.; Schreiber, S. L.; Munoz, B. Cinnamides as Selective Small-Molecule Inhibitors of a Cellular Model of Breast Cancer Stem Cells. *Bioorg. Med. Chem. Lett*. **2013**, *23*, 1834-1838.

(46) Legoabe, L.; Kruger, J.; Petzer, A.; Bergh, J. J.; Petzer, J. P. Monoamine Oxidase Inhibition by Selected Anilide Derivatives. *Eur. J. Med. Chem*. **2011**, *46*, 5162-5174.

(47) SMART and SAINT *Software Reference Manuals Version 6.45*; Bruker Analytical X-ray Systems, Inc.: Madison, WI, 2003.

(48) *Bruker AXS, SADABS, Program for Empirical Absorption Correction of Area Detector Data V 2004/1*; Bruker AXS Inc.: Madison, Wisconsin, USA, 2004.

(49) Sheldrick, G. M. Crystal Structure Refinement with SHELXL. *Acta Crystallogr., Sect. A*: *Found. Crystallogr*. 2008, A64, 112-122.

(50) Dolomanov, O. V.; Bourhis, L. J.; Gilea, R. J.; Howard, J. A. K.; Puschmann, H. OLEX2: A Complete Structure Solution, Refinement and Analysis Program. *J. Appl. Crystallogr*. **2009**, *42*, 339-341.

^{1}H, ^{13}C NMR Spectra of the Products:

Figure 2.1. ^{1}H NMR Spectrum of (*E*)-3-(4-(*tert*-butyl)phenyl)-*N*-phenylacrylamide (**2.1e**):

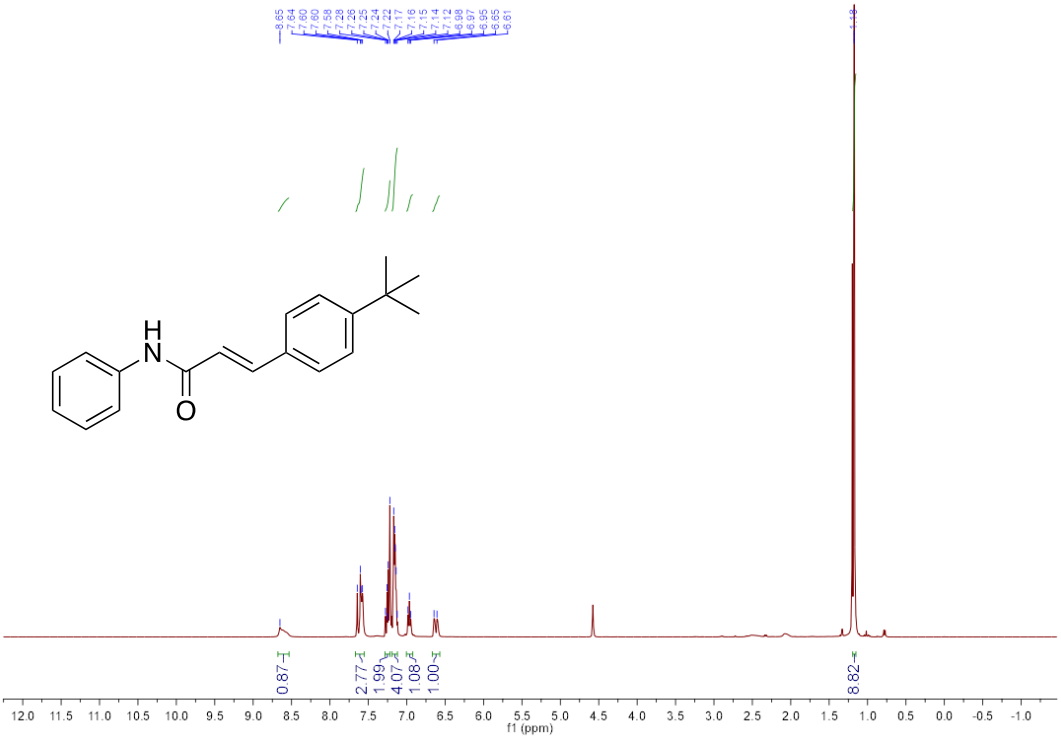


Figure 2.2. ^{13}C NMR Spectrum (*E*)-3-(4-(*tert*-butyl)phenyl)-*N*-phenylacrylamide (**2.1e**)**:**

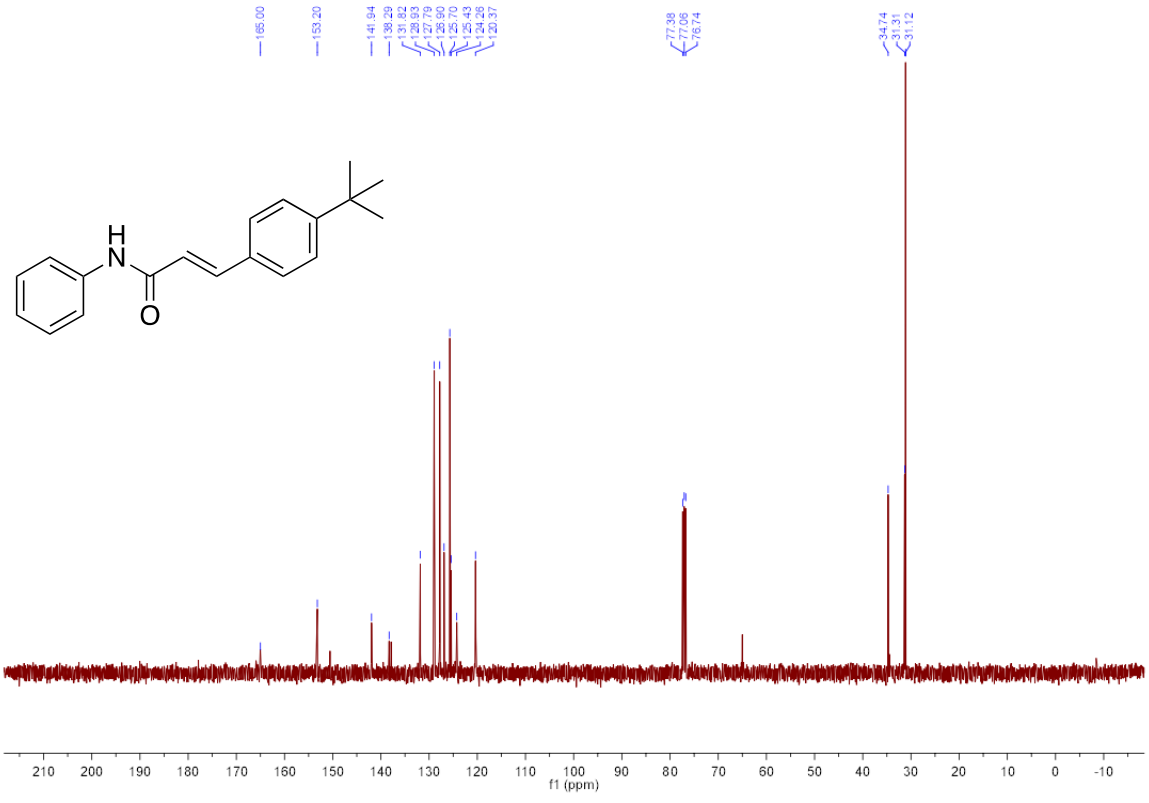


Figure 2.3. ^{1}H NMR Spectrum of (*E*)-*N*-phenyl-3-(4-(trifluoromethyl)phenyl)acrylamide (**2.1m**):

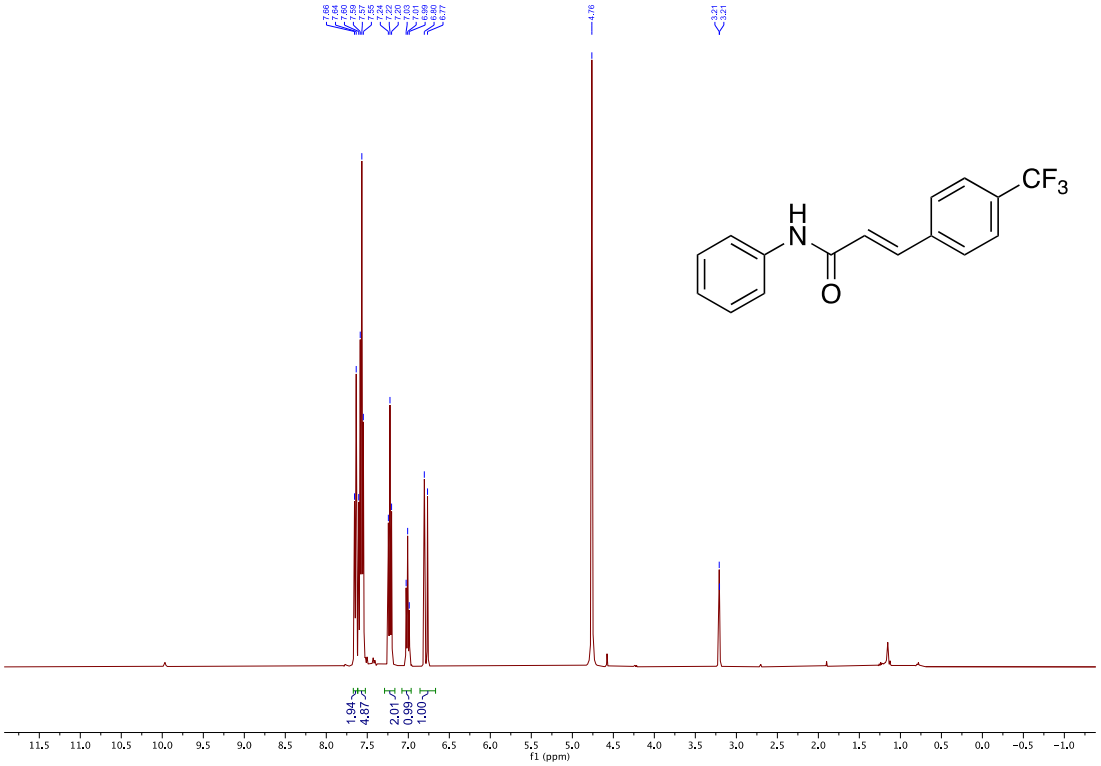


Figure 2.4. ^{13}C NMR Spectrum of (*E*)-*N*-phenyl-3-(4-(trifluoromethyl)phenyl)acrylamide (**2.1m**):

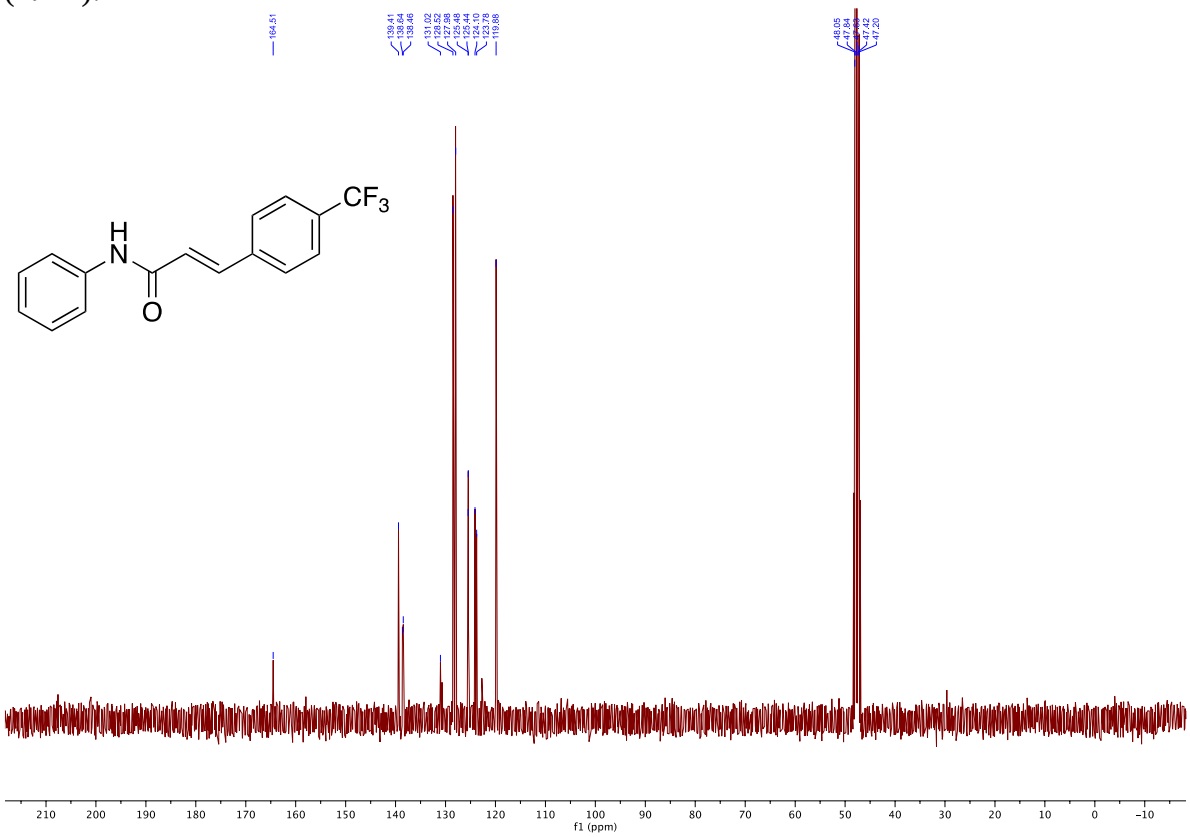


Figure 2.5. ^{1}H NMR spectrum of (*E*)-*N*-(2,3-dimethylphenyl)-3-(4(trifluoromethyl)phenyl)acrylamide (**2.2j**)**:**

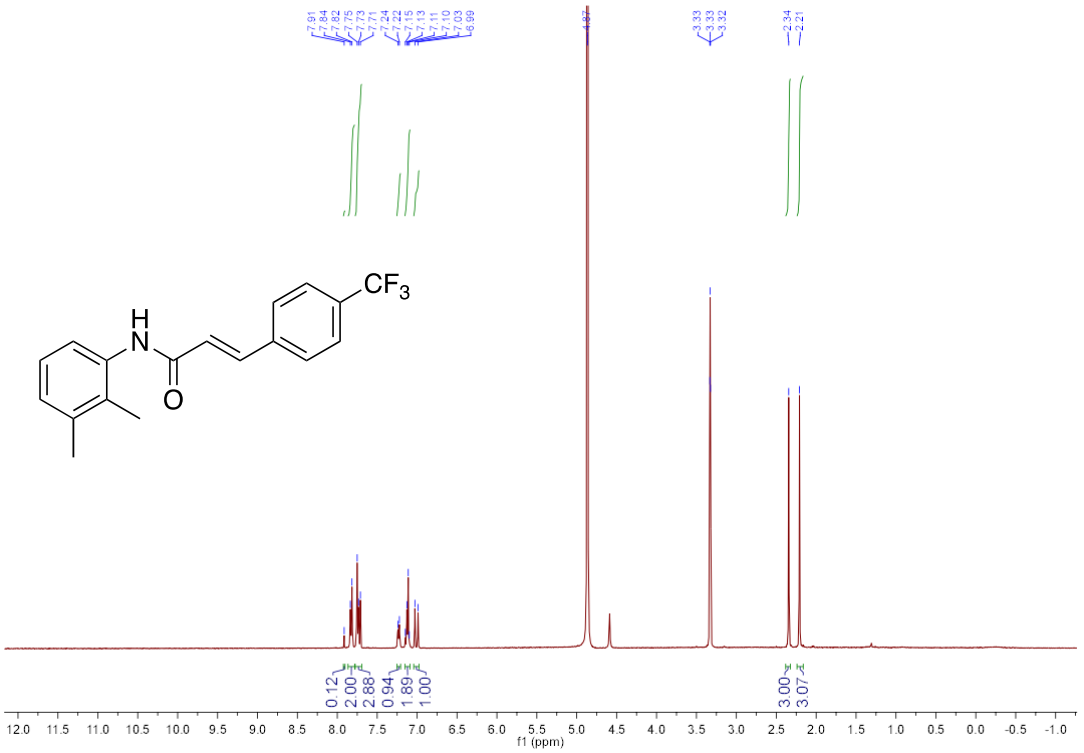
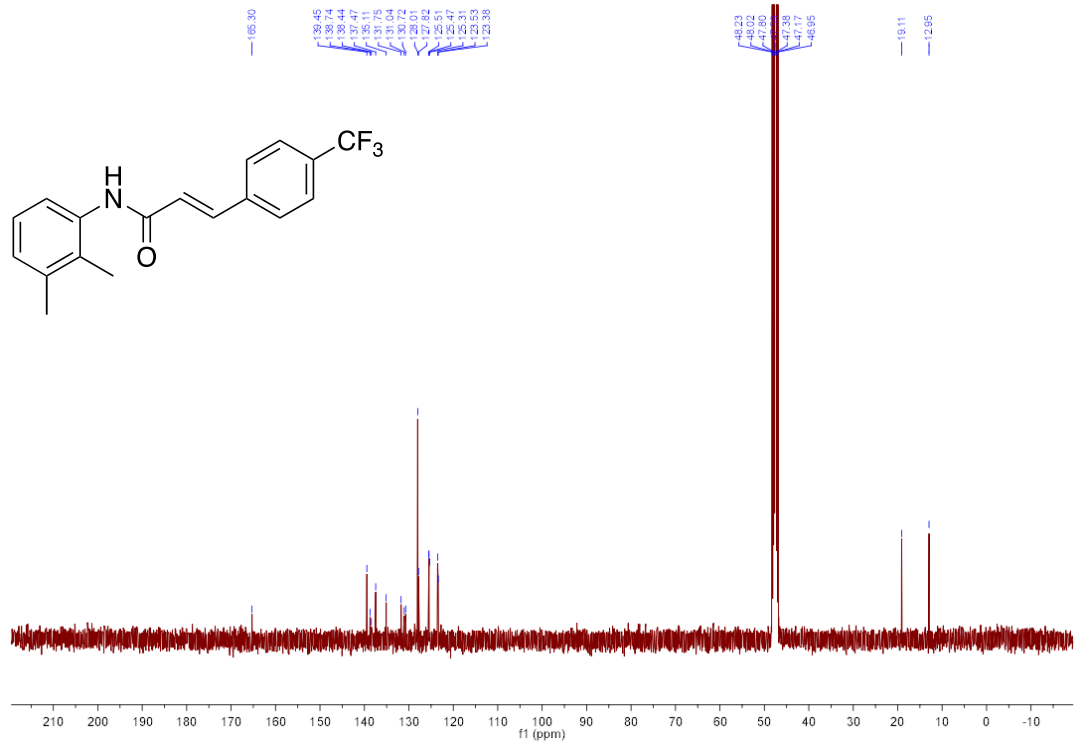


Figure 2.6. ^{13}C NMR Spectrum of (*E*)-*N*-(2,3-dimethylphenyl)-3-(4-(trifluoromethyl)phenyl)acrylamide **(2.2j):**



CHAPTER 3

Manganese(I) Catalyzed Alkenylation of Phosphine Oxides Using Alcohols with Liberation of Hydrogen and Water

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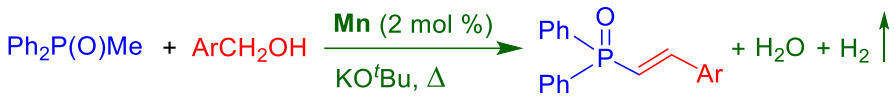
3.1 ABSTRACT

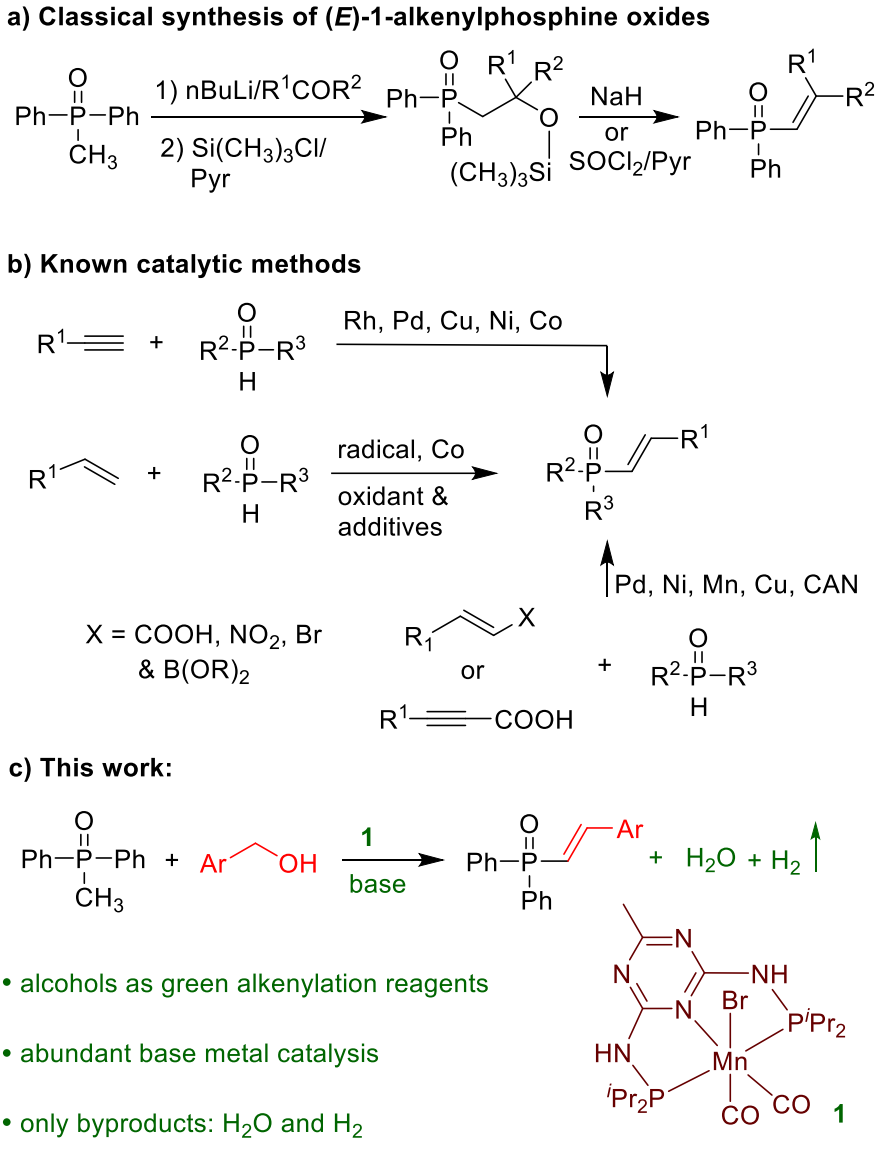


Herein, a catalytic cross-coupling of methyldiphenylphosphine oxide with arylmethyl alcohols leading to the alkenylphosphine oxides is reported. A manganese pincer catalyst catalyzes the reactions, which provides exclusive formation of trans-alkenylphosphine oxides. Mechanistic studies indicate that reactions proceed via aldehyde intermediacy and the catalyst promotes the C=C bond formation. Reactions are facilitated by dearomatization, and aromatization metal-ligand cooperation operates in catalyst. Use of abundant base metal catalyst and formation of water and H_2 as the only byproducts make this catalytic protocol sustainable and environmentally benign.

3.2 INTRODUCTION

Organophosphorus compounds are important functional motifs in chemistry and biology. In particular, alkenylphosphine oxides play a vital role as biologically active compounds and are highly useful in agricultural, industrial, and medicinal chemistry.[1-3] In addition, alkenylphosphine oxides have widespread synthetic utility as the C=C bond undergoes diverse transformations, including nucleophilic addition of phosphines, amines, and carbanions.[4] These compounds are also used as valuable building blocks in material science[5] and serve as precursors for many phosphine ligands.[6] Owing to such diverse applications, a number of methods have been developed for the synthesis of alkenylphosphine oxides. However, the

Scheme 3.1. Synthetic Methods for Alkenylphosphine Oxides



conventional methods involve the multistep synthesis using a stoichiometric amount of strong bases and tedious experimental procedures.[7] For example, lithium base promoted coupling of methyl diphenylphosphine oxide with aldehyde or ketone provided the 2-hydroxyalkyldiphenylphosphine oxide, which was converted to the corresponding O-trimethylsilyl derivative, and further reaction with base or thionyl chloride/pyridine resulted in

alkenylphosphine oxides (**Scheme 3.1**).[8] Transition metal catalyzed or radical-mediated addition of diarylphosphine oxides to alkynes[9,10] or alkenes[11] has been extensively applied for the synthesis of alkenylphosphine oxides (**Scheme 3.1**). The defunctionalization C−P cross-coupling strategy has been utilized to obtain P-alkenyl compounds, which involved catalytic cross-coupling of propargylic acid or *α,β*-unsaturated carboxylic acid or functionalized alkenes with diarylphosphine oxides.[12,13]

Direct synthesis of alkenylphosphine oxide from methyldiphenylphosphine oxides and alcohols can be a desirable method and remains unknown. In recent years, acceptorless dehydrogenative coupling of alcohols with carbon nucleophiles afforded the atom economical and sustainable chemical transformations and advanced chemical synthesis.[14] However, such coupling of alcohols leading to the construction of an alkene functionality remains limited. Synthesis of vinyl nitriles from alcohols and arylmethyl nitriles was developed by our group and others.[15] We have demonstrated the manganese pincer catalyzed direct olefination of ketones and amides using alcohols, and also cross-coupling of secondary allylic alcohols with primary alcohols.[16] Catalytic methods for alkenylation of heteroarylmethyl compounds and sulfone derivatives using alcohols have been developed.[17]

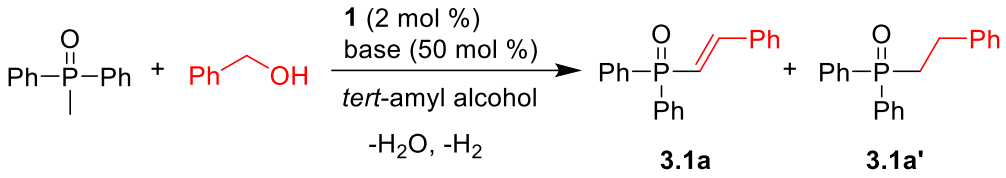
These results prompted us to explore the potential reactivity of Kempe's manganese pincer complex **1** as a catalyst for the dehydrogenative coupling of methyldiphenylphosphine oxides and alcohols toward the synthesis of alkenylphosphine oxides. Achieving selectivity for the alkene functionality is a challenge and crucial for this transformation as the competing borrowing hydrogen pathway[18] can utilize the in situ generated molecular hydrogen to reduce the C=C double bond and result in a corresponding alkylation product.[19] A similar transformation leading to *α*-alkylation of methyldiphenylphosphine oxides was reported by Wang.[19a] In continuation of our efforts in the development of sustainable synthetic methods, herein we report a dehydrogenative coupling of methyldiphenylphosphine oxide and alcohols

(**Scheme 3.1**). Remarkably, the reaction is catalyzed by earth-abundant, and cheap base metal-manganese, and liberated H_2 and H_2O are the only byproducts.

3.3 RESULTS AND DISCUSSIONS

At the outset of our investigations, methyldiphenylphosphine oxide (0.5 mmol), benzyl alcohol (0.5 mmol), manganese pincer catalyst **1** (2 mol %), and KO^{t}Bu (50 mol %) were reacted in tertamyl alcohol at 135 °C. The reaction resulted in 61% yield, which comprised alkenyl and alkylation products with a ratio of 93:7 (**3.1a**/**3.1a′**, Table 3.1, entry 1). Use of different bases provided the diminished yields or no reaction (Table 3.1, entries 2-5) perhaps due to the low acidity of the methyl protons. As the KO^{t}Bu emerged as a choice of base, further optimization was carried out by using 1 equiv of the base and increased catalyst load of 5 mol % (entries 6 and 7). Different solvents such as 1,4-dioxane provided lower yield, and toluene was found incompatible (entries 8 and 9). On the basis of these observations, further experiments were performed using 2 mol % of catalyst **1**, 50 mol % of KO^{t}Bu base in tert-amyl alcohol for a

Table 3.1. **Optimization for α-Alkenylation of Phosphine Oxides using Catalyst 1**[a]



entry	base	temp. (° C)	time (h)	yield (%)[b]	ratio (**3.1a/3.1a′**)[c]
1	KO^{t}Bu	135	24	61	93/7
2	NaO^{t}Bu	135	24	26	94/6
3	Cs_2CO_3	135	24	15	94/6
4	LiO^{t}Bu	135	24	--	--
5	K_2CO_3	135	24	--	--
6[d]	KO^{t}Bu	135	24	57	93/7
7[e]	KO^{t}Bu	135	24	59	94/6
8[f]	KO^{t}Bu	135	24	57	93/7
9[g]	KO^{t}Bu	135	24	trace	--

10	KO^{t}Bu	135	36	67	93/7
11	**KO^{t}Bu**	**135**	**48**	**79**	**93/7**
12[h]	KO^{t}Bu	135	48	66	94/6
13	KO^{t}Bu	120	24	40	94/6
14	KO^{t}Bu	150	24	58	92/8
15[i]	KO^{t}Bu	135	48	trace	--
16	--	135	48	--	--

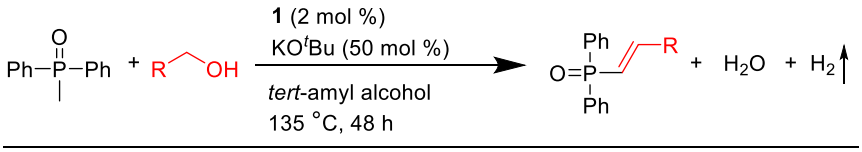
[a] Reaction conditions: methyldiphenylphosphine oxide (0.5 mmol), benzyl alcohol (0.5 mmol), *tert*-amyl alcohol (2 mL), catalyst **1**, and base were heated in an open system under a nitrogen flow. [b] Isolated yields after column chromatography. [c] Determined from ^{1}H NMR analysis of crude reaction mixture. [d]100 mol% base used. [e] 5 mol % catalyst used. [f] 1,4-Dioxane was used as a solvent. [g]Toluene was used as a solvent. [h] 25 mol % of KO^{t}Bu was used. [I] No catalyst was used.

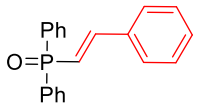
prolonged period; after 36 h, an improved yield of 67% with a selectivity of 93:7 (**3.1a**/**3.1a′**, entry 10) was observed. The reaction carried out for 48 h emerged as the optimal condition for the alkenylation of phosphine oxide with 79% yield of the product having 93:7 (**3.1a**/**3.1a′**) selectivity (entry 11). Decreasing the base load to 25 mol % also decreased the product yield (entry 12). Lowering the reaction temperature to 120 °C or increasing to 150 °C failed to provide the product in desired yields (entries 13 and 14). Control experiments without catalyst or base resulted in a trace amount of product or no reaction, indicating that both catalyst and base are essential for this transformation (entries 15 and 16). Notably, in all reactions, only the selective formation of *E*-alkene was observed.

Having established the optimal experimental conditions, an assortment of benzyl alcohols was subjected to manganese-catalyzed alkenylation with methyldiphenylphosphine oxide (Table 3.2). Benzyl alcohols bearing electron-donating substituents provided the alkenyl phosphine products in moderate to good yields. *m*-Methyl, *p*-methyl, and *p*-ethylbenzyl alcohols resulted

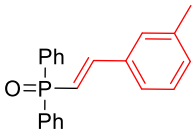
in 66%, 65%, and 55% of products **3.1b**, **3.1c**, and **3.1d**, respectively. *p*-Isopropyl, *p*-isobutyl, and 4-tertbutybenzyl alcohols afforded the trans-olefination products **3.1e**-**3.1g** in moderate to good yields. A methoxy and ethoxy substituent at meta- and para- positions produced the alkenyl products **3.1h**-**3.1j** in moderate yields. Reaction with 3,4-dimethoxybenzyl alcohol and piperonyl alcohol afforded the products **3.1k** and **3.1l** in 55% and 63%, respectively. While *m*-phenoxybenzyl alcohol yielded only 43% of product **3.1m**, p-benzyloxybenzyl alcohol produced 71% of product **3.1n**. Unfortunately, the electron-rich 4-N,Ndimethylbenzyl alcohol provided both the alkenyl and alkylation (in 1:1 ratio) products **3.1o**. *p*-Thiomethylbenzyl alcohol afforded 67% of the product **3.1p**. *p*-Phenylbenzyl alcohol provided the corresponding alkenyl product **3.1q** in 54% yield. Further, polyarylmethyl alcohols were tested, and they delivered the corresponding products in moderate to excellent yields. 1-Naphthalenemethanol and 2-naphthalenemethanol resulted in alkenyl products **3.1r** and **3.1s** in 60% and 40% isolated yields, respectively. Higher polyarylmethanols such as 9-anthracenemethanol afforded the alkenyl products **3.1t** in 49% yield, whereas 1-pyrenemethanol provided both alkylation and alkenyl products in a 1:1 ratio (**3.1u**, 60% yield). Interestingly, ferrocenemethanol also produced the alkenylphosphine oxide **3.1v** in 62% yield. Benzyl alcohols having electron-withdrawing substituents, in general, provided the products in low to moderate yields. While reaction of m-fluorobenzyl alcohol provided product **3.1w** in 51% yield, m-chlorobenzyl alcohol resulted in only 20% of the alkenyl product **3.1x**, and a major amount of alcohol remains unreacted. Notably, the single-crystal X-ray analyses of alkenyl diphenylphosphine oxides **3.1e**, **3.1k**, and **3.1w** corroborated the trans-geometry of the alkenyl functionality.

Table 3.2. **Manganese Catalyzed *α*-Alkenylation of Phosphine Oxides Using Diverse Primary Alcohols and ORTEP Structures of Products 3.1e, 3.1k, and 3.1w**[a]

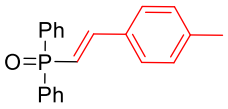




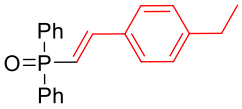
3.1a, 79%, 62%[b]



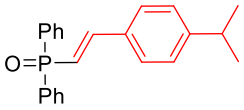
3.1b, 66%



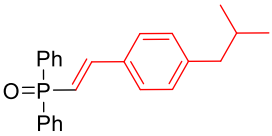
3.1c, 65%[c]



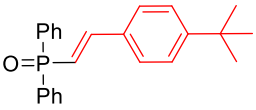
3.1d, 55%



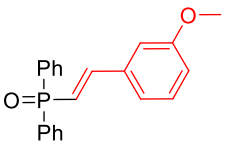
3.1e, 80%



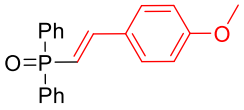
3.1f, 62%



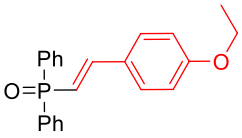
3.1g, 77%



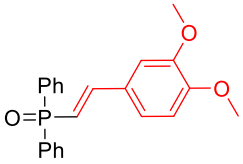
3.1h, 45%



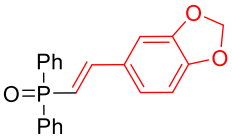
3.1i, 75%



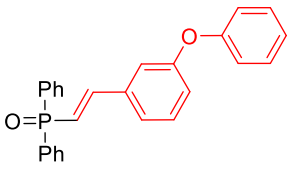
3.1j, 62%



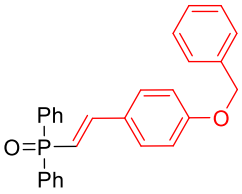
3.1k, 55%



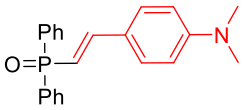
3.1l, 63%



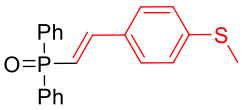
3.1m, 43%



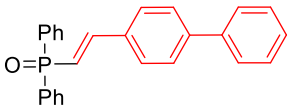
3.1n, 71%



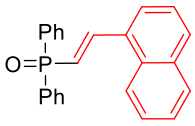
3.1o, 55%[d]



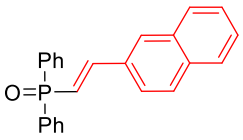
3.1p, 67%



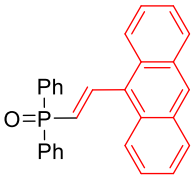
3.1q, 54%



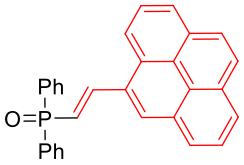
3.1r, 60%



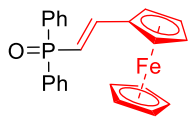
3.1s, 40%



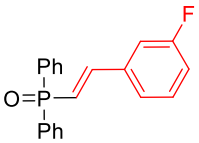
3.1t, 49%



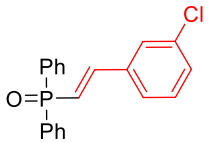
3.1u, 60%[d]



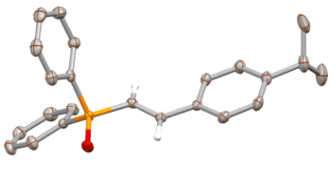
3.1v, 62%



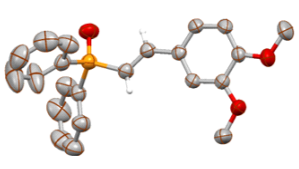
3.1w, 51%



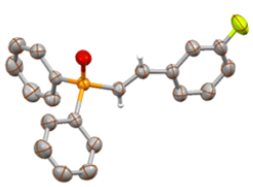
3.1x, 20%



3.1e



3.1k

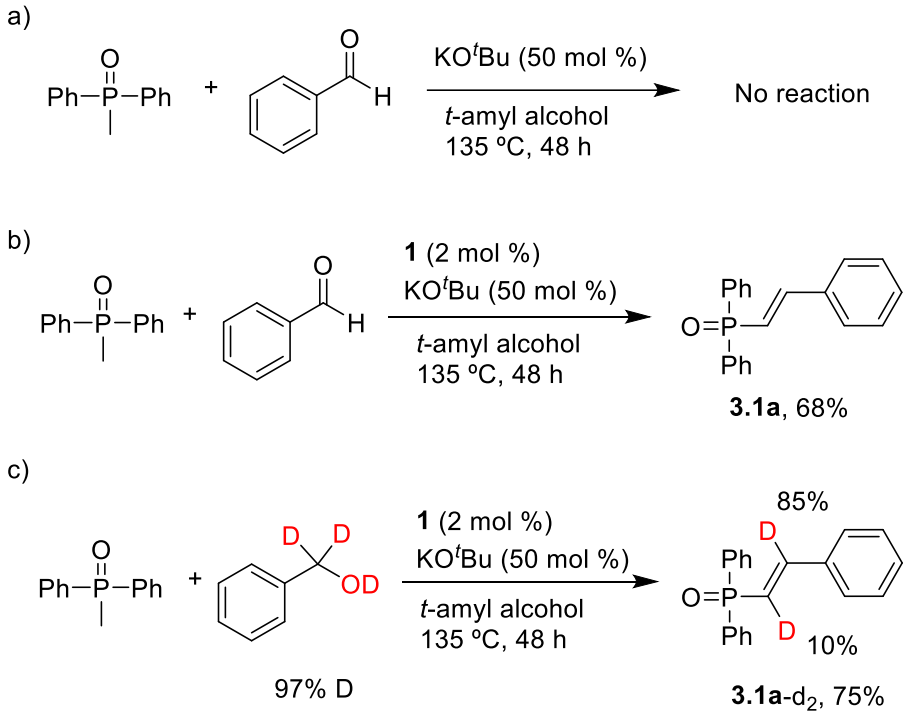


3.1w

[a] Reaction conditions: methyldiphenylphosphine oxide (0.5 mmol), alcohol (0.5 mmol), *tert*-amyl alcohol (2 mL), catalyst **1** (0.01 mmol, 2 mol %), and KO^{t}Bu (50 mol %) were heated in an open system under a nitrogen flow. Reported yields correspond to isolated products after column chromatography. Ellipsoids of ORTEP structures are drawn with 50% probability. [b] Yield of the 0.5 g scale reaction performed for 60 h. [c] 20% alkylation product was observed. [d]50% alkylation product was observed.

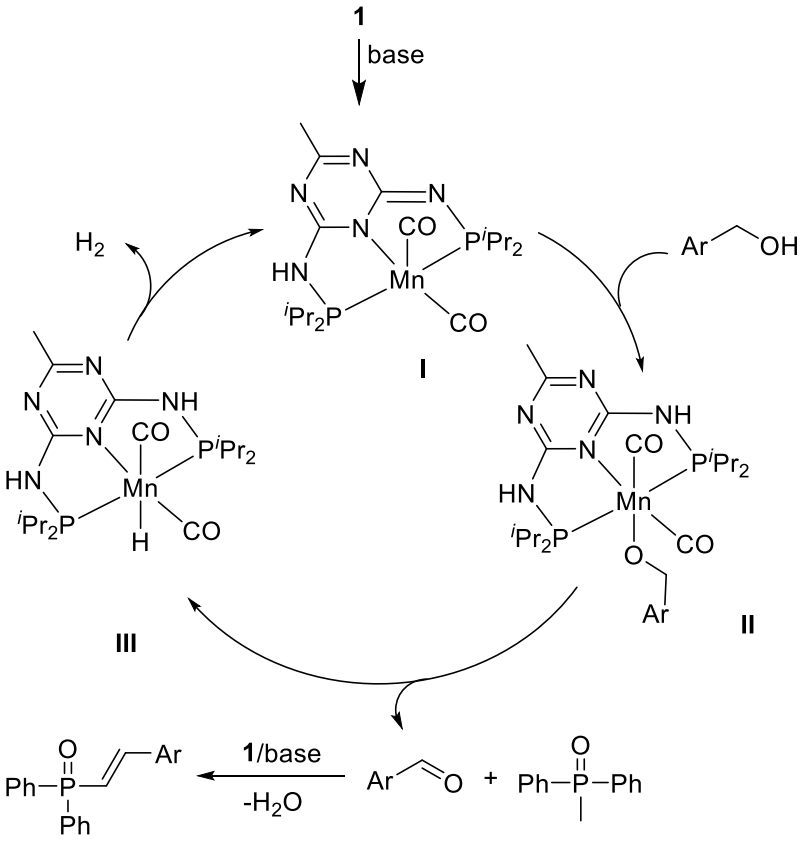
In order to understand the reaction pathways, experiments were performed using benzaldehyde. Control experiment involving methyldiphenylphosphine oxide and benzaldehyde with 50 mol % base and in the absence of catalyst **1** failed to provide the desired alkenyl product (**Scheme 3.2a**). However, a similar experiment in the presence of catalyst **1** (2 mol %) resulted in alkenyl product 2a in 68% yield (**Scheme 3.2b**). These two experiments confirm that the reaction proceeds via the aldehyde intermediate, and the catalyst is necessary for C=C bond formation. Further, manganese catalyzed alkenylation of methyldiphenylphosphine oxide was performed using benzyl alcohol-d_3, which provided the alkenyl product **3.1a**-d_2 in 75% yield. While 85% deuterium was found in β-carbon, a minor deuterium scrambling leading to the 10% deuterium incorporationmat the α-carbon of the alkene functionality was observed. The 10% deuteration observed at the α-carbon may be due to H/D exchange with partially deuterated heavy water eliminated in the aldol condensation step.

Scheme 3.2: Mechanistic Studies



A plausible mechanism for α-alkenylation of methyldiphenylphosphine oxides is depicted in **Scheme 3.3**. Upon reaction of catalyst 1 with base, a dearomatized coordinatively unsaturated intermediate **I** is generated. The reaction of intermediate I with alcohol results in facile O-H activation, which produces the alkoxy-ligated manganese complex **II**. Similar alkoxy-ligated manganese complexes are characterized by Milstein, Yu, and Liu.[20-22] Intermediate II undergoes *β*-hydride elimination to provide the corresponding aldehyde and Mn-hydride complex **III**. The in situ generated aldehyde undergoes catalyst and base promoted C=C bond formation with methyldiphenylphosphine oxides to provide the alkenylphosphine oxide product. The catalyst might have a role in increasing the electrophilicity of the in situ generated aldehyde, thereby facilitating the aldol condensation step.[23] Intermediate **III** further liberates the molecular hydrogen, which produces dearomatized intermediate **I** to complete one loop in a catalytic cycle. This catalytic coupling reaction is facilitated by the aromatization-dearomatization metal-ligand cooperation[24] operative in the catalytic system, which maintains the +1 oxidation state in all the intermediates involved in the catalytic cycle.

Scheme 3.3: Proposed Mechanism for Alkenylation of Methyldiphenylphosphine oxide using Alcohols



3.4 CONCLUSION

In summary, a manganese pincer catalyzed atom economical, environmentally benign catalytic protocol for the synthesis of alkenylphosphine oxide is reported using benzylic alcohols. An assortment of primary alcohols react with methyldiphenyl phosphine oxides to provide the alkenylation product. Contrary to previous reports for the synthesis of such compounds, this reaction uses readily available alcohols as a coupling partner. The reaction proceeds via an acceptorless dehydrogenation pathway in which water and hydrogen are the only byproducts.

3.5 EXPERIMENTAL SECTION

General Experimental: All catalytic reactions were performed under an inert atmosphere using standard Schlenk techniques. All stoichiometric reactions were performed in a nitrogen atmosphere MBRAUN glovebox. Chemicals were purchased from Acros, Sigma-Aldrich,

Alfa-Aesar, and Himedia Chemicals and used without further purification. Dry solvents were prepared according to standard procedures. Infrared (IR) spectra were recorded in PerkinElmer FTIR and Thermo-Nicolet FT-IR spectrophotometers. High-resolution mass spectra (HRMS) were obtained on a Bruker micrOTOF-Q II Spectrometer and are reported as m/z (relative intensity). Accurate masses are reported for the molecular ion $[M + Na]^+$, $[M+H]^+$, $[M]^+$. Nuclear magnetic resonance spectra (^{1}H NMR and ^{13}C NMR) were recorded at a Bruker AV-700 (^{1}H at 700 MHz and ^{13}C at 175 MHz) and Bruker AV-400 (^{1}H at 400 MHz and ^{13}C at 100.6 MHz). ^{1}H NMR chemical shifts are referenced in parts per million (ppm) with respect to tetramethyl silane (TMS, δ 0.00 ppm), and ^{13}C {^{1}H} NMR chemical shifts are referenced in parts per million (ppm) with respect to $CDCl_3$ (δ 77.160 ppm). Coupling constants are reported in hertz (Hz). ^{1}H NMR spectroscopy abbreviations: s, singlet; d, doublet; t, triplet; q, quartet; dd, doublet of doublets; dt, doublet of triplets; dq, doublet of quartets; td, triplet of doublets; qd, quartets of doublets; ddd, doublets of doublets of doublets; m, multiplet; br, broad. Assignment of spectra was done based on one-dimensional (dept-135) NMR techniques.

General Procedure for Optimization of *α*-Alkenylation of Phosphine Oxides Using Alcohols. To a Schlenk flask (25 mL) equipped with a stir bar were added catalyst **1** (0.01 mmol, 2 mol %), base (50 mol %, until otherwise indicated), methyldiphenylphosphine oxide (0.5 mmol), benzyl alcohol (0.5 mmol), and tert-amyl alcohol (2 mL) under a nitrogen atmosphere in a glovebox. The reaction mixture was taken out of the glovebox, equipped with a condenser, and the solution was heated at 135 °C (oil bath temperature) with stirring in an open system under nitrogen flow for 24-48 h. After cooling, the reaction mixture was transferred to an RB flask and the solvent was evaporated under reduced pressure. The resultant residue was dissolved in chloroform and washed with water and brine. The collected organic layer was dried over anhydrous sodium sulfate and concentrated in vacuum. The resultant

residue was purified by column chromatography (silica gel, 100-200 mesh). The yields were calculated for the isolated product.

General Procedure for *α*-Alkenylation of Phosphine Oxides Using Alcohols.

To a Schlenk flask (25 mL) equipped with a stir bar were added catalyst **1** (0.01 mmol, 2 mol %), KO^{t}Bu (0.25 mmol, 50 mol %), methyldiphenylphosphine oxide (0.5 mmol), alcohol (0.5 mmol), and tert-amyl alcohol (2 mL) under a nitrogen atmosphere in a glovebox. The reaction mixture was taken out of the glovebox, equipped with a condenser, and the solution was heated at 135 °C (oil bath temperature) with stirring in an open system under nitrogen flow for 48 h. After cooling, the reaction mixture was transferred to an RB flask. The solvent was removed under reduced pressure; the reaction mixture was dissolved in chloroform and washed with water and brine. The collected organic layer was dried over anhydrous sodium sulfate and concentrated in vacuum. The resultant residue was purified by silica gel (100-200 mesh) column chromatography using an ethyl acetate/hexane mixture as an eluent. Yields were calculated for isolated products.

Procedure for Control Experiment with Aldehyde.

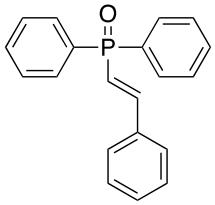
To a Schlenk flask (25 mL) equipped with a stir bar were added catalyst **1** (0.01 mmol, 2 mol %), KO^{t}Bu (0.25 mmol, 50 mol %), methyldiphenylphosphine oxide (0.5 mmol), benzaldehyde (0.5 mmol), and tert-amyl alcohol (2 mL) under a nitrogen atmosphere in a glovebox. The reaction mixture was taken out of the glovebox, equipped with a condenser, and the solution was heated at 135 °C (oil bath temperature) with stirring in an open system under nitrogen flow for 48 h. After cooling, the reaction mixture was transferred to an RB flask and the solvent was evaporated under reduced pressure. The resultant residue was dissolved in chloroform and washed with water and brine. The collected organic layer was dried over anhydrous sodium sulfate and concentrated in vacuum. The residue obtained was purified by column chromatography (silica gel, 100-200 mesh). Yield was calculated for the isolated product.

Procedure for Deuteration Scrambling Experiment with Benzyl Alcohol-d_3.

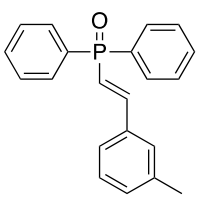
To a Schlenk flask (25 mL) equipped with a stir bar were added catalyst 1 (0.01 mmol, 2 mol %), KO^{t}Bu (0.25 mmol, 50 mol %), methyldiphenylphosphine oxide (0.5 mmol), benzyl alcohol-d3 (0.5 mmol), and *tert*-amyl alcohol (2 mL) under a nitrogen atmosphere in a glovebox. The reaction mixture was taken out of the glovebox, equipped with a condenser, and the solution was heated at 135 °C (oil bath temperature) with stirring in an open system under nitrogen flow for 48 h. After cooling, the reaction mixture was transferred to an RB flask and the solvent was evaporated under reduced pressure. The resultant residue was dissolved in chloroform and washed with water and brine. The collected organic layer was dried over anhydrous sodium sulfate and concentrated in vacuum. The residue obtained was purified by column chromatography (silica gel, 100-200 mesh). Yield was calculated for the isolated product.

Spectral Data of *α*-Alkenyl Phosphine Oxide Products

(*E*)-Diphenyl(styryl)phosphine Oxide (3.1a):[12] Purified by silica-gel column chromatography using an ethyl acetate/hexane (50:50) mixture as an eluent. White solid. Yield (120 mg, 79%; 435 mg, 62% for the 0.5 g scale reaction). IR (DCM): 748, 810, 1115, 1172, 1436, 1602, 3049 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.67 (s, 5H), 7.50-7.36 (m, 9H), 7.28 (m, 2H), 6.76 (t, J = 18.6 Hz, 1H). $^{13}C\{^1H\}$ NMR (176 MHz, $CDCl_3$): 147.7, 135.2 (d, $J_{C\text{-}P}$ = 17.7 Hz), 133.1 (d, J = 105.9 Hz), 132.0 (d, J = 1.5 Hz), 131.5 (d, J = 9.9 Hz), 130.2, 129.0, 127.9, 128.8 (d, J = 12.0 Hz), 119.4 (d, J = 104.5 Hz). ^{31}P NMR (162 MHz, $CDCl_3$): δ 24.56.

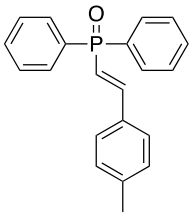


(*E*)-(3-Methylstyryl)diphenylphosphine Oxide (3.1b):[12] Purified by silica-gel column chromatography using an ethyl acetate/hexane (50:50) mixture as an eluent. White solid. Yield (105 mg, 66%). IR (DCM): 748, 1105, 1184, 1440, 1596, 3054 cm^{-1}. ^{1}H NMR (700 MHz, $CDCl_3$): δ 7.68−7.62 (m, 4H), 7.45 (t, J =



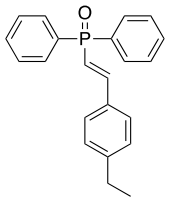
7.3 Hz, 2H), 7.41-7.36 (m, 4H), 7.24 (d, *J* = 9.2 Hz, 2H), 7.20-7.16 (m, 2H), 7.09 (d, *J* = 7.4 Hz, 1H), 6.73 (dd, J_1 = 22.2, J_2 = 17.5 Hz, 1H), 2.27 (s, 3H). ^{13}C NMR (176 MHz, $CDCl_3$): δ 147.9, 138.7, 135.2 (d, J_{C-P} = 18.0 Hz), 133.1 (d, J_{C-P} = 106.3 Hz), 132.0, 131.6 (d, J_{C-P} = 9.9 Hz), 131.1, 128.9, 128.8 (d, J_{C-P} = 12.1 Hz), 128.5, 125.2, 119.0 (d, J_{C-P} = 105.0 Hz), 21.4. ^{31}P NMR (162 MHz, $CDCl_3$): δ 25.67. MS-ESI: m/z 341.1, $[M + Na]^+$.

(*E*)-(4-Methylstyryl)diphenylphosphine Oxide (3.1c):[12] Purified by silica-gel column



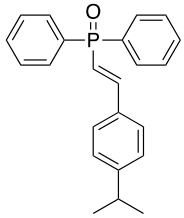
chromatography using an ethyl acetate/hexane (10:90) mixture as an eluent. White solid. Yield (103 mg, 65%). IR (DCM): 748, 1113, 1188, 1440, 1605, 3051 cm^{-1}. Minor amount of alkylated product is also present (20%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.70-7.66 (m, 5H), 7.47-7.38 (m, 9H), 7.34 (d, *J* = 8.0 Hz, 2H), 7.10 (d, *J* = 7.8 Hz, 2H), 6.98 (s, 1H), 6.78-6.60 (t, *J* = 18.4 Hz, 1H), 2.29 (s, 3H), 2.22 (s, 1H). ^{13}C NMR (176 MHz, $CDCl_3$): δ 147.7 (d, J_{C-P} = 3.4 Hz), 140.6, 133.2 (d, J_{C-P} = 105.7 Hz), 132.5 (d, J_{C-P} = 18.0 Hz), 131.9 (d, J_{C-P} = 2.2 Hz), 131.5 (d, J_{C-P} = 9.9 Hz), 130.9 (d, J_{C-P} = 9.3 Hz), 129.7, 129.4, 128.8 (d, J_{C-P} = 11.7 Hz), 128.7 (d, J_{C-P} = 12.1 Hz), 128.0, 127.9, 126.8 (d, J_{C-P} = 28.2 Hz), 117.9 (d, J_{C-P} = 105.3 Hz), 21.5. ^{31}P NMR (162 MHz, $CDCl_3$): δ 31.72, 24.83. MS-ESI: m/z 341.1, $[M + Na]^+$.

(*E*)-(4-Ethylstyryl)diphenylphosphine Oxide (3.1d): Purified by silica-gel column

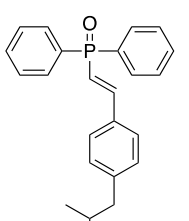


chromatography using an ethyl acetate/hexane (10:90) mixture as an eluent. White solid. Yield (91 mg, 55%). IR (DCM): 751, 1107, 1191, 1443, 1603, 3048 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.73-7.60 (m, 4H), 7.45-7.34 (m, 9H), 7.11 (d, *J* = 7.9 Hz, 2H), 6.74-6.65 (t, *J* = 20 Hz, 1H), 2.55 (q, *J* = 7.6 Hz, 2H), 1.13 (t, *J* = 7.6 Hz, 3H). ^{13}C NMR (176 MHz, $CDCl_3$): δ 147.7, 146.9, 133.1 (d, J_{C-P} = 105.0 Hz), 132.7 (d, J_{C-P} = 17.7 Hz), 131.9, 131.5 (d, J_{C-P} = 9.2 Hz), 128.6 (d, J_{C-P} = 11.6 Hz), 128.4, 127.9, 28.8, 15.4. ^{31}P NMR (162 MHz, $CDCl_3$): δ 24.92. HRMS (ESI) Calcd. for $C_{22}H_{21}OPNa$ $[M + Na]^+$: 355.1222, Found: 355.1232.

(*E*)-(4-Isopropylstyryl)diphenylphosphine Oxide (3.1e):[11a] Purified by silica-gel column chromatography using an ethyl acetate/hexane (50:50) mixture as an eluent. White solid. Yield (138 mg, 80%). IR (DCM): 746, 1099, 1187, 1439, 1596, 3049 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.10-7.89 (m, 1H), 7.67 (s, 3H), 7.45-7.37 (m, 9H), 7.16 (t, *J* = 7.3 Hz, 2H), 6.71 (s, 1H), 2.90-2.74 (m, 1H), 1.16 (d, *J* = 6.6 Hz, 6H). $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$): δ 151.4, 147.7, 131.9, 131.9, 131.5, 131.4, 128.6, 128.5, 127.9, 127.7, 126.9, 126.1, 124.3, 34.0, 23.8. ^{31}P NMR (162 MHz, $CDCl_3$): δ 25.56. MS-ESI: m/z 369.1, $[M + Na]^+$.



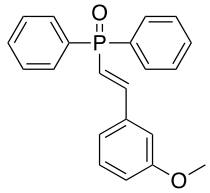
(*E*)-(4-Isobutylstyryl)diphenylphosphine Oxide (3.1f): Purified by silica-gel column chromatography using ethyl acetate/hexane (50:50) mixture as an eluent. Yellow solid. Yield (112 mg, 62%). IR (DCM): 751, 1103, 1191, 1444, 1608, 3048 cm^{-1}. ^{1}H NMR (700 MHz, $CDCl_3$): δ 7.70 (s, 4H), 7.46 – 7.28 (m, 9H), 7.09 (d, *J* = 6.4 Hz, 2H), 6.73 (s, 1H), 2.42 (d, *J* = 6.6 Hz, 1H), 1.82 – 1.78 (m, 1H), 0.83 (d, *J* = 6.0 Hz, 6H). ^{13}C NMR (176 MHz, $CDCl_3$): δ 147.8, 144.4, 133.1 (d, J_{C-P} = 108.7 Hz), 131.9, 131.6, 129.9, 129.7, 128.7, 128.3 (d, J_{C-P} = 6.8 Hz), 127.8, 45.3, 30.3, 22.4. ^{31}P NMR (162 MHz, $CDCl_3$): δ 25.40. HRMS (ESI) Calcd. for $C_{24}H_{25}OP$ $[M + H]^+$: 361.1716, Found: 361.1704.



(*E*)-(4-(*tert*-Butyl)styryl)diphenylphosphine oxide (3.1g):[11a] Purified by silica-gel column chromatography using ethyl acetate/hexane (50:50) mixture as an eluent. White solid. Yield (139 mg, 77%). IR (DCM): 748, 1098, 1191, 1443, 1603, 3046 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.67 (dd, J_1 = 11.1, J_2 = 7.8 Hz, 4H), 7.47 – 7.37 (m, 9H), 7.32 (d, *J* = 8.3 Hz, 2H), 6.80 – 6.64 (dd, J_1 = 18 Hz, J_2 = 21.6 Hz, 1H), 1.23 (s, 9H). ^{13}C NMR (176 MHz, $CDCl_3$): δ 153.6, 147.4, 133.2 (d, J_{C-P} = 103.8 Hz), 132.4 (d, J_{C-P} = 17.5 Hz), 131.8, 131.4 (d, J_{C-P} = 8.8 Hz), 128.6 (d, J_{C-P} = 11.4 Hz),

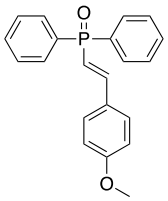
127.6, 125.8, 118.2 (d, J_{C-P} = 104.7 Hz), 34.8, 31.2. ^{31}P NMR (162 MHz, $CDCl_3$): δ 24.90. MS-ESI: *m/z* 383.1, $[M + Na]^+$.

(*E*)-(3-Methoxystyryl)diphenylphosphine oxide (3.1h):[13a] Purified by silica-gel column



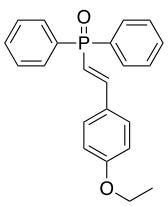
chromatography using ethyl acetate/hexane (50:50) mixture as an eluent. White solid. Yield (75 mg, 45%). IR (DCM): 751, 1099, 1195, 1452, 1601, 3041 cm^{-1}. ^{1}H NMR (700 MHz, $CDCl_3$): δ 7.78 (dd, J_1 = 11.8, J_2 = 7.6 Hz, 4H), 7.57 (t, J = 7.2 Hz, 2H), 7.52 – 7.47 (m, 5H), 7.32 (t, J = 7.9 Hz, 1H), 7.14 (d, J = 7.6 Hz, 1H), 7.07 (s, 1H), 6.94 (dd, J_1 = 8.2, J_2 = 2.1 Hz, 1H), 6.87 – 6.79 (m, 1H), 3.84 (s, 3H). ^{13}C NMR (176 MHz, $CDCl_3$): δ 160.1, 147.7, 136.6 (d, J_{C-P} = 18.1 Hz), 133.0 (d, J_{C-P} = 107.5 Hz), 132.1, 131.6 (d, J_{C-P} = 9.9 Hz), 130.0, 128.8 (d, J_{C-P} = 12.1 Hz), 120.6, 119.7 (d, J_{C-P} = 104.4 Hz), 116.1, 112.9, 55.5. ^{31}P NMR (162 MHz, $CDCl_3$): δ 24.54. MS-ESI: *m/z* 357.1, $[M + Na]^+$.

(*E*)-(4-Methoxystyryl)diphenylphosphine oxide (3.1i):[12] Purified by silica-gel column



chromatography using ethyl acetate/hexane (10:90) mixture as an eluent. White solid. Yield (125 mg, 75%). IR (DCM): 748, 1107, 1199, 1447, 1598, 3051 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.75 – 7.69 (m, 3H), 7.67 (m, 2H), 7.47 – 7.43 (m, 3H), 7.38 (m, 4H), 7.27 – 7.23 (m, 1H), 6.92 – 6.81 (m, 3H). 3.75 (s, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ 158.1, 143.2 (d, J_{C-P} = 15.1 Hz), 133.5 (d, J_{C-P} = 105.6 Hz), 131.7 (d, J_{C-P} = 3 Hz), 131.5, 131.4, 131.3, 128.8, 128.6 (d, J_{C-P} = 9.9 Hz), 124.2, 124.0, 120.6, 119.5 (d, J_{C-P} = 104.5 Hz), 111.21, 55.46. ^{31}P NMR (162 MHz, $CDCl_3$): δ 25.37. MS-ESI: *m/z* 357.1, $[M + Na]^+$.

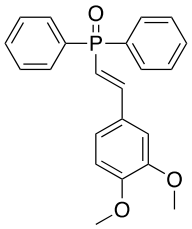
(*E*)-(4-Ethoxystyryl)diphenylphosphine oxide (3.1j): Purified by silica-gel column



chromatography using ethyl acetate/hexane (50:50) mixture as an eluent. White solid. Yield (108 mg, 62%). IR (DCM): 751, 1098, 1195, 1440, 1610, 3051 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.80 – 7.74 (m, 4H), 7.55-7.51 (m, 2H), 7.49-7.43 (m, 6H), 7.41 – 7.36 (m, 1H), 6.88 (d, J = 8.7 Hz, 2H), 6.74 – 6.61 (m, 1H), 4.05 (q, J =

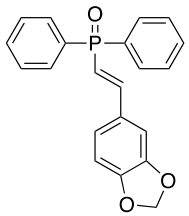
7.0 Hz, 2H), 1.42 (t, J = 7.0 Hz, 3H). ^{13}C NMR (176 MHz, $CDCl_3$): δ 160.7, 147.2, 133.4 (d, $J_{C\text{-}P}$ = 106.2 Hz), 131.8, 131.4 (d, $J_{C\text{-}P}$ = 9.7 Hz), 129.4, 128.6 (d, $J_{C\text{-}P}$ = 11.8 Hz), 127.8 (d, $J_{C\text{-}P}$ = 18.2 Hz), 116.0 (d, $J_{C\text{-}P}$ = 106.6 Hz), 114.8, 63.4, 14.8. ^{31}P NMR (162 MHz, $CDCl_3$): δ 24.93. HRMS (ESI) Calcd. for $C_{22}H_{21}O_2PNa$ $[M + Na]^+$: 371.1171, Found: 371.1167.

(*E*)-(3,4-Dimethoxystyryl)diphenylphosphine oxide (**3.1k**):[13e] Purified by silica-gel column



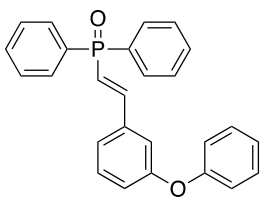
chromatography using ethyl acetate/hexane (60:40) mixture as an eluent. White solid. Yield (100 mg, 55%). IR (DCM): 748, 1103, 1196, 1442, 1608, 3045 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.78 (s, 4H), 7.63 – 7.38 (m, 7H), 7.11 – 7.05 (m, 2H), 6.86 (d, J = 8.1 Hz, 1H), 6.71 (s, 1H), 3.90 (s, 6H). ^{13}C NMR (176 MHz, $CDCl_3$): δ 151.0, 149.3, 147.5, 133.2 (d, $J_{C\text{-}P}$ = 108.6 Hz), 131.9, 131.5, 128.7 (d, $J_{C\text{-}P}$ = 10.2 Hz), 128.3 (d, $J_{C\text{-}P}$ = 17.2 Hz), 122.2, 116.5 (d, $J_{C\text{-}P}$ = 102.4 Hz), 111.1, 109.7, 56.1, 56.0. ^{31}P NMR (162 MHz, $CDCl_3$): δ 25.44. MS-ESI: *m/z* 387.1, $[M + Na]^+$.

(*E*)-(2-(Benzo[*d*][1,3]dioxol-5-yl)vinyl)diphenylphosphine oxide (**3.1l**):[13a] Purified by



silica-gel column chromatography using ethyl acetate/hexane (60:40) mixture as an eluent. White solid. Yield (109 mg, 63%). IR (DCM): 749, 1100, 1196, 1444, 1612, 3046 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.70-7.65 (m, 4H), 7.48 – 7.27 (m, 7H), 6.98 (s, 1H), 6.91 (d, J = 8.0 Hz, 1H), 6.73 (d, J = 8.0 Hz, 1H), 6.55 (t, J = 18.4 Hz, 1H), 5.92 (s, 2H). ^{13}C NMR (176 MHz, $CDCl_3$): δ 149.5, 148.5, 147.3 (d, $J_{C\text{-}P}$ = 3.7 Hz), 133.3 (d, $J_{C\text{-}P}$ = 105.7 Hz), 132.0, 131.5 (d, $J_{C\text{-}P}$ = 9.9 Hz), 129.8 (d, $J_{C\text{-}P}$ = 18.4 Hz), 128.7 (d, $J_{C\text{-}P}$ = 12.1 Hz), 124.1, 116.8 (d, $J_{C\text{-}P}$ = 106.1 Hz), 108.6, 106.5, 101.7. ^{31}P NMR (162 MHz, $CDCl_3$): δ 24.98. MS-ESI: *m/z* 371.1, $[M + Na]^+$.

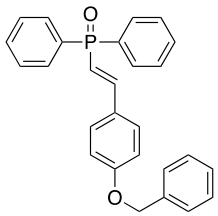
(*E*)-(3-Phenoxystyryl)diphenylphosphine oxide (**3.1m**): Purified by silica-gel column



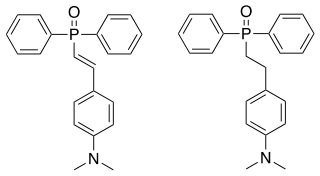
chromatography using ethyl acetate/hexane (60:40) mixture as an eluent. White solid. Yield (85 mg, 43%). IR (DCM): 750, 1103, 1198, 1439, 1608, 3051, 3083 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.86-7.75

(m, 4H), 7.58-7.51 (m, 6H), 7.41 – 7.27 (m, 4H), 7.26 – 7.10 (m, 3H), 7.02 (d, J = 8.0 Hz, 3H), 6.85 (dd, J_1 = 21.3, J_2 =14.1 Hz, 1H). ^{13}C NMR (176 MHz, $CDCl_3$): δ 157.9, 157.2 (d, J_{C-P} = 74.8 Hz), 156.8, 147.2, 137.0 (d, J_{C-P} = 16.2 Hz), 132.7 (d, J_{C-P} = 106.6 Hz), 132.1, 131.5, 130.3, 130.0, 129.9, 129.7 (d, J_{C-P} = 37.0 Hz), 128.8 (d, J_{C-P} = 9.8 Hz), 123.7, 123.6, 123.3 (d, J_{C-P} = 33.6 Hz), 122.9, 120.5, 120.0 (d, J_{C-P} = 103.1 Hz), 119.1, 117.7. ^{31}P NMR (162 MHz, $CDCl_3$): δ 24.92. HRMS (ESI) Calcd. for $C_{26}H_{21}O_2P$ $[M + H]^+$: 397.1279, Found: 397.1281.

(*E*)-(4-(Benzyloxy)styryl)diphenylphosphine oxide (**3.1n**): Purified by silica-gel column chromatography using ethyl acetate/hexane (50:50) mixture as an eluent. White solid. Yield (146 mg, 71%). IR (DCM): 757, 1096, 1195, 1442, 1609, 3049 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.76-7.63 (t, J = 7.6 Hz, 4H), 7.47-7.38 (m, 8H), 7.35-7.18 (m, 6H), 6.89 (d, J = 8.3 Hz, 2H), 6.59 (t, J = 18.8 Hz, 1H), 5.01 (s, 2H). ^{13}C NMR (176 MHz, $CDCl_3$): δ 160.4, 147.2, 136.5, 133.3 (d, J_{C-P} = 106.1 Hz), 131.9, 131.5 (d, J_{C-P} = 8.9 Hz), 129.5, 128.7, 128.7, 128.6, 128.2, 127.5, 116.4 (d, J_{C-P} = 105.8 Hz), 115.2, 70.1. ^{31}P NMR (162 MHz, $CDCl_3$): δ 24.99. HRMS (ESI) Calcd. for $C_{26}H_{21}O_2P$ $[M + H]^+$: 411.1436, Found: 411.1440.

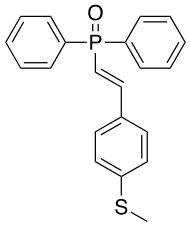


(*E*)-(4-(Dimethylamino)styryl)diphenylphosphine oxide and **(4-(dimethylamino)phenethyl)diphenylphosphine oxide** (**3.1o**):[25] Purified by silica-gel column chromatography using ethyl acetate/hexane (50:50) mixture as an eluent. White solid. Yield (95 mg, 55%). IR (DCM): 756, 1105, 1196, 1440, 1612, 3051 cm^{-1}. *Both alkenyl and alkylation products are present in 50:50 ratio*. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.66 (dt, J_1 = 20.8, J_2 =10.4 Hz, 4H), 7.43-7.34 (m, 6H), 7.31 (d, J = 8.8 Hz, 2H), 7.28-7.17 (m, 1H), 3.65 (ddd, J_1 = 6.6, J_2 = 4.2, J_3 = 2.5 Hz, 3H), 2.90 (s, 6H), 1.75 (ddd, J_1 = 6.6, J_2 = 4.2, J_3 = 2.5 Hz, 3H). ^{13}C NMR (176 MHz, $CDCl_3$): δ 151.7, 147.9 (d, J_{C-P} = 4.1 Hz), 133.8 (d, J_{C-P} = 105.4 Hz), 131.7 (d, J_{C-P} = 2.5 Hz), 131.5 (d, J_{C-P} = 9.8 Hz), 129.4, 128.6 (d, J_{C-P} = 12.0 Hz), 123.2 (d, J_{C-P} = 18.5 Hz), 112.4 (d,



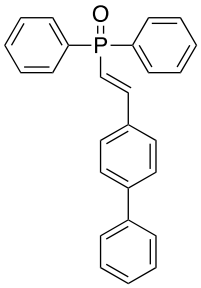
J_{C-P} = 109.1 Hz), 111.8, 40.3. ^{31}P NMR (162 MHz, $CDCl_3$): δ 25.72. MS-ESI: *m/z* 370.1, [M + Na]$^+$.

(*E*)-(4-(Methylthio)styryl)diphenylphosphine oxide (**3.1p**):[13a] Purified by silica-gel column



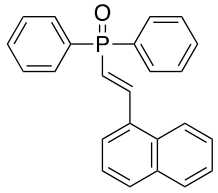
chromatography using ethyl acetate/hexane (50:50) mixture as an eluent. White solid. Yield (117 mg, 67%). IR (DCM): 758, 1098, 1199, 1438, 1612, 3055 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.67 (s, 4H), 7.47 – 7.31 (m, 9H), 7.12 (d, *J* = 7.8 Hz, 2H), 6.71 (s, 1H), 2.39 (s, 3H). ^{13}C NMR (176 MHz, $CDCl_3$): δ 147.0, 141.7, 133.1 (d, J_{C-P} = 105.3 Hz), 131.9, 131.8 (d, J_{C-P} = 15.9 Hz), 131.5, 128.7, 128.2, 126.1, 118.1 (d, J_{C-P} = 106.9 Hz), 15.3. ^{31}P NMR (162 MHz, $CDCl_3$): δ 24.64. MS-ESI: *m/z* 373.1, [M + Na]$^+$.

(*E*)-(2-([1,1'-Biphenyl]-4-yl)vinyl)diphenylphosphine oxide (**3.1q**):[9a] Purified by silica-gel



column chromatography using ethyl acetate/hexane (50:50) mixture as an eluent. White solid. Yield (102 mg, 54%). IR (DCM): 756, 1102, 1201, 1441, 1610, 3052, 3081 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.09 (d, *J* = 8.4 Hz, 1H), 7.71 (s, 4H), 7.60-7.50 (m, 7H), 7.47-7.34 (m, 8H), 7.28 (m, 1H), 6.81 (t, *J* = 19 Hz, 1H). ^{13}C NMR (176 MHz, $CDCl_3$): δ 147.3, 143.0, 140.3, 134.2 (d, J_{C-P} = 18.0 Hz), 133.1 (d, J_{C-P} = 106.0 Hz), 132.1, 131.5 (d, J_{C-P} = 9.9 Hz), 130.9 (d, J_{C-P} = 9.2 Hz), 129.0, 128.8 (d, J_{C-P} = 12.1 Hz), 128.4, 127.9, 127.6, 127.4 (d, J_{C-P} = 15.7 Hz), 127.2, 119.2 (d, J_{C-P} = 104.4 Hz). ^{31}P NMR (162 MHz, $CDCl_3$): δ 25.10. MS-ESI: *m/z* 403.1, [M + Na]$^+$.

(*E*)-(2-(Naphthalen-1-yl)vinyl)diphenylphosphine oxide (**3.1r**):[12] Purified by silica-gel



column chromatography using ethyl acetate/hexane (50:50) mixture as an eluent. White solid. Yield (106 mg, 60%). IR (DCM): 1097, 1196, 1438, 1609, 2979, 3049, 3080 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.35 (s, 1H), 8.15 (s, 1H), 7.99-7.79 (m, 6H), 7.72 (d, *J* = 7.5 Hz, 1H).7.53 (s, 8H), 7.35 (s, 1H), 7.28-7.03 (m, 1H). ^{13}C NMR (176 MHz, $CDCl_3$): δ 145.0, 133.9, 133.6, 132.9, 132.0, 131.6, 131.1, 130.4,

128.8, 128.7, 126.9, 126.2, 125.6 (d, J_{C-P} = 12.9 Hz), 125.4, 124.8, 123.4. ^{31}P NMR (162 MHz, $CDCl_3$): δ 24.18. MS-ESI: *m/z* 377.1, $[M + Na]^+$.

(*E*)-(2-(Naphthalen-2-yl)vinyl)diphenylphosphine oxide (**3.1s**):[9a] Purified by silica-gel column chromatography using ethyl acetate/hexane (50:50) mixture as an eluent. White solid. Yield (71 mg, 40%). IR (DCM): 837, 1102, 1198, 1440, 1610, 2981, 3048 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.64 (s, 1H), 8.06 (d, *J* = 8.5 Hz, 1H), 7.91 (d, *J* = 8.0 Hz, 1H), 7.86-7.82 (m, 2H), 7.76-7.70 (m, 4H), 7.63 (d, *J* = 8.2 Hz, 1H), 7.56-7.43 (m, 7H), 7.19 (s, 1H), 6.92 (s, 1H). ^{13}C NMR (176 MHz, $CDCl_3$): δ 148.0, 136.0, 134.3, 133.4, 132.9 (d, J_{C-P} = 69.8 Hz), 132.6, 132.1, 131.6 (d, J_{C-P} = 10.0 Hz), 129.6 (d, J_{C-P} = 4.9 Hz), 128.9, 128.8 (d, J_{C-P} = 2.6 Hz), 128.7, 128.7, 128.4, 127.9 (d, J_{C-P} = 7.9 Hz), 127.3, 126.9, 125.6, 123.5, 119.2 (d, J_{C-P} = 106.7 Hz). ^{31}P NMR (162 MHz, $CDCl_3$): δ 25.84. HRMS (ESI) Calcd. for $C_{24}H_{19}O_2PNa$ $[M + Na]^+$: 377.1174, Found: 377.1178.

(*E*)-(2-(Anthracen-9-yl)vinyl)diphenylphosphine oxide (**3.1t**): Purified by silica-gel column chromatography using ethyl acetate/hexane (50:50) mixture as an eluent. Yellow solid. Yield (99 mg, 49%). IR (DCM): 773, 840, 1048, 1202, 1447, 1609, 2984, 3049, 3081 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.37-8.27 (m, 2H), 8.08 (dd, J_1 =6.2, J_2 = 2.3 Hz, 2H), 7.88 (dd, J_1 = 6.3, J_2 = 3.2 Hz, 2H), 7.82-7.76 (m, 4H), 7.50-7.41 (m, 6H), 7.37-7.29 (m, 4H), 6.79 (t, *J* = 6.8 Hz, 1H). ^{13}C NMR (176 MHz, $CDCl_3$): δ 145.4, 134.1, 132.9 (d, J_{C-P} = 106.7 Hz), 132.1, 131.5 (d, J_{C-P} = 8.3 Hz), 131.3, 130.7 (d, J_{C-P} = 16.7 Hz), 129.1, 128.9, 128.8, 128.1, 127.3 (d, J_{C-P} = 45.8 Hz), 126.4, 125.4, 125.1, 123.7, 115.8. ^{31}P NMR (162 MHz, $CDCl_3$): δ 24.11. HRMS (ESI) Calcd. for $C_{28}H_{21}OPNa$ $[M + Na]^+$: 427.1217, Found: 427.1222.

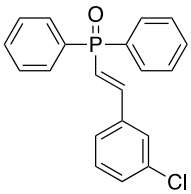
(*E*)-Diphenyl(2-(pyren-4-yl)vinyl)phosphine oxide and Diphenyl(2-(pyren-4-yl)ethyl)phosphine oxide (**3.1u**): Purified by silica-gel column chromatography using ethyl acetate/hexane (50:50) mixture as an eluent. White solid. Yield (128 mg, 60%). IR (DCM): 756, 840, 1097, 1196, 1445, 1610, 2981, 3048, 3079 cm^{-1}. *Both alkenyl and alkylation products are present in 50:50 ratio*. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.67-8.55 (m, 1H), 8.37 (d, J = 9.3 Hz, 1H), 8.27 (d, J = 8.1 Hz, 1H), 8.17 (d, J = 7.6 Hz, 2H), 8.11 (dd, J_1 = 6.9, J_2 = 2.6 Hz, 2H), 8.08 (d, J = 3.0 Hz, 1H), 8.02-7.92 (m, 4H), 7.84-7.73 (m, 5H), 7.56-7.42 (m, 8H), 7.20 (s, 3H), 7.08 (dd, J_1 = 23.2, J_2 = 17.3 Hz, 1H), 3.61 (dd, J_1 = 16.2, J_2 = 8.3 Hz, 1H), 2.75 (dd, J_1 = 16.5, J_2 = 10.9 Hz, 1H). $^{13}C\{^{1}H\}$ NMR (176 MHz, $CDCl_3$): δ 144.7, 133.3, 132.6, 132.3, 132.0, 131.9, 131.6, 131.5, 131.4, 130.9, 130.8, 128.8, 128.8, 128.7, 128.6, 128.3, 127.8, 127.4, 127.3, 127.0, 126.9, 126.3, 126.0, 125.8, 125.1, 125.0, 124.9, 124.7, 124.1, 122.8, 122.5. ^{31}P NMR (162 MHz, $CDCl_3$): δ 32.11, 24.91. HRMS (ESI) Calcd. for $C_{30}H_{22}OP$ $[M + H]^+$: 429.1163, Found: 429.1163.

(*E*)-Diphenyl(2-vinyl-ferrocene)phosphine oxide (**3.1v**): Purified by silica-gel column chromatography using ethyl acetate/hexane (50:50) mixture as an eluent. White solid. Yield (128 mg, 62%). IR (DCM): 697, 1049, 1102, 1203, 1626, 1932, 1989, 2048, 2981, cm^{-1}. ^{1}H NMR (700 MHz, $CDCl_3$): δ 7.70-7.17 (m, 10H), 6.31 (s, 2H), 5.20 (s, 1H), 4.34 (d, J = 45.2 Hz, 4H), 4.04 (s, 4H). ^{31}P NMR (162 MHz, $CDCl_3$): δ 24.80. HRMS (ESI) Calcd. for $C_{24}H_{22}OPFe$ $[M + H]^+$: 413.095, Found: 413.095.

(*E*)-(3-Fluorostyryl)diphenylphosphine oxide (**3.1w**):[26] Purified by silica-gel column chromatography using ethyl acetate/hexane (60:40) mixture as an eluent. White solid. Yield (82 mg, 51%). IR (DCM): 726, 1196, 1440, 1610, 3051 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.68 (t, J = 7.2 Hz, 4H), 7.50-7.39 (m, 7H), 7.30-7.18 (m, 2H), 7.15 (d, J = 9.6 Hz, 1H), 6.98 (t, J = 7.3 Hz, 1H), 6.80 (t, J = 15.0 Hz,

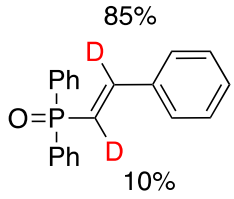
1H). ^{13}C NMR (176 MHz, $CDCl_3$): δ 163.2 (d, J_{C-F} = 247.0 Hz), 146.3, 137.5 (d, J_{C-P} = 7.3 Hz), 137.4 (d, J_{C-P} = 7.4 Hz), 132.7 (d, J_{C-P} = 107.5 Hz), 132.2, 131.5 (d, J_{C-P} = 9.9 Hz), 130.6 (d, J_{C-P} = 8.2 Hz), 128.8 (d, J_{C-P} = 12.1 Hz), 124.0, 121.1 (d, J_{C-P} = 103.7 Hz), 117.1 (d, J_{C-F} = 21.4 Hz), 114.1 (d, J_{C-F} = 21.9 Hz). ^{31}P NMR (162 MHz, $CDCl_3$): δ 24.12. MS-ESI: *m/z* 345.1, $[M + Na]^+$.

(*E*)-(3-Chlorostyryl)diphenylphosphine oxide (**3.1x**):[11a] Purified by silica-gel column



chromatography using ethyl acetate/hexane (50:50) mixture as an eluent. Yellow solid. Yield (34 mg, 20%). IR (DCM): 1102, 1186, 1440, 1610, 3047 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.77 (s, 4H), 7.60 – 7.51 (m, 8H), 7.42-7.32 (m, 3H), 6.90 (s, 1H). ^{13}C{^{1}H} NMR (176 MHz, $CDCl_3$): δ 146.0, 137.0, 136.9, 134.9, 132.1, 131.5, 130.2, 130.0, 128.8, 128.7, 127.4, 126.3. ^{31}P NMR (162 MHz, $CDCl_3$): δ 24.20.

(*E*)-Diphenyl(2-phenylvinyl-1,2-d2)phosphine oxide (**2a**-d_2): Purified by silica-gel column



chromatography using ethyl acetate/hexane (50:50) mixture as an eluent. White solid. Yield (114 mg, 75%). IR (DCM): 743, 813, 1119, 1181, 1446, 1605, 3055 cm^{-1}.^{1}H NMR (400 MHz, $CDCl_3$): δ 7.80-7.75 (m, 4H), 7.57-7.46 (m, 8H), 7.30-7.18 (m, 3H), 6.91 – 6.82 (m, 1H). ^{2}D NMR (400 MHz, $CHCl_3$): δ 7.52. ^{13}C NMR (176 MHz, $CDCl_3$): δ 147.7, 135.2 (dd, J_1 = 17.8, J_2 = 13.0 Hz), 133.1 (d, J = 105.9 Hz), 132.0 (d, J = 1.5 Hz), 131.5 (d, J = 9.9 Hz), 130.2, 129.0, 128.8 (d, J = 12.0 Hz), 127.92, 119.3 (dd, J_1 = 104.6, J_2 = 25.2 Hz). HRMS (ESI) Calcd. for $C_{20}H_{16}DOP$ $[M]^+$: 305.1068, Found: 305.1074.

X-Ray Analysis of α-Alkenyl Phosphine Oxide Products 3.1e, **3.1k** and **3.1w**: Crystals suited for single crystal X-Ray diffraction measurements were mounted on a glass fiber. Geometry and intensity data were collected with a Rigaku Smartlab X-ray diffractometer equipped with graphite-monochromated Cu-Kα radiation (λ = 1.54184 Å, multilayer optics). Intensities were integrated with SAINT+[27] and corrected for absorption with SADABS[28]. The

structures were solved by direct methods and refined on F^2 with SHELXL-97[29] using Olex-2[30] software.

Crystal Data of α-Alkenyl Phosphine Oxide Product **3.1e**: $C_{23}H_{23}OP$, white solid, M = 346.38 gm/mol, monoclinic with space group P121/n 1, a = 10.5848 (2) Å, b = 10.7353 (19) Å, c = 17.1475 (6) Å, α = 90°, β = 91°, γ = 90°, V = 1948.21 (9) $Å^3$, Z = 4, F(000) = 736, μ-(CuKα) = 1.287 mm^{-1} , $2\theta_{max}$ = 75.086, ρ_{calcd} = 1.181 g/cm^3 , T = 100.00(10) K, 3944 Reflections collected, 3831 unique, R_1 = 0.0327, WR_2 = 0.0845 (all data). The structure has been deposited at the CCDC data center and can be retrieved using the deposit number **CCDC 2077423**.

Crystal Data of α-Alkenyl Phosphine Oxide Product **3.1k**: $C_{22}H_{21}O_3P$, white solid, M = 364.12 gm/mol, monoclinic with space group P121/c 1, a = 11.1492 (1) Å, b = 8.9181 (1) Å, c = 20.0809 (2) Å, α = 90°, β = 99.8°, γ = 90°, V = 1967.60 (3) $Å^3$, Z = 4, F(000) = 716, μ-(CuKα) = 1.342 mm^{-1} , $2\theta_{max}$ = 75.2070, ρ_{calcd} = 1.145 g/cm^3 , T = 290.00 (5) K, 3991 Reflections collected, 3660 unique, R_1 = 0.1581, WR_2 = 0.4147 (all data). The structure has been deposited at the CCDC data center and can be retrieved using the deposit number **CCDC 2077424**.

Crystal Data of α-Alkenyl Phosphine Oxide Product **3.1w**: $C_{20}H_{16}FOP$, white solid, M = 322.30 gm/mol, monoclinic with space group P121/n 1, a = 8.6776 (2) Å, b = 17.9368 (3) Å, c = 11.2529 (2) Å, α = 90°, β = 107.4°, γ = 90°, V = 1671.07 (6) $Å^3$, Z = 4, F(000) = 672, μ-(CuKα) = 1.554 mm^{-1} , $2\theta_{max}$ = 74.9380, ρ_{calcd} = 1.281 g/cm^3 , T = 185.00 (50) K, 3353 Reflections collected, 3115 unique, R_1 = 0.0418, WR_2 = 0.1137 (all data). The structure has been deposited at the CCDC data center and can be retrieved using the deposit number **CCDC 2077425**.

3.6 NOTES AND REFERENCES

(1) (a) Corbridge, D. E. C. Phosphorus: Chemistry, Biochemistry and Technology, 6th ed.; CRC Press: London, 2013. (b) Sobkowski, M.; Kraszewski, A.; Stawinski, J. *Recent Advances in H-Phosphonate Chemistry. Part 1. H-Phosphonate Esters: Synthesis and Basic Reactions. In Phosphorus Chemistry II: Synthetic Methods*. Montchamp, J. -L., Ed.; Springer International Publishing: Cham, 2015; p 137.

(2) (a) Montchamp, J. -L. Phosphinate Chemistry in the 21st Century: A Viable Alternative to the Use of Phosphorus Trichloride in Organophosphorus Synthesis. *Acc. Chem. Res.* **2011**, *47*, 77-87. (b) Ma, Y.-N.; Li, S.-X.; Yang, S.-D. New Approaches for Biaryl-Based Phosphine Ligand Synthesis via P═O Directed C–H Functionalizations. *Acc. Chem. Res.* **2017**, *50*, 1480-1492.

(3) (a) Moonen, K.; Laureyn, I.; Stevens, C. V. Synthetic Methods for Azaheterocyclic Phosphonates and Their Biological Activity. *Chem. Rev*. **2004**, *104*, 6177−6216. (b) Corbridge, D. E. C. *Phosphorus: Chemistry, Biochemistry and Technology*, 6th ed.; CRC Press: London, 2013. (c) Horsman, G. P.; Zechel, D. L. Phosphonate Biochemistry. *Chem. Rev.* **2017**, *117*, 5704−5783. (d) Ni, H.; Chan, W. L. Lu, Y. Phosphine-Catalyzed Asymmetric Organic Reactions. *Chem. Rev.* **2018**, *118*, 9344-9411.

(4) (a) Barbaro, P.; Bianchini, C.; Giambastiani, G.; Togni, A. The first tridentate phosphine ligand combining planar, phosphorus and carbon chirality. *Chem. Commun.* **2002**, *22*, 2672-2673. (b) Maj, A. M.; Pietrusiewicz, K. M.; Suisse, I.; Agbossou, F.; Montreux, A. P-Chiral β-Aminophosphine Oxides vs. β-Aminophosphines as Auxiliaries for Ruthenium Catalysed Enantioselective Transfer Hydrogenation of Arylketones. *J. Organomet. Chem.* 2001, *626*, 157-160.

(5) Baumgartner, T.; Reáu, R. Organophosphorus π-Conjugated Materials. *Chem. Rev.* **2006**, *106*, 4681−4727.

(6) (a) Grushin, V. V. Mixed Phosphine−Phosphine Oxide Ligands. *Chem. Rev*. **2004**, *104*, 1629-1662. (b) Inoue, H.; Nagaoka, Y.; Tomioka, K. A New Methodology for Synthesis of a Chiral Phosphinocarboxylic Acid through Michael Cyclization−Aldol Tandem Reaction of Chiral α,β,χ,ψ-Unsaturated Bisphosphine Oxide and Application in Palladium-Catalyzed Asymmetric Allylic Alkylation. *J. Org. Chem*. **2002**, *67*, 5864-5867.

(7) Coudray, L.; Montchamp, J. -L. Recent Developments in the Addition of Phosphinylidene-Containing Compounds to Unactivated Unsaturated Hydrocarbons: Phosphorus-Carbon Bond-Formation via Hydrophosphinylation and Related Processes. *Eur. J. Org. Chem.* **2008**, 3601-3613.

(8) Santelli-Rouvier, C. A Simple Preparation of Vinyl- or Allyldiphenylphosphine Oxides. *Synth*. **1988**, *1*, 64-66.

(9) (a) Liu, W.-Q.; Lei, T.; Zhou, S.; Yang, X.-L.; Li, J.; Chen, B.; Sivaguru, J.; Tung, C.-H.; Wu, L.-Z. Cobaloxime Catalysis: Selective Synthesis of Alkenylphosphine Oxides under Visible Light. *J. Am. Chem. Soc*. **2019**, *141*, 13941−13947. (b) Chen, T.; Zhao, C.-Q.; Han, L.-B. Hydrophosphorylation of Alkynes Catalyzed by Palladium: Generality and Mechanism. *J. Am. Chem. Soc.* **2018**, *140*, 3139–3155. (c) Niu, M.; Fu, H.; Jiang, Y.; Zhao, Y. Copper Catalyzed Addition of H-Phosphine Oxides to Alkynes Forming Alkenylphosphine Oxides. *Chem. Commun*. **2007**, 272-274. (d) Han, L-.B.; Zhang, C.; Yazawa, H.; Shimada, S. Efficient and Selective Nickel-Catalyzed Addition of H-P(O) and H-S Bonds to Alkynes. *J. Am. Chem. Soc*. **2004**, *126*, 5080–5081. (e) Zhao, C. Q.; Han, L. B.; Goto, M.; Tanaka, M. Rhodium-Catalyzed Hydrophosphorylation of Terminal Alkynes Leading to Highly Selective Formation of

(*E*)-Alkenylphosphonates: Complete Reversal of Regioselectivity to the Palladium-Catalyzed Counterpart. *Angew. Chem. Int. Ed.* **2001**, *40*, 1929–1932.

(10) Huang, T.; Saga, Y.; Guo, H.; Yoshimura, A.; Ogawa, A.; Han, L.-B. Radical Hydrophosphorylation of Alkynes with $R_2P(O)H$ Generating Alkenylphosphine Oxides: Scope and Limitations. *J. Org. Chem.* **2018**, *83*, 8743−8749.

(11) Wang, X.; Xiao, Bo.; Cheng, J.-B.; Yang, B.; Li, G.-Z. Ceric(IV) Ammonium Nitrate Mediated Phosphorylation of Alkenes: Easy Access to (E)-Vinylphosphonates. *Eur. J. Org. Chem*. **2019**, 2065–2070. (b) Gui, Q.; Hu, L.; Chen, X.; Liu, J.; Tan, Z. Stereoselective Synthesis of Vinylphosphonates and Phosphine Oxides via Silver-catalyzed Phosphorylation of Styrenes. *Chem. Commun.* **2015**, *51*, 13922– 13924.

(12) (a) Hu, G; Gao, Y; Zhao, Y. Copper-Catalyzed Decarboxylative C–P Cross-Coupling of Alkynyl Acids with H-Phosphine Oxides: A Facile and Selective Synthesis of (E)-1-Alkenylphosphine Oxides. *Org. Lett*. **2014**, *16*, 4464–4467.

(13) (a) Liu, L.; Zhou, D.; Dong, J.; Zhou, Y.; Yin, S.-F.; Han, L.-B. Transition-Metal-Free C-P Bond Formation via Decarboxylative Phosphorylation of Cinnamic Acids with P(O)H Compounds. *J. Org. Chem.* **2018**, *83*, 4190–4196. (b) Xue, J.-F.; Zhou, S.-F.; Liu, Y.-Y.; Pan, X.; Zou, J.-P.; Asekun, O. T. Manganese(III)-Mediated Alkenyl C_{sp2}–P Bond Formation from the Reaction of β-Nitrostyrenes with Dialkyl Phosphites. *Org. Biomol. Chem.* **2015**, *13*, 4896–4902. (c) Wu, Y.; Liu, L.; Yan, K.; Xu, P.; Gao, Y.; Zhao, Y. Nickel-Catalyzed Decarboxylative C–P Cross-Coupling of Alkenyl Acids with P(O)H Compounds. *J. Org. Chem.* **2014**, *79*, 8118–8127. (d) Li, X.; Yang, F.; Wu, Y.; Wu, Y. Rh(I)-Catalyzed Decarboxylative Transformations of Arenecarboxylic Acids: Ligand- and Reagent-Controlled Selectivity toward Hydrodecarboxylation or Heck−Mizoroki Products. *Org. Lett.* **2014**, *16*, 992–995. (e) Liu, L.; Wang, Y.; Zeng, Z.; Xu, P.; Gao, Y.; Yin, Y.; Zhao, Y. Nickel(II)-Magnesium-Catalyzed Cross-

Coupling of 1,1-Dibromo-1-alkenes with Diphenylphosphine Oxide: One-Pot Synthesis of (E)-1-Alkenylphosphine Oxides or Bisphosphine Oxides. *Adv. Synth. Catal.* **2013**, *355*, 659–666. (f) Evano, G.; Tadiparthi, K.; Couty, F. Copper-Mediated Cross-Coupling of 1,1-Dibromo-1-Alkenes with Dialkyl Phosphites: a Convenient Synthesis of 1-Alkenylphosphonates. *Chem. Commun.* **2011**, *47*, 179–181. (g) Kabalka, G. W.; Guchhait, S. K. Synthesis of (E)- and (Z)- Alkenylphosphonates Using Vinylboronates. *Org. Lett.* **2003**, *5*, 729–731.

(14) For reviews, see: (a) Crabtree, R. H. Homogeneous Transition Metal Catalysis of Acceptorless Dehydrogenative Alcohol Oxidation: Applications in Hydrogen Storage and to Heterocycle Synthesis. *Chem. Rev*. **2017**, *117*, 9228−9246. (b) Gunanathan, C.; Milstein, D. Applications of Acceptorless Dehydrogenation and Related Transformations in Chemical Synthesis. *Science* **2013**, *341*, 1229712.

(15) (a) Yadav, V.; Landge, V. G.; Subaramanian, M.; Balaraman, E. Manganese-Catalyzed α-Olefination of Nitriles with Secondary Alcohols. *ACS Catal*. **2020**, *10*, 947−954. (b) Thiyagarajan, S.; Gunanathan, C. Ruthenium-Catalyzed α-Olefination of Nitriles Using Secondary Alcohols. *ACS Catal*. **2018**, *8*, 2473−2478. (c) Chakraborty, S.; Das, U. K.; Ben-David, Y.; Milstein, D. Manganese Catalyzed α-Olefination of Nitriles by Primary Alcohols. *J. Am. Chem. Soc*. **2017**, *139*, 11710−11713.

(16) (a) Gawali, S. S.; Pandia, B. K.; Gunanathan C. Manganese(I)-Catalyzed *α*-Alkenylation of Ketones Using Primary Alcohols. *Org. Lett*. **2019**, *21*, 3842−3847. (b) Pandia, B. K.; Gunanathan C. Manganese(I) Catalyzed *α*-Alkenylation of Amides using Alcohols with Liberation of Hydrogen and Water. *J. Org. Chem.* **2021**, *86*, 9994-10005. (c) Pandia, B. K.; Pattanaik, S.; Gunanathan C. Manganese(I) Catalyzed Cross-Coupling of Secondary Allylic Alcohols and Primary Alcohols. *Tetrahedron* **2021**, *101*, 132472.

(17) (a) Das, J.; Vellakkaran, M.; Sk, M.; Banerjee, D. Iron-Catalyzed Coupling of Methyl N-Heteroarenes with Primary Alcohols: Direct Access to E-Selective Olefins. *Org. Lett*. **2019**, *21*, 7514−7518. (b) Ramalingam, B. M.; Ramakrishna, I.; Baidya, M. Nickel-Catalyzed Direct Alkenylation of Methyl Heteroarenes with Primary Alcohols. *J. Org. Chem*. **2019**, *84*, 9819−9825. (c) Zhang, G.; Irrgang, T.; Dietel, T.; Kallmeier, F.; Kempe, R. Manganese-Catalyzed Dehydrogenative Alkylation or α-Olefination of Alkyl-Substituted N-Heteroarenes with Alcohols. *Angew. Chem. Int. Ed*. **2018**, *57*, 9131−9135. (d) Barman, M. K.; Waiba, S.; Maji, B. Manganese-Catalyzed Direct Olefination of Methyl-Substituted Heteroarenes with Primary Alcohols. *Angew. Chem. Int. Ed*. **2018**, *57*, 9126–9130. (e) Waiba, S.; Barman, M. K.; Maji, B. Manganese-Catalyzed Acceptorless Dehydrogenative Coupling of Alcohols with Sulfones: A Tool to Access Highly Substituted Vinyl Sulfones. *J. Org. Chem*. **2019**, *84*, 973–982.

(18) For reviews, see: (a) Corma, A.; Navas, J.; Sabater, M. J. Advances in One-Pot Synthesis Through Borrowing HydrogenCatalysis. *Chem. Rev*. **2018**, *118*, 1410−1459. (b) Crabtree, R. H. Homogeneous Transition Metal Catalysis of Acceptorless Dehydrogenative Alcohol Oxidation: Applications in Hydrogen Storage and to Heterocycle Synthesis. *Chem. Rev*. **2017**, *117*, 9228−9246. (c) Gunanathan, C.; Milstein, D. Bond Activation and Catalysis by Ruthenium Pincer Complexes. *Chem. Rev*. **2014**, *114*, 12024−12087.

(19) (a) Li, W.-Z.; Wang, Z.-X. Nickel Catalyzed Coupling of $R_2P(O)Me$ (R = aryl or alkoxy) with (hetero)arylmethyl alcohols. *Org. Biomol. Chem.* **2021**, *19*, 2233-2242. (b) Gawali, S. S.; Pandia, B. K.; Pal, S.; Gunanathan, C. Manganese(I)-Catalyzed Cross-Coupling of Ketones and Secondary Alcohols with Primary Alcohols. *ACS Omega* **2019**, *4*, 10741−10754. (c) Thiyagarajan, S.; Gunanathan, C. Catalytic Cross-Coupling of Secondary Alcohols. *J. Am. Chem. Soc*. **2019**, *141*, 3822−3827. (d)

Thiyagarajan, S.; Gunanathan, C. Facile Ruthenium(II)-Catalyzed α-Alkylation of Arylmethyl Nitriles Using Alcohols Enabled by Metal−Ligand Cooperation. *ACS Catal*. **2017**, *7*, 5483−5490.

(20) (a) Zhang, G.; Irrgang, T.; Dietel, T.; Kallmeier, F.; Kempe, R. Manganese-Catalyzed Dehydrogenative Alkylation or α-Olefination of Alkyl-Substituted N-Heteroarenes with Alcohols. *Angew. Chem., Int. Ed*. **2018**, *57*, 9131−9135. (b) Kallmeier, F.; Irrgang, T.; Dietel, T.; Kempe, R. Highly Active and Selective Manganese C=O Bond Hydrogenation Catalysts: The Importance of the Multidentate Ligand, the Ancillary Ligands, and the Oxidation State. *Angew. Chem., Int. Ed*. **2016**, *55*, 11806−11809.

(21) Das, U. K.; Ben-David, Y.; Diskin-Posner, Y.; Milstein, D. N-Substituted Hydrazones by Manganese-Catalyzed Coupling of Alcohols with Hydrazine: Borrowing Hydrogen and Acceptorless Dehydrogenation in One System. *Angew. Chem., Int. Ed*. **2018**, *57*, 2179−2182.

(22) (a) Liu, T.; Wang, L.; Wu, K.; Yu, Z. Manganese-Catalyzed β-Alkylation of Secondary Alcohols with Primary Alcohols under Phosphine-Free Conditions. *ACS Catal*. **2018**, *8*, 7201−7207. (b) Fu, S.; Shao, Z.; Wang, Y.; Liu, Q. Manganese-Catalyzed Upgrading of Ethanol into 1-Butanol. *J. Am. Chem. Soc*. **2017**, *139*, 11941-11948.

(23) Corma, A.; Navas, J.; Sabater, M. J. Advances in One-Pot Synthesis through Borrowing Hydrogen Catalysis. *Chem. Rev*. **2018**, *118*, 1410-1459.

(24) (a) Khusnutdinova, J. R.; Milstein, D. Metal-Ligand Cooperation. *Angew. Chem., Int. Ed*. **2015**, *54*, 12236−12273. (b) Gunanathan, C.; Milstein, D. Metal_Ligand Cooperation by Aromatization-Dearomatization: A New Paradigm in Bond Activation and “Green” Catalysis. *Acc. Chem. Res.* **2011**, *44*, 588-602.

(25) Gloyna, D.; Brendt, K.-G.; Koppel, H.; Henning, H.-G. Darstellung und ^{1}H-NMR-spektroskopische Untersuchungen von β-substituierten Äthylen-diphenylphosphinoxiden. *J. Prakt. Chem*. **1976**, *318*, 327-335.

(26) Tang, L.; Wen, L.; Sun, T.; Zhang, D.; Yang, Z.; Feng, C.; Wang, Z. Solvent-Controlled Copper-Catalyzed Radical Decarboxylative Coupling for Alkenyl C(sp^2)−P Bond Formation. *Asian J. Org. Chem*. **2017**, *6*, 1683-1692.

(27) SMART and SAINT Software Reference Manuals Version 6.45; Bruker Analytical X-ray Systems, Inc.: Madison, WI, 2003.

(28) Bruker AXS, SADABS, Program for Empirical Absorption Correction of Area Detector Data V 2004/1, Bruker AXS Inc., Madison, Wisconsin, USA, 2004.

(29) Sheldrick, G. M. A Short History of SHELX. *Acta Crystallogr.* **2008**, *A64*, 112-122.

(30) Dolomanov, O. V.; Bourhis, L. J.; Gilea, R. J.; Howard, J. A. K.; Puschmann, H. *J. Appl. Crystallogr*. **2009**, *42*, 339-341.

^{1}H, ^{13}C and ^{31}P NMR Spectra of the Alkenylphosphine Oxide Products:

Figure 3.1. ^{1}H NMR spectrum of (*E*)-(4-(*tert*-butyl)styryl)diphenylphosphine oxide (**3.1g**, 400 MHz, $CDCl_3$):

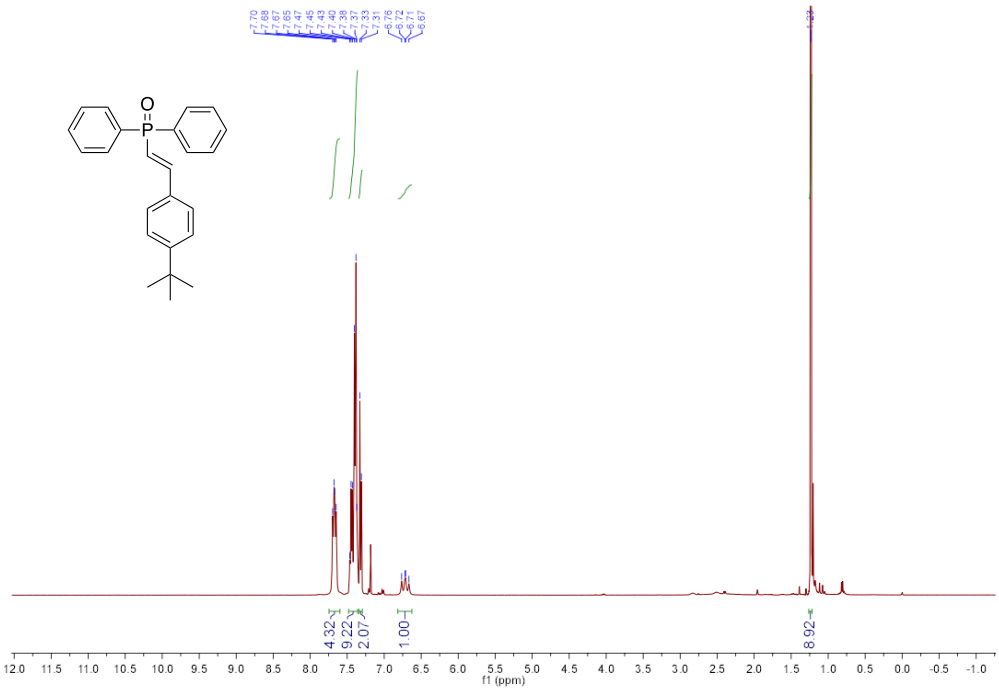


Figure 3.2. ^{13}C{^{1}H} NMR spectrum of (*E*)-(4-(*tert*-butyl)styryl)diphenylphosphine oxide (**3.1g**, 176 MHz, $CDCl_3$):

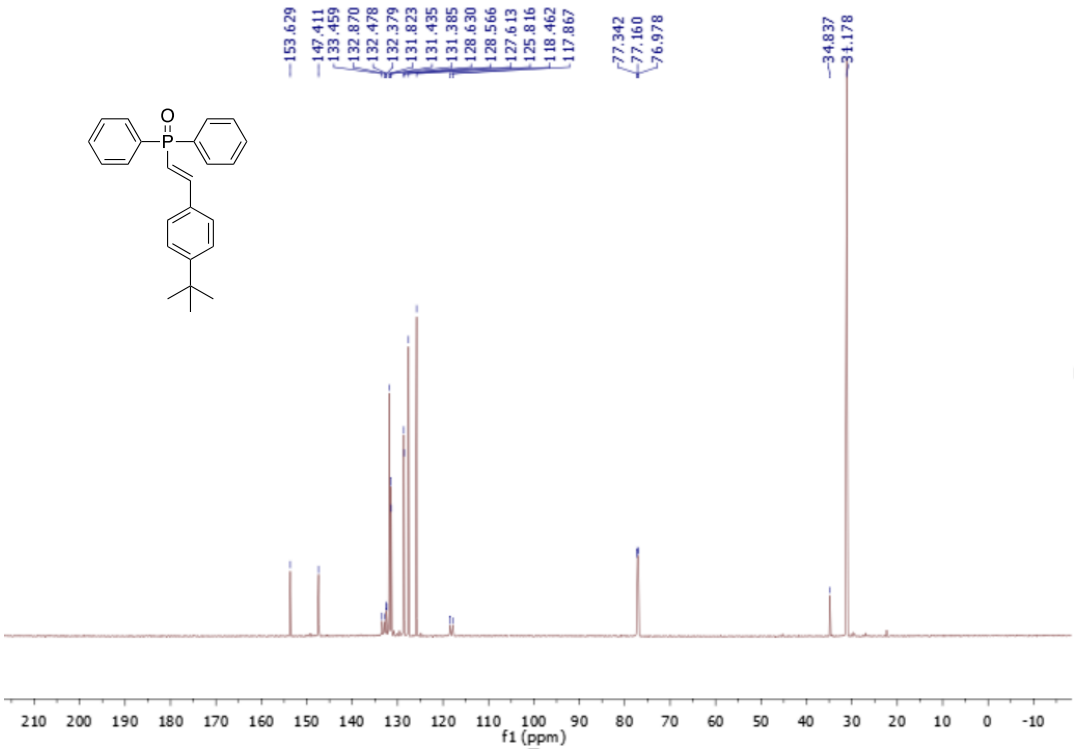


Figure 3.3. ^{31}P NMR spectrum of (*E*)-(4-(*tert*-butyl)styryl)diphenylphosphine oxide (**3.1g**, 162 MHz, $CDCl_3$):

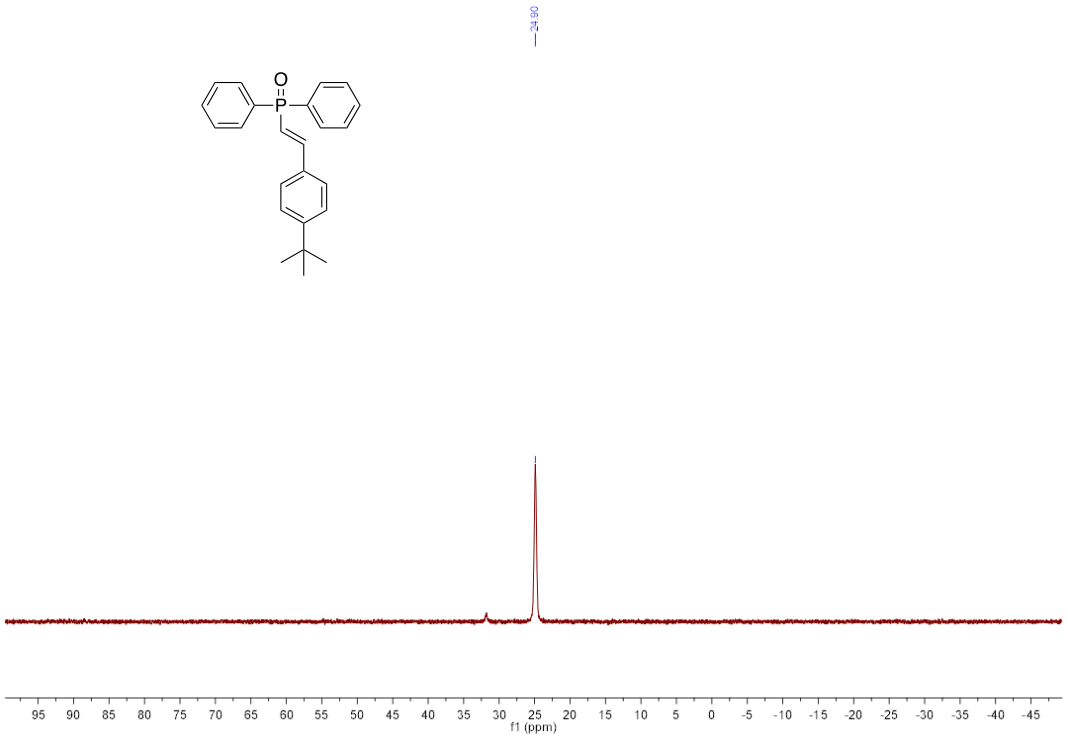


Figure 3.4. ^{1}H NMR spectrum of (*E*)-(4-(benzyloxy)styryl)diphenylphosphine oxide (**3.1n**, 400 MHz, $CDCl_3$):

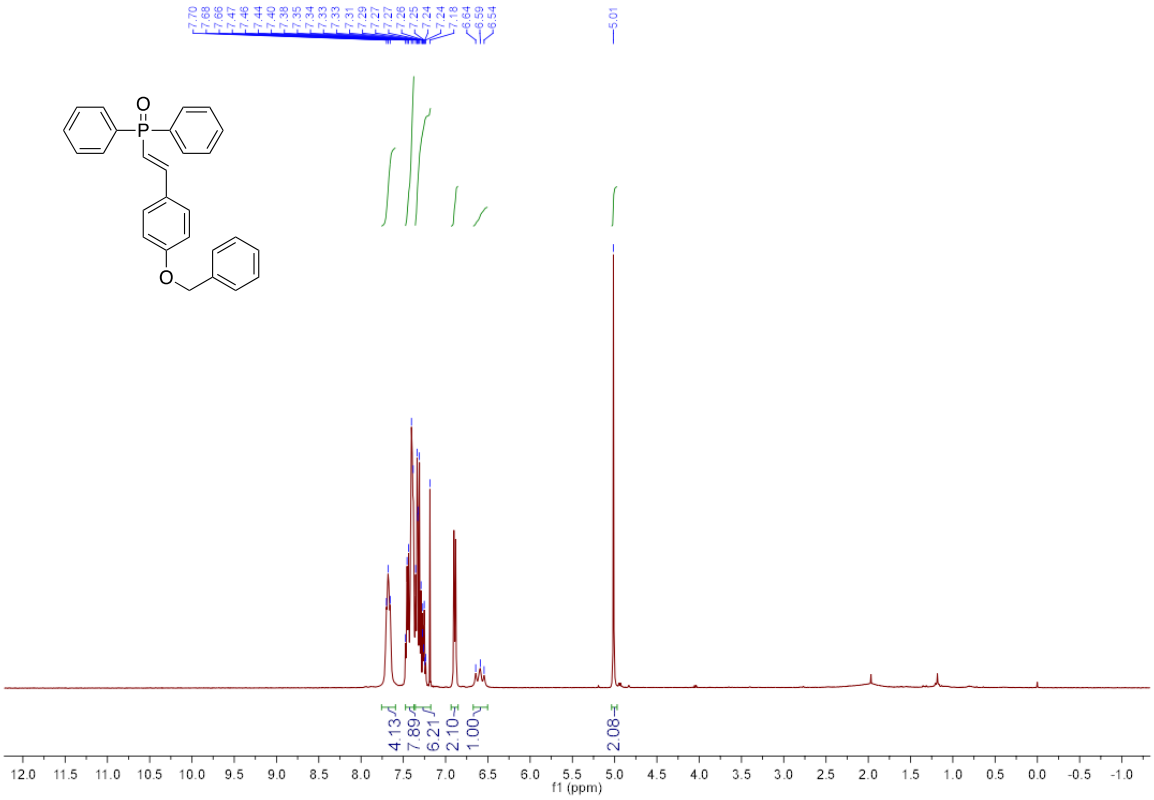


Figure 3.5. $^{13}C\{^{1}H\}$ NMR spectrum of (*E*)-(4-(benzyloxy)styryl)diphenylphosphine oxide (**3.1n**, 101 MHz, $CDCl_3$):

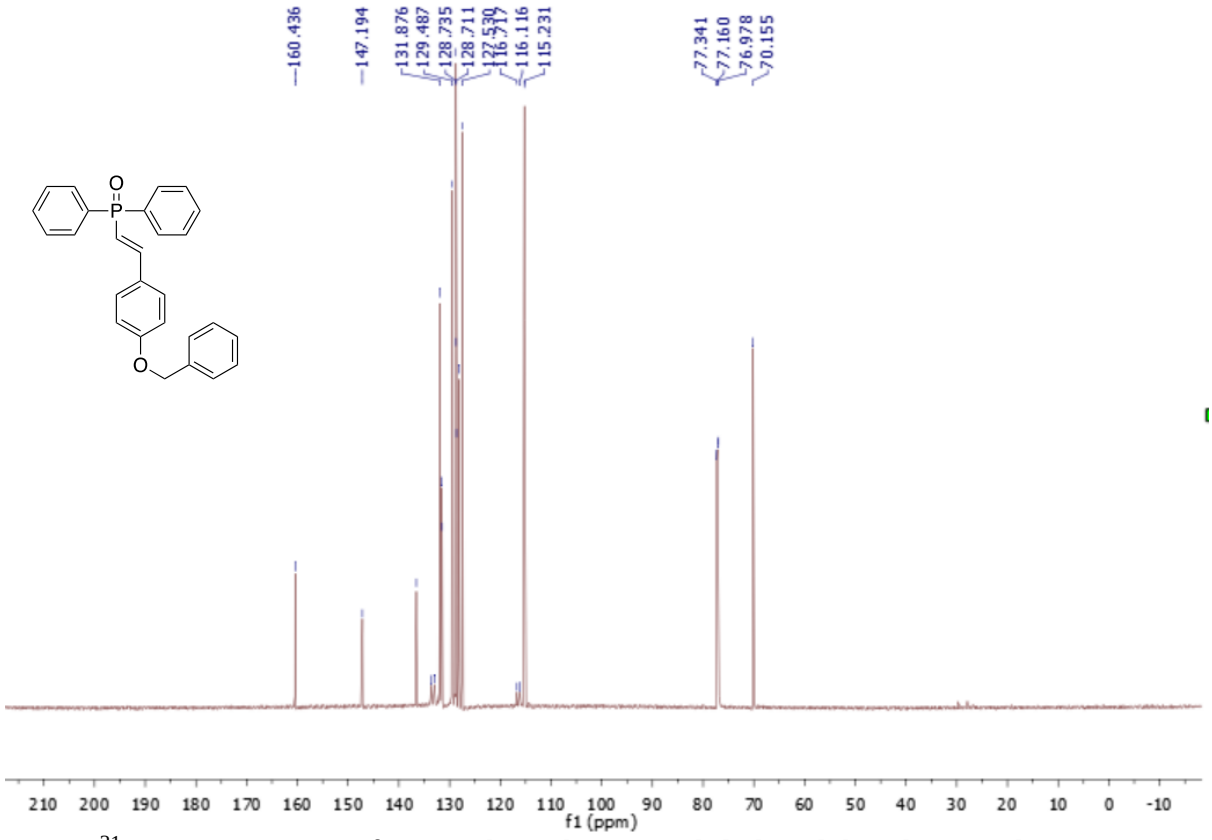


Figure 3.6. ^{31}P NMR spectrum of (*E*)-(4-(benzyloxy)styryl)diphenylphosphine oxide (**3.1n**, 162 MHz, $CDCl_3$):

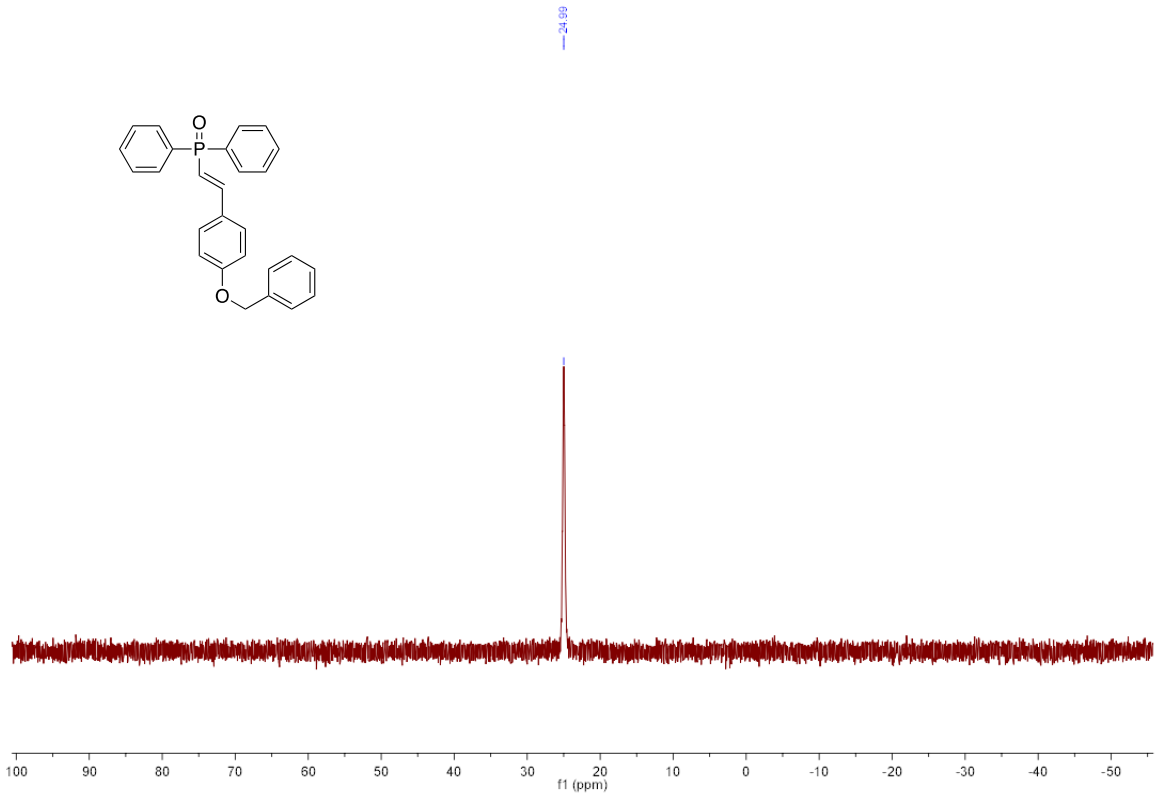


Figure 3.7. ^{1}H NMR spectrum of (*E*)-(2-(naphthalen-2-yl)vinyl)diphenylphosphine oxide (**3.1s**, 400 MHz, $CDCl_3$):

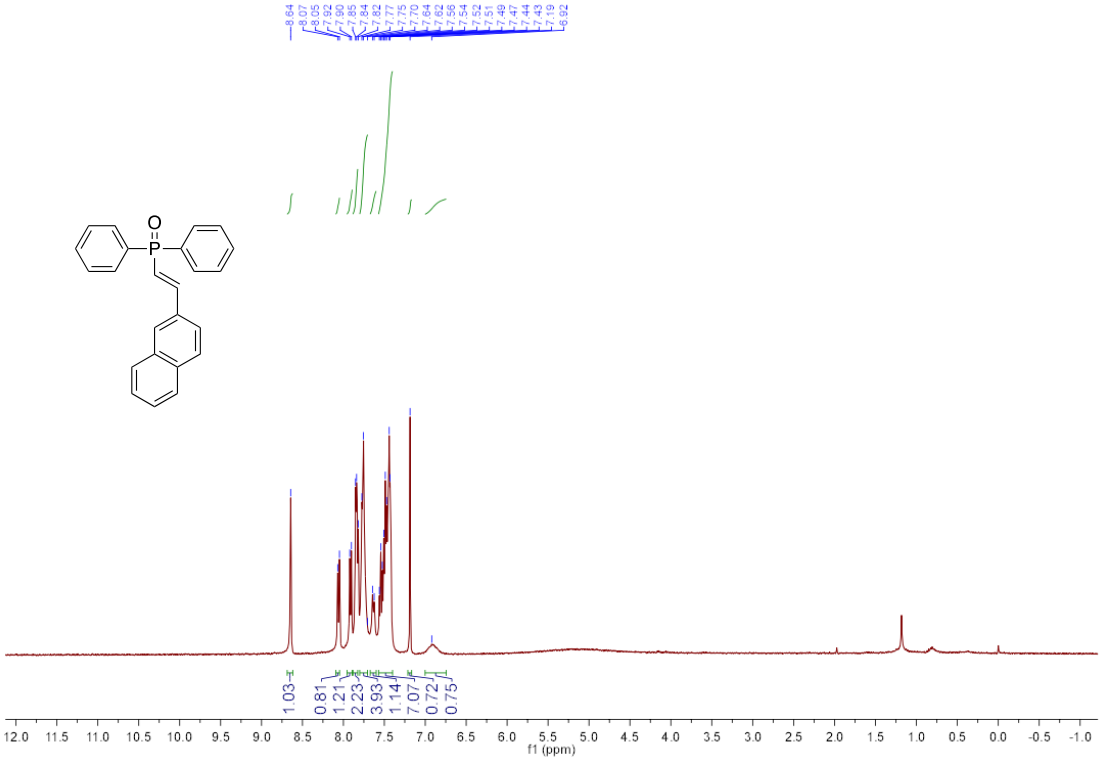


Figure 3.8. ^{13}C{^{1}H} NMR spectrum of (*E*)-(2-(naphthalen-2-yl)vinyl)diphenylphosphine oxide (**3.1s**, 176 MHz, $CDCl_3$):

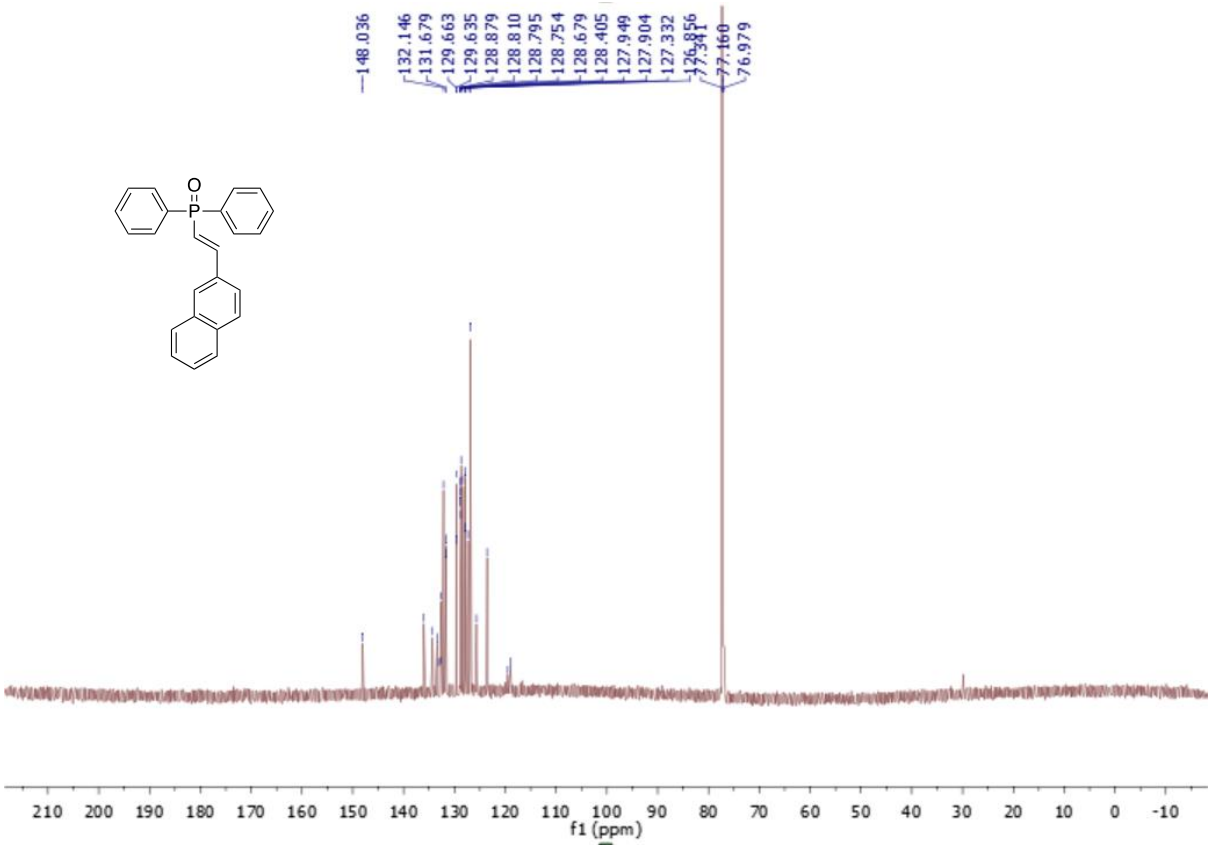
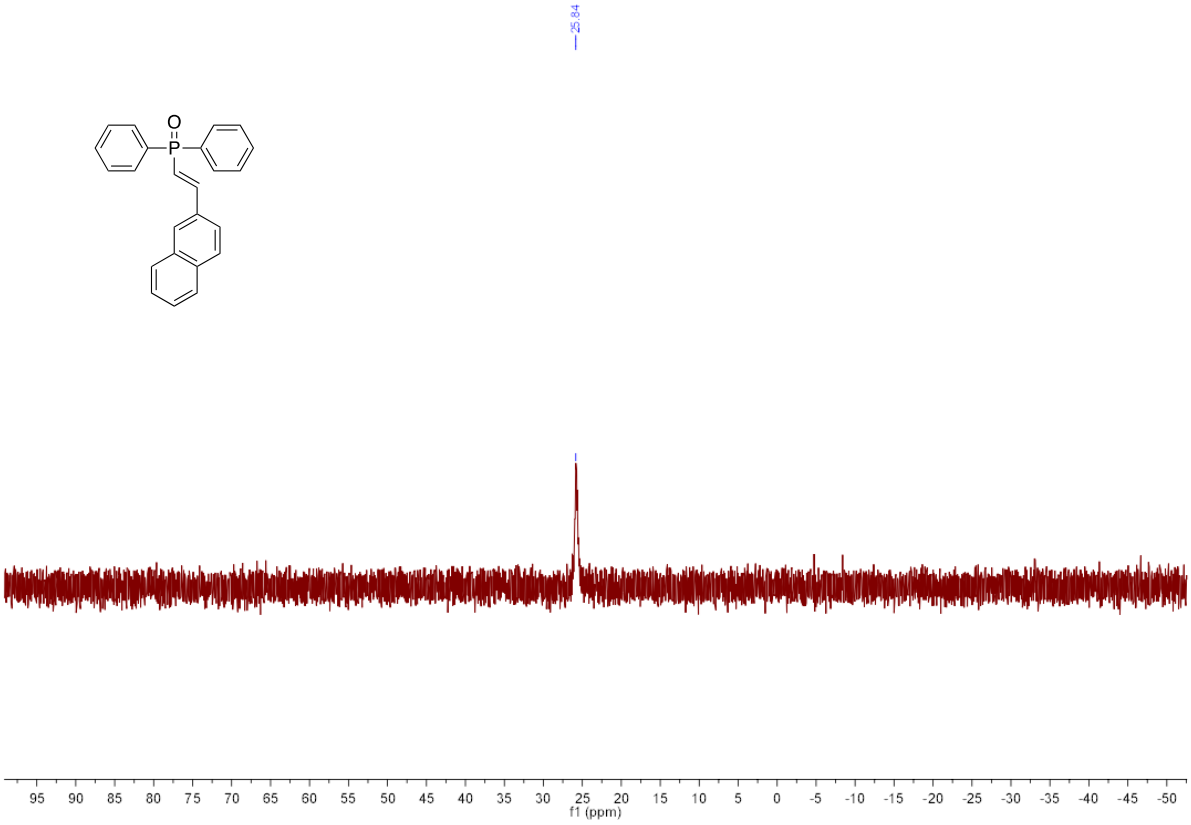


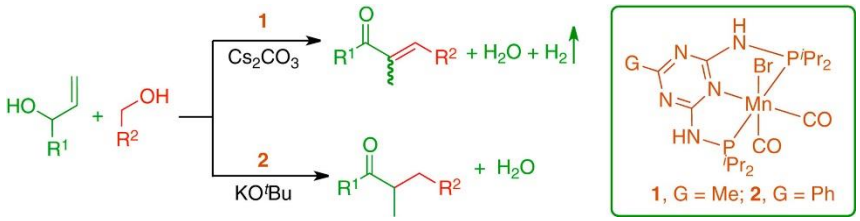
Figure 3.9. ^{31}P NMR spectrum of (*E*)-(2-(naphthalen-2-yl)vinyl)diphenylphosphine oxide (**3.1s**, 162 MHz, $CDCl_3$):



CHAPTER 4

Manganese(I) Catalyzed Cross-Coupling of Secondary Allylic Alcohols and Primary Alcohols

4.1 ABSTRACT



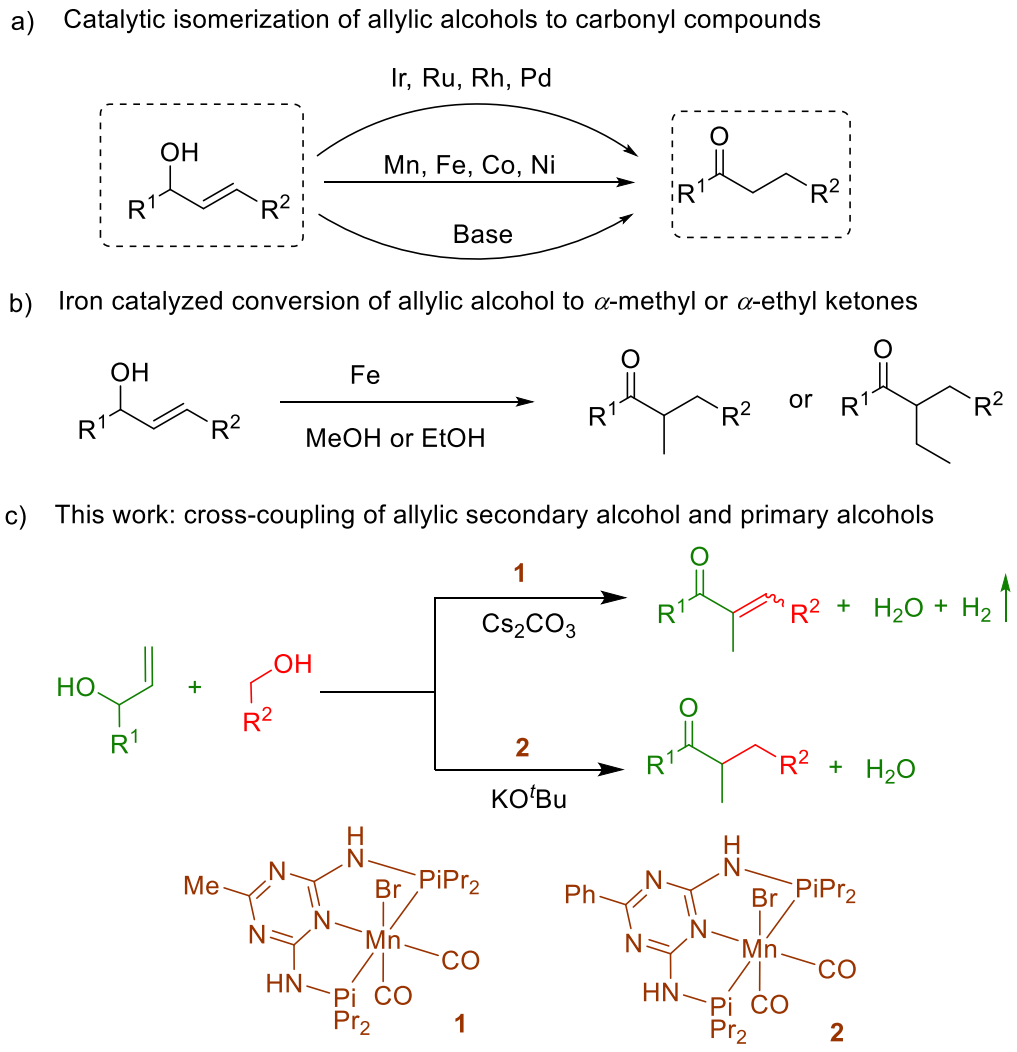
Cross-coupling of alcohols to value-added products by using sustainable catalytic reactions has gained attention in recent years. Isomerization of secondary allylic alcohol to the corresponding enolizable ketone is an atom economical and known transformation. Herein, a selective cross-coupling of secondary allylic alcohol and primary alcohol is reported to afford the corresponding α-alkenyl or alkylation products. These catalytic protocols proceed via acceptorless dehydrogenative coupling (ADC) or borrowing hydrogen (BH) strategies, which liberates water and/or hydrogen as the only byproducts. Highly abundant manganese-based pincer catalysts catalyze the reactions.

4.2 INTRODUCTION

Allylic alcohols are readily available and serve as resourceful building blocks of C3 precursors to synthesize diverse organic compounds with myriad applications. The allylic alcohol motif is found to be present in a number of important pharmaceuticals compounds.[1] Allylic alcohols are excellent candidates in the development of atom economical and sustainable green protocols. In recent years, transition metal-catalyzed isomerization of allylic alcohols to carbonyl compounds via redox isomerization is widely explored.[2] The redox isomerization circumvents the two-step oxidation and reduction pathway and directly affords the desired carbonyl compound. Complexes of noble metals such as iridium, ruthenium, rhodium, and

palladium are well known to catalyze this reaction (**Scheme 4.1a**).[3] Further, complexes of abundant base metals such as iron, cobalt, nickel, and manganese catalyzed isomerization of allylic alcohols to carbonyl compounds have been reported recently (**Scheme 4.1a**).[4] Base promoted isomerization of allylic alcohols to carbonyl compounds has been reported (**Scheme 4.1a**).[5]

Scheme 4.1. Advances in the Redox Isomerization of Allylic Alcohols and Further Alkylation



α,β-Unsaturated ketones are abundantly present in nature and highly promising industrial feedstock chemicals.[6] Ketones have widespread utilities in the synthesis of natural products,

polymers, important biological and pharmaceutical compounds.[7] Conventionally, *α,β*-unsaturated ketones are synthesized via aldol condensation, which involves the use of aldehydes.[8] Conventional synthesis of a-disubstituted ketones employs strong bases (nBuLi, LDA, etc.) and toxic alkyl halides.[9] This protocol is dependent on enolate generation, which requires cryogenic conditions and has various disadvantages such as generation of stoichiometric metal halides, over alkylation, and undesired self-coupling of carbonyl compounds. The advancement in catalysis allowed to displace this waste generating synthesis, which involves multistep synthesis by direct use of inexpensive, readily available, and environmentally benign alcohols as alkylating reagents.[10] One-pot derivatization of the allylic alcohols to *α,β* -unsaturated ketones and *α*-disubstituted ketones are interesting and important transformations. Towards this goal, Morrill and co-workers reported the iron catalyzed one-pot conversion of allylic alcohols to *α*-methyl ketones (**Scheme 4.1b**).[11]

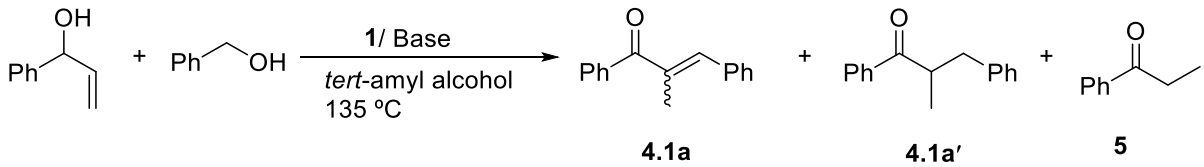
In the last two decades, a range of green organic transformations has been developed employing the acceptorless dehydrogenative coupling (ADC)[12,13] and borrowing hydrogen (BH) pathways using alcohols as coupling partners.[14,15] In recent years, a number of cross-coupling reactions are developed, which proceeded following ADC or BH strategies. Cross-coupling of primary alcohols and secondary alcohols are well-known to produce the corresponding unsaturated or saturated carbonyl compounds.[16] Our group discovered the cross-coupling of two different secondary alcohols leading to the *β*-disubstituted ketones.[17] We have also reported the manganese pincer catalyzed cross-coupling of secondary and primary alcohols[18], *α*-alkenylation of ketones, amides, and diphenylmethyl phosphineoxide using primary alcohols.[19] These studies established that Kempe's PNP-Mn(I) pincer complex having "methyl" substitution embedded in the heteroaryl backbone (precatalyst **1**, **Scheme 4.1c**) leads to the alkenylation reactions[19], whereas the similar precatalyst **2** with "phenyl" substitution results in favorable alkylation reactions.[18] In continuation of our interest in the development of base-

metal catalyzed sustainable cross-coupling reactions and to extend the synthetic scope of allylic alcohols in cross-coupling reactions, herein, we report the manganese catalyzed synthesis of *α*-alkenyl and *α*-alkyl ketones from the direct cross-coupling of secondary allylic alcohols and primary alcohols (**Scheme 4.1c**).

4.3 RESULTS AND DISCUSSIONS

Optimization studies towards cross-coupling of secondary allylic alcohol and primary alcohols were carried with α-vinylbenzyl alcohol and benzyl alcohol as benchmark substrates. Initially, α-vinylbenzyl alcohol (0.5 mmol) and benzyl alcohol (0.6 mmol) were subjected to cross-coupling using precatalyst **1** (1 mol %), and KO^{t}Bu (10 mol %), which resulted in 99% conversion of α-vinylbenzyl alcohol. Under this strong basic condition, predominant alkylation and minor alkenylation, as well as redox isomerization products, were observed (**Table 4.1**, entry 1).

Table 4.1. Optimization for Cross-Coupling of α-Vinylbenzyl Alcohol with Benzyl Alcohol Catalyzed by a Manganese Pincer Catalyst 1[a]



entry	base	base load (mol %)	catalyst load **1** (mol %)	time (h)	conversion (%) [b]	yield (%)	ratio (**4.1a/4.1a′/5**)[c]
1	KO^{t}Bu	10	1	24	99	71	10/70/20
2	NaO^{t}Bu	10	1	24	99	69	15/80/5
3	Cs_2CO_3	20	2	24	99	65	80/20
4	Cs_2CO_3	10	2	24	90	66	85/15
5	Cs_2CO_3	10	1	15	75	56	80/5/15

6	Cs_2CO_3	10	0.5	20	75	57	70/20/10
7	Cs_2CO_3	10	1.5	24	99	66	94/6
8	Cs_2CO_3	10	1.5	20	89	61	94/6
9	Cs_2CO_3	8	1.5	20	85	65	92/3/5
10	**Cs_2CO_3**	**8**	**1.5**	**24**	**90**	**68**	**97/3**
11[d]	Cs_2CO_3	8	1.5	24	87	61	96/4/0
11	--	--	1.5	24	--	--	--
12	Cs_2CO_3	8	--	24	--	--	--

[a] Reaction conditions: α-vinylbenzyl alcohol (0.5 mmol), benzyl alcohol (0.6 mmol), *tert*-amyl alcohol (2 mL), precatalyst **1**, and base were heated at 135 °C under nitrogen flow. Yields were calculated after isolation by column chromatography. [b] Conversion of α-vinylbenzyl alcohol was determined by ^{1}H NMR analysis using 1,4-dioxane (0.25 mmol) as an internal standard. [c] Products ratio calculated from ^{1}H NMR spectral analysis of crude reaction mixture. [d] Reaction was carried out using ^{t}BuOH as a solvent.

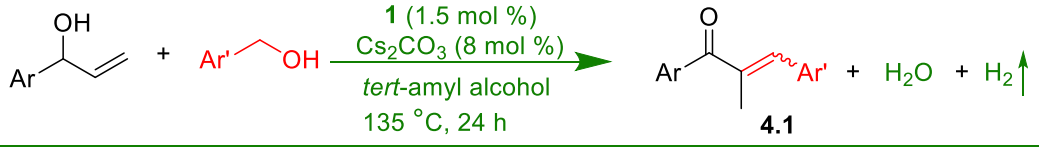
A similar result was obtained by use of NaO^{t}Bu (**Table 4.1**, entry 2). Hence, in order to switch the selectivity towards alkenylation, the mild base Cs_2CO_3 was tested; a catalytic experiment with precatalyst **1** (2 mol %), and Cs_2CO_3 (20 mol %), provided complete conversion of α-vinylbenzyl alcohol with the selectivity of 80:20 for alkenyl and alkylation products, respectively (**Table 4.1**, entry 3). When the amount of base was reduced to 10 mol %, conversion of α-vinylbenzyl alcohol decreased to 90% with a slight increase in selectivity for alkenylation (85:15 ratio, **Table 4.1**, entry 4). As the use of Cs_2CO_3 base provided the desired alkenylation as a major reaction, further experiments were performed by changing the amount of base, catalyst load, and reaction time (**Table 4.1**, entries 5-9). The results obtained from these experiments guided us to carry out a reaction with 8 mol % of Cs_2CO_3 and 1.5 mol % of

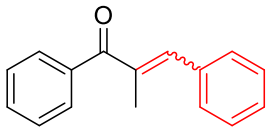
precatalyst **1** for 24 h, which resulted in 90% conversion and 68% yield with the 97:3 ratio of alkenyl and alkylation products (**Table 4.1**, entry 10). This experiment was selected as an optimized reaction condition as the presence of unreacted propiophenone and the formation of alkylation products are minimized in the reaction mixture. Experiment performed using tert-butanol as a solvent under similar conditions provided slightly lower conversion, and diminished yield of products (**Table 4.1**, entry 11). Control experiments without base, precatalyst and base alone resulted in no product formation confirming the necessity of catalyst and base for the desired cross-coupling (**Table 4.1**, entries 12-13).

With optimal conditions in hand, α-vinylbenzyl alcohol was subjected to the manganese(I) catalyzed cross-coupling with different primary alcohols (**Table 4.2**). As discussed in optimization, reaction with benzyl alcohol resulted in product **4.1a** as a mixture of *E* and *Z* isomers in a 68% yield. In general, benzyl alcohols bearing electron-donating and electron withdrawing groups provided good to moderate yields as a mixture of *E* and *Z* isomers. The reaction of 4-isopropylbenzyl alcohol provided product **4.1b** in 60%. With 4-methoxy and 3,4-dimethoxy substituted benzyl alcohols, corresponding alkenyl products **4.1c** and **4.1d** were isolated in 62% and 55% yields, respectively. Piperonyl alcohol and 3-phenoxybenzyl alcohol provided cross-coupling products **4.1e** and **4.1f** in moderate yields. (4-(Dimethylamino)phenyl)methanol as a coupling partner, product **4.1g** was obtained in 57% yield as a mixture of *E* and *Z* isomers. The reaction of secondary allylic alcohol with benzyl alcohols having electron-withdrawing substituents resulted in alkenyl cross-coupling compounds in moderate yields. Reaction with 4-phenylbenzyl alcohol and 1-naphthalene methanol afforded the products **4.1h**-**4.1i** in 54% and 45% yields, respectively. 3-Fluorobenzyl alcohol provided **4.1j** in 61% yield. Heteroaryl alcohols such as furfuryl alcohol and 2-thiophenmethanol afforded corresponding products **4.1k** and **4.1l** in 74% and 71% yields,

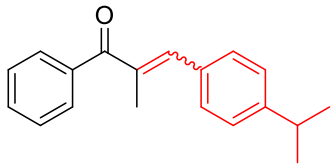
respectively. The incorporation of electron-donating substituents on secondary allylic alcohol resulted in a moderate cross-coupling reaction. The reaction of (p-tolyl)prop-2-en-1-ol with

Table 4.2. Synthesis of Methyl Branched α-Alkenyl Ketones: Cross-Coupling of Secondary Allylic Alcohols and Primary Alcohols[a]

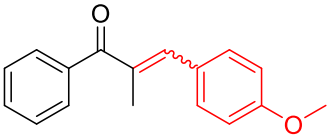




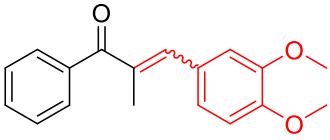
4.1a, 68% & 61%[b]
E/*Z* 98:2



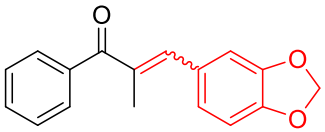
4.1b, 60%
E/*Z* 98:2



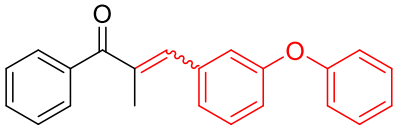
4.1c, 62%
E/*Z* 99:1



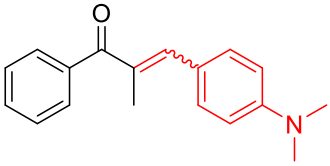
4.1d, 55%
E/*Z* 99:1



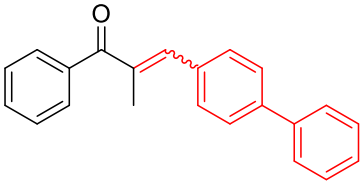
4.1e, 55%



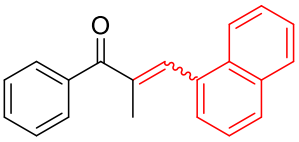
4.1f, 57%
E/*Z* 87:13



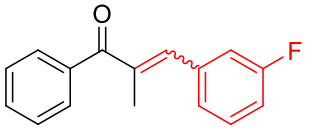
4.1g, 57%
E/*Z* 95:5



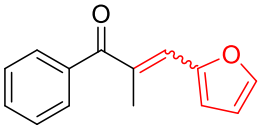
4.1h, 54%
E/*Z* 97:3



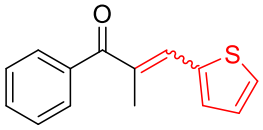
4.1i, 45%
E/*Z* 72:28



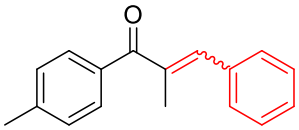
4.1j, 61%
E/*Z* 87:13



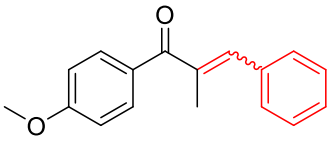
4.1k, 74%
E/*Z* 65:35



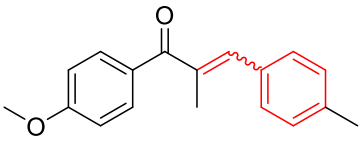
4.1l, 71%
E/*Z* 65:35



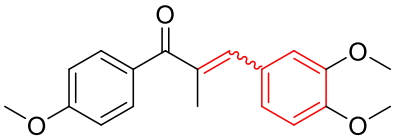
4.1m, 51%
E/*Z* 64:36



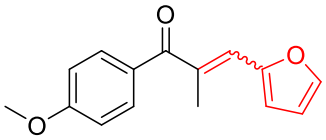
4.1n, 49%
E/*Z* 85:15



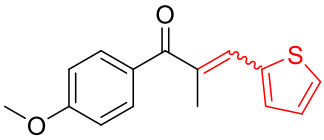
4.1o, 53%
E/*Z* 60:40



4.1p, 65% [c]
E/*Z* 87:13



4.1q, 47% [c]
E/*Z* 95:5



4.1r, 58% [d]
E/*Z* 95:5

[a] Reaction conditions: secondary allylic alcohol (0.5 mmol), aryl alcohol (0.6 mmol), *tert*-amyl alcohol (2 mL), precatalyst **1** (1.5 mol %) and Cs_2CO_3 (8 mol %) were heated at 135 °C under nitrogen flow. Yields correspond to isolated pure compounds. [b] Yield of the 0.5 g scale

reaction, performed for 36 h. [c] A mixture of alkenyl and alkyl products was isolated (1:1 ratio). [d] Presence 10% alkylation product was also found in the reaction mixture.

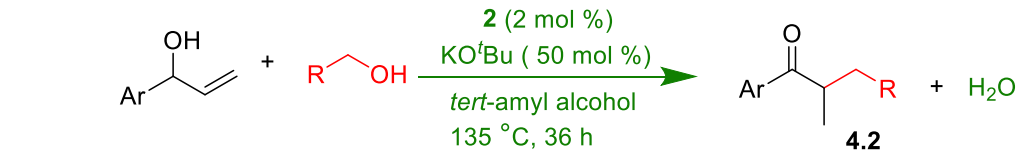
---

benzyl alcohol provided the corresponding product **4.1m** in 51% yield as a mixture of *E* and *Z* isomers. Similarly, when (4-methoxyphenyl)prop-2-en-1-ol was subjected to cross-coupling with benzyl alcohol, product **4.1n** was obtained in a 49% yield. The reaction of (4-methoxyphenyl)prop-2-en-1-ol with 4-methylbenzyl alcohol afforded product **4.1o** in 53% yield. However, upon reaction with 3,4-dimethoxybenzyl alcohol and furfuryl alcohol, a mixture of alkenylation and alkylation products **4.1p-4.1q** were obtained. Reaction with 2-thiophene methanol provided the corresponding alkenylated product **4.1r** in 58% yield.

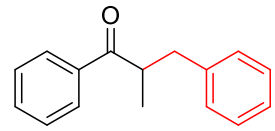
Based on our previous reports[18] on cross-coupling of secondary and primary alcohols using manganese pincer catalyst **2** and our initial observations in optimization studies on cross-coupling of secondary allylic alcohols with primary alcohols in which use of strong base favored the predominant formation of alkylation product (**Table 4.1**, entries 1-2), we set out to explore the possible α-alkylation of secondary allylic alcohols. Thus, reaction of α-vinylbenzyl alcohol with benzyl alcohol and thiophene-2-methanol with precatalyst **2** (2 mol %) and KO^{t}Bu base (50 mol %) provided the corresponding alkylation products **4.2a**, and **4.2b** in 68% and 64% yields, respectively (**Table 4.3**). Notably, the alkylation also occurred using aliphatic alcohols such as 1-hexanol and the corresponding product **4.2c** was isolated in 51% yield. Further, different secondary allylic alcohols were tested in the manganese catalyzed α-alkylation reaction, which afforded the corresponding alkylated products. The reaction of (p-tolyl)prop-2-en-1-ol with benzyl alcohol provided the product **4.2d** in 60% yield. 1-(Naphthalen-1-yl)prop-2-en-1-ol reacted with thiophene-2-methanol and provided product **4.2e** in 44% yield. Reaction of 1-(4-methoxyphenyl)prop-2-en-1-ol with 3-phenoxybenzyl alcohol afforded the corresponding alkylated product **4.2f** in 62% yield. Notably, the α-

methylalkyl ketones are obtained directly from secondary allylic alcohols and primary alcohols under BH conditions.

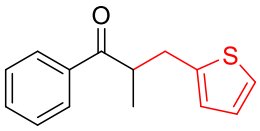
Table 4.3. Cross-Coupling of Allylic Secondary Alcohols and Primary Alcohols for Synthesis of α-Alkylated Ketones [a]



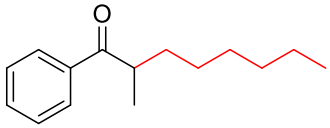
4.2



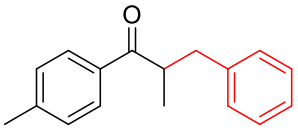
4.2a, 68%



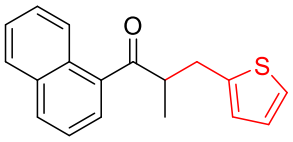
4.2b, 64%



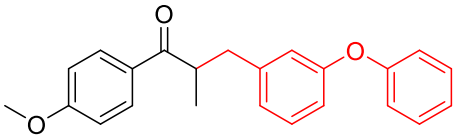
4.2c, 51%



4.2d, 60%



4.2e, 44%



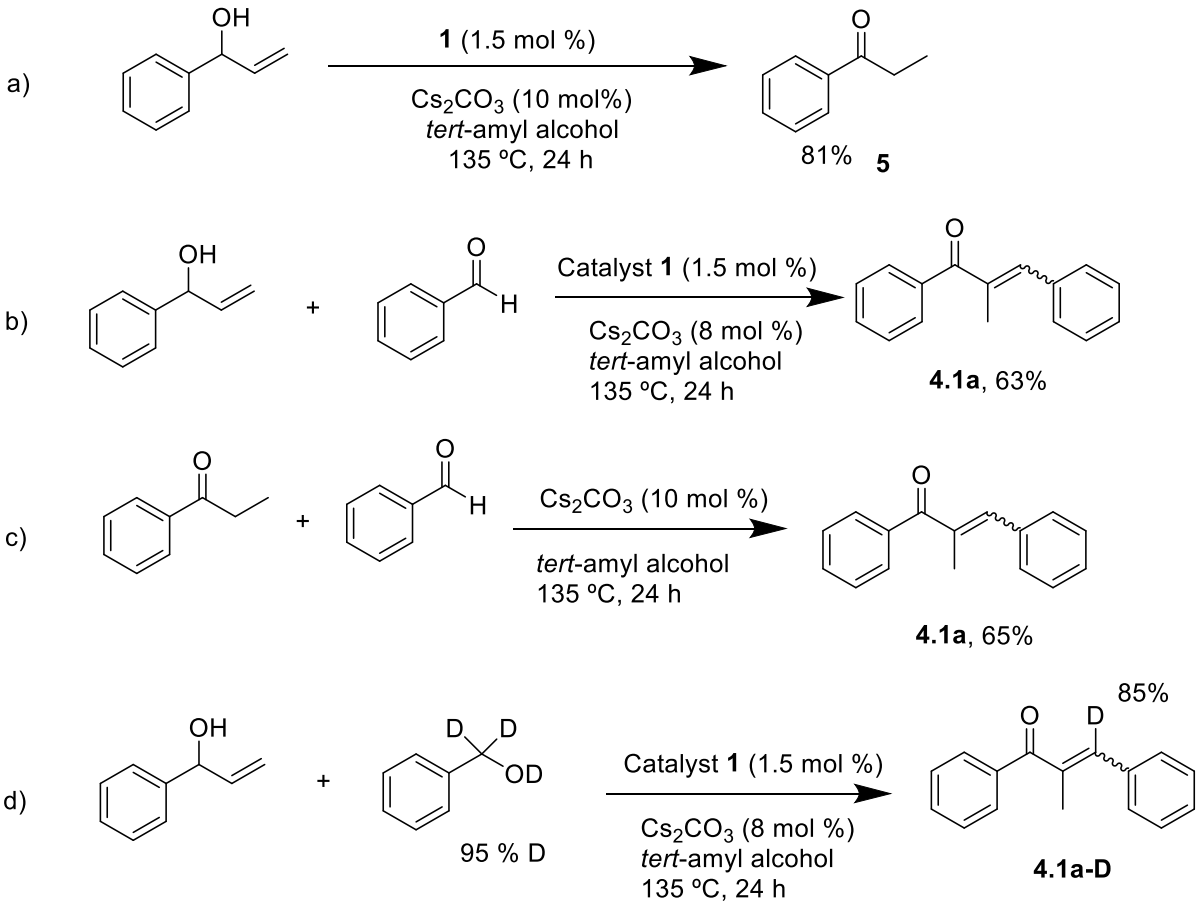
4.2f, 62%

[a] Reaction conditions: secondary allylic alcohol (0.5 mmol), primary alcohol (1 mmol), *tert*-amyl alcohol (2 mL), catalyst **2** (2 mol %), and KO^{t}Bu (50 mol %) were heated at 135 °C under nitrogen flow for 36 h.

Experiments aimed at understanding the reaction pathways of manganese catalyzed cross-coupling of secondary allylic alcohols with primary alcohols were performed in Scheme 2. The reaction of α-vinylbenzyl alcohol with precatalyst **1** (1.5 mol %) and Cs_2CO_3 (10 mol %) provided propiophenone in 81% yield (**Scheme 4.2a**). This observation revealed that the reaction proceeds via the redox isomerization pathway. Reaction of α-vinylbenzyl alcohol with benzaldehyde under optimized reaction condition for alkenylation afforded product **4.1a** in 63% yield, indicating the involvement of aldehyde intermediacy resulting from oxidation of primary alcohols by the manganese catalysts (**Scheme 4.2b**). Further, when propiophenone and

benzaldehyde were reacted with Cs_2CO_3 (10 mol %) for 24 h at 135 °C, alkenyl product **4.1a** was obtained in a 65% yield (**Scheme 4.2c**). These experiments establish that secondary allylic alcohols undergo redox isomerization leading to ketones, and primary alcohols are oxidized to aldehydes by manganese pincer catalysts, and the subsequent base promoted aldol condensation furnishes the α-alkenylation products. Catalytic cross-coupling using benzyl alcohol-d_3 provided the 85% deuterium incorporation at the alkenyl proton of product **4.1a**, confirming the aldol condensation (**Scheme 4.2d**).

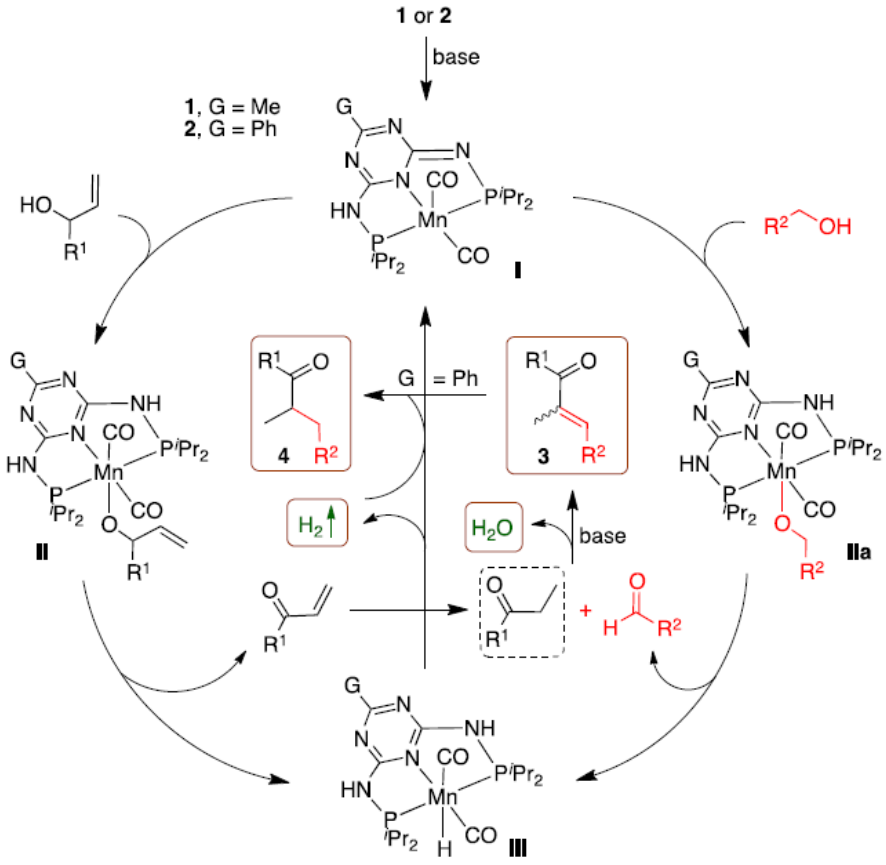
Scheme 4.2. Mechanistic Studies on Manganese Catalyzed Cross-Coupling of Secondary Allylic Alcohols with Primary Alcohols.



Based on mechanistic studies (**Scheme 4.2**) and previous reports[4], a plausible catalytic pathway for cross-coupling of secondary allylic alcohols with primary alcohols is proposed in Scheme

4.3. A dearomatized coordinatively unsaturated intermediate **I** is generated upon the reaction of precatalysts with base. The reaction of intermediate **I** with secondary allylic alcohols as well as primary alcohols result in alkoxy-ligated complexes **II** and **IIa**, respectively, via facile O-H activation of alcohol functionalities.[20] Involvement of alkoxy-ligated manganese complexes in oxidative functionalization of alcohols are also established previously by Milstein, Yu and Liu.[21,22] Perhaps, β-hydride elimination or by other mechanistic pathways from intermediate **II**, and **IIa** produce α,β-unsaturated ketone and aldehyde intermediates, respectively and a common Mn-hydride complex **III**.[18] Selective hydrogenation of in-situ generated α,β-unsaturated ketone by Mn-hydride complex **III** leads to the formation of propiophenone intermediate. The in-situ generated propiophenone and aldehyde undergo base promoted aldol condensation to provide the α-alkenylation products **4.3**. In the case of alkylation, α-alkenyl compounds **4.3** are further hydrogenated by the Mn-hydride intermediate **III** (G = Ph) under strong basic conditions, leading to the formation of α-alkylation products **4.4**.[23] The stoichiometrically equivalent amounts of secondary allylic alcohols and primary alcohols undergo oxidation leading to the formation of two equivalent of hydrogen. One equivalent of hydrogen is utilized by **III** for the hydrogenation of α,β-unsaturated ketone to propiophenone. One equivalent of molecular hydrogen is liberated when α-alkenylation products **4.3** are formed as the reaction proceeds by ADC pathway. Whereas the second equivalent hydrogen is also utilized in the hydrogenation of α-alkenyl compounds **4.3**, which produce the α-alkylation products **4.4** following BH pathway, and water is the only by-product resulting from this tandem process. Either hydrogenation of α,β-unsaturated ketone or liberation of molecular hydrogen from intermediate **III** leads to regeneration of dearomatized intermediate **I** to complete a catalytic cycle. Metal-ligand cooperation by dearomatizationaromatization is operative in this catalytic cycle, which allowed the oxidation state of manganese to remain +1 in all the intermediates.

Scheme 4.3. Proposed Mechanism for Manganese Pincer-Catalyzed Cross-Coupling of Secondary Allylic Alcohols and Primary Alcohols.



4.4 CONCLUSION

In summary, an abundant base metal, manganese-catalyzed cross-coupling of secondary allylic alcohols and primary alcohols to α-alkenylation and α-alkylation is attained in which the reactions followed ADC or BH pathways. Remarkably, water and/or molecular hydrogen are the only byproducts of this reaction. Overall, the aromatization-dearomatization pathway is operative in the catalysts, facilitating the oxidation of the primary alcohol and redox isomerization of the allylic alcohol. Base promoted condensation between aldehydes and propiophenone provided the α-alkenylation reactions, whereas the hydrogenation of α-alkenylation products led to the formation of α-alkylation products.

4.5 EXPERIMENTAL SECTION

General Information. All catalytic reactions were performed under an inert atmosphere using standard Schlenk techniques. All stoichiometric reactions were performed in nitrogen atmosphere MBRAUN glove box. Chemicals were purchased from Acros, Sigma-Aldrich, Alfaaesar, Himedia Chemicals and used without further purification. Dry solvents were prepared according to standard procedures. Infrared (IR) spectra were recorded in PerkinElmer FT-IR and Thermo-Nicolet FT-IR spectrophotometers. High-resolution mass spectra (HRMS) were obtained on Bruker micrOTOF-Q II Spectrometer and are reported as m/z (relative intensity). Accurate masses are reported for the molecular ion $[M+Na]^+$, $[M+H]^+$, $[M]^+$. Nuclear magnetic resonance spectra (^{1}H NMR and ^{13}C NMR) were recorded at Bruker AV-700 (^{1}H at 700 MHz and ^{13}C at 175 MHz) and Bruker AV-400 (^{1}H at 400 MHz and ^{13}C at 100.6 MHz). ^{1}H NMR chemical shifts are referenced in parts per million (ppm) with respect to tetramethylsilane (TMS, d 0.00 ppm) and ^{13}C{^{1}H} NMR chemical shifts are referenced in parts per million (ppm) with respect to $CDCl_3$ (d 77.160 ppm). Coupling constants are reported in Hertz (Hz). ^{1}H NMR spectroscopy abbreviations: s, Singlet; d, doublet; t, triplet; q, quartet; dd, doublet of doublets; dt, doublet of triplets; dq, doublet of quartets; td, triplet of doublets; qd, quartets of doublets; ddd, doublets of doublets of doublets; m, multiplet; br, broad. Assignment of spectra was done based on one-dimensional (dept-135) NMR techniques.

General Procedure for Optimization of Cross-Coupling of Secondary Allylic Alcohols and Primary Alcohols. To a Schlenk flask (25 mL) equipped with a stir bar, precatalyst **1**, base, α-vinylbenzyl alcohol (0.5 mmol), benzyl alcohol (0.6 mmol), and *tert*-amyl alcohol (2 mL) were added under nitrogen atmosphere in a glove box. The reaction mixture was taken out of the glove box, equipped with a condenser, and the solution was heated at 135 °C (oil bath temperature) with stirring in an open system under nitrogen flow for 24 h. After cooling, the reaction mixture was transferred to an RB flask, and the solvent was evaporated under reduced

pressure. Further, 1,4-dioxane (0.25 mmol) was added (as an internal standard) to the mixture, dissolved in $CDCl_3$ (1 mL), and subjected to ^1H NMR analysis from which the conversion was calculated.

Procedure for Quantification of Hydrogen Gas Evolved in Cross-Coupling of α-Vinylbenzyl Alcohol with Benzyl Alcohol. To a Schlenk flask (25 mL) equipped with a stir bar, precatalyst **1** (1.5 mol %), Cs_2CO_3 (8 mol %), α-vinylbenzyl alcohol (0.5 mmol), benzyl alcohol (0.6 mmol), and *tert*-amyl alcohol were added under nitrogen atmosphere in a glove box. The reaction mixture was taken out of the glove box, equipped with a condenser, and the solution was heated at 135 °C (oil bath temperature) with stirring for 24 h. The side arm of Schlenk tube was connected to a gas burette via cold trap (to remove solvent vapours). The number of moles of hydrogen evolved was calculated by taking the vapour pressure of water at 298 K = 23.7695 Torr. Volume of water displaced = 13.1 mL, atmospheric presure = 758.3124 Torr, R = 62.3635 L Torr K^{-1} mol^{-1}, nH_2 = [(Patm - Pwater) * V]/RT = 0.000521 mol. Expected value = 0.0005 mol or 0.5 mmol.

General Procedure for Cross-Coupling of Allylic Secondary Alcohols with Primary Alcohols (for Alkenylation). To a Schlenk flask (25 mL) equipped with a stir bar, precatalyst **1** (1.5 mol %), Cs_2CO_3 (8 mol %), α-vinylbenzyl alcohol (0.5 mmol), alcohol (0.6 mmol), and *tert*-amyl alcohol were added under nitrogen atmosphere in a glove box. The reaction mixture was taken out of the glove box, equipped with a condenser, and the solution was heated at 135 °C (oil bath temperature) with stirring in an open system under nitrogen flow for 24 h. After cooling, the reaction mixture was transferred to an RB flask. The solvent was removed under reduced pressure. The residue was purified by silica gel (100-200 mesh) column chromatography using ethyl acetate/hexane mixture as eluent. Yields were calculated for isolated products.

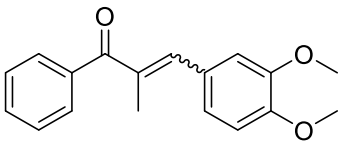
Spectral Data of *α*-Alkenyl Products

(*E*)-2-Methyl-1,3-diphenylprop-2-en-1-one (4.1a).[24] Purified by silica-gel column chromatography using hexane as an eluent. Colourless liquid. Yield (76 mg, 68%). Yield for 0.5 g scale reaction (505 mg, 61%). IR (DCM): 695, 1014, 1261, 1439, 1608, 1668, 2923, 3051 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.67 (d, *J* = 7.8 Hz, 2H), 7.47 (t, *J* = 7.2 Hz, 1H), 7.39 (d, *J* = 7.3 Hz, 2H), 7.36-7.33 (m, 4H), 7.30-7.27 (m, 1H), 7.11 (s, 1H), 2.20 (s, 3H). $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$): δ 199.3, 142.0, 136.9, 135.8, 131.6, 129.6, 129.4, 129.1, 128.6, 128.5, 128.4, 128.2, 128.2, 14.4.

(*E*)-3-(4-isopropylphenyl)-2-methyl-1-phenylprop-2-en-1-one (**4.1b**).[25] Purified by silica-gel column chromatography using ethyl acetate/hexane (0.5:99.5) mixture as an eluent. Colourless liquid. Yield (79 mg, 60%). IR (DCM): 697, 1012, 1439, 1598, 1664, 2941, 3055 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.78 (d, *J* = 7.7 Hz, 2H), 7.57 (t, *J* = 7.2 Hz, 1H), 7.49 (t, *J* = 7.5 Hz, 2H), 7.41 (t, *J* = 9.0 Hz, 2H), 7.32 (d, *J* = 8.0 Hz, 2H), 7.22 (s, 1H), 3.01-2.9 (m, 1H), 2.34 (s, 3H),1.32 (d, *J* = 6.8 Hz, 2H). $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$): δ 199.6, 149.8,142.6, 138.8, 136.1, 133.4, 131.6, 130.0, 129.6, 128.2, 126.7, 34.0, 23.9, 14.5.

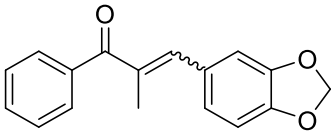
(*E*)-3-(4-methoxyphenyl)-2-methyl-1-phenylprop-2-en-1-one (**4.1c**).[19a] Purified by silica-gel column chromatography using ethyl acetate/hexane mixture (1:99) as an eluent. Colourless liquid. Yield (78 mg, 62%). IR (DCM): 695, 738, 1011, 1596, 1665, 2924, 3055, 3085 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.70-7.72 (m, 2H), 7.51-7.55 (m, 1H), 7.39-7.46 (m, 4H), 7.16 (s, 1H), 6.92-6.95 (m, 2H), 3.84 (s, 3H), 2.28 (d, *J* = 1.2 Hz, 3H). $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$): δ 199.7, 160.1, 142.8, 139.1, 135.0, 131.7, 131.5, 129.5, 128.5, 128.3, 114.1, 55.5, 14.5.

(*E*)-3-(2,3-dimethoxyphenyl)-2-methyl-1-phenylprop-2-en-1-one (**4.1d**).[19a] Purified by



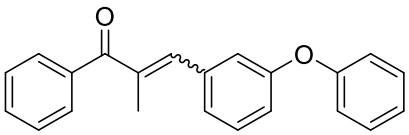
silica-gel column chromatography using ethyl acetate/hexane mixture (1:99) as an eluent. Colorless oil. Yield (78 mg, 55%). IR (DCM): 1012, 1456, 1510, 1602, 1659, 2929, 3057 cm^{-1}.^{1}H NMR (400 MHz, $CDCl_3$): δ 7.80 (d, *J* = 7.6 Hz, 2H), 7.54 (t, *J* = 7.2 Hz, 1H), 7.45 (t, *J* = 7.2 Hz, 2H), 7.36 (s, 1H), 7.10 (t, *J* = 8.0 Hz), 7.02 (d, *J* = 7.6 Hz, 1H), 6.94 (d, *J* = 8.4 Hz, 1H), 3.87 (s, 3H), 3.74 (s, 3H), 2.18 (s, 3H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 199.5, 152.9, 147.6, 138.5, 138.0, 137.6, 131.9, 130.4, 129.8, 128.2, 123.9, 121.9, 112.9, 61.0, 56.0, 14.5.

(*E*)-3-(benzo[d][1,3]dioxol-5-yl)-2-methyl-1-phenylprop-2-en-1-one (**4.1e**). Purified by



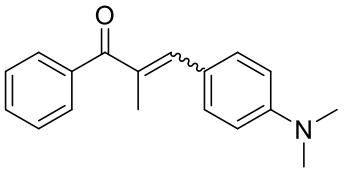
silica-gel column chromatography using ethyl acetate/hexane (1:99) mixture as an eluent. White solid. Yield (73 mg, 55%). IR (DCM): 773, 1038, 1444, 1586, 1664, 2905, 3051 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.63 (d, *J* = 7.7 Hz, 2H), 7.45 (t, *J* = 7.3 Hz, 1H), 7.37 (t, *J* = 7.4 Hz, 2H), 7.02 (s, 1H), 6.90 (s, 1H), 6.80 (dd, J_1 = 27.7, J_2 = 8.1 Hz, 2H), 5.93 (s, 2H), 2.19 (s, 3H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 199.6, 148.1, 147.9, 142.5, 138.8, 135.4, 131.6, 130.0, 129.5, 128.3, 125.0, 109.7, 108.5, 101.5, 14.5.

1-(4-methoxyphenyl)-2-methyl-3-(3-phenoxyphenyl)prop-2-en-1-one (**4.1f**). Purified by



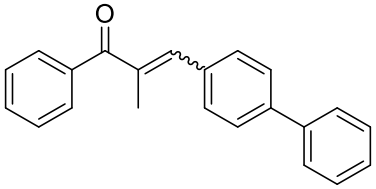
silica-gel column chromatography using ethyl acetate/ hexane (0.5:99.5) mixture as an eluent. White solid. Yield (90 mg, 57%). IR (DCM): 795, 1177, 1253, 1440, 1602, 1665, 2976, 3055, 3081 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.87-7.74 (m, 1H), 7.65 (d, *J* = 7.6 Hz, 2H), 7.45 (t, *J* = 7.4 Hz, 1H), 7.36 (t, *J* = 7.4 Hz, 2H), 7.27 (m, 4H), 7.08-7.00 (m, 3H), 6.98-6.90 (m, 5H), 6.66 (dd, J_1 = 17.4, J_2 = 10.0 Hz, 1H), 2.14 (s, 3H), 2.07 (s, 1H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 199.3, 157.4, 156.8, 141.2, 138.3, 137.5, 137.4, 131.7, 129.8, 129.8, 129.5, 128.2, 124.5, 123.6, 119.6, 119.0, 118.8, 14.5.

(*E*)-3-(4-(dimethylamino)phenyl)-2-methyl-1-phenylprop-2-en-1-one (**4.1g**).[26] Purified by



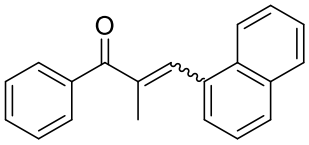
silica-gel column chromatography using ethyl acetate/ hexane (1:99) mixture as an eluent. Yellow solid. Yield (75 mg, 57%). IR (DCM): 795, 1168, 1439, 1610, 1661, 2929, 3052 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.59 (d, *J* = 7.7 Hz, 2H), 7.42 (t, *J* = 7.0 Hz, 1H), 7.36 (d, *J* = 7.2 Hz, 2H), 7.34-7.27 (m, 2H), 7.08 (s, 1H), 6.62 (d, *J* = 8.5 Hz, 2H), 2.93 (s, 6H), 2.23 (s, 3H). $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$): δ 199.8, 150.7, 144.6, 139.7, 132.4, 132.0, 130.9, 129.4, 128.1, 123.6, 111.7, 40.2, 14.4.

(*E*)-3-([1,10-biphenyl]-4-yl)-2-methyl-1-phenylprop-2-en-1-one (**4.1h**).[27] Purified by silica-



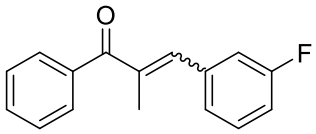
gel column chromatography using hexane as an eluent. Colourless liquid. Yield (80 mg, 54%). IR (DCM): 738,1128, 1441, 1595, 1668, 2923, 3057, 3077 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.69 (d, *J* = 7.7 Hz, 2H), 7.56 (t, *J* = 8.6 Hz, 4H), 7.47 (m, 2H), 7.43-7.35 (m, 5H), 7.30 (t, *J* = 7.1 Hz, 1H), 7.16 (d, *J* = 14.1 Hz, 1H), 2.25 (s, 3H). $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$): δ 199.5, 142.0, 141.5, 140.4, 138.7, 136.9, 134.8, 131.7, 130.4, 129.6, 129.0, 128.3, 127.8, 127.2, 127.2, 14.7.

(*E*)-2-Methyl-3-(naphthalen-1-yl)-1-phenylprop-2-en-1-one (**4.1i**).[24] Purified by silica-gel

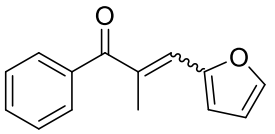


column chromatography using ethyl acetate/hexane (0.5:99.5) mixture as an eluent. White solid. Yield (61 mg, 45%). IR (DCM): 696, 832,1097,1196,1438,1609,1664, 2979, 3049, 3080 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.02 (d, *J* = 8.3 Hz, 1H), 7.82-7.77 (m, 4H), 7.74-7.71 (m, 1H), 7.65-7.60 (m, 2H), 7.53-7.34 (m, 9H), 7.18 (s, 1H), 7.11 (dd, J_1 = 14.2, J_2 = 7.0 Hz, 1H), 7.06-7.01 (m, 1H), 6.96 (t, *J* = 7.8 Hz, 1H), 2.25 (s, 3H), 2.07 (s, 1H). $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$): δ 199.3, 140.3, 139.0, 131.9, 129.5, 128.8, 128.8, 128.7, 128.4, 128.0, 126.8, 126.5, 126.2, 125.8, 125.2, 124.5, 22.3, 14.6.

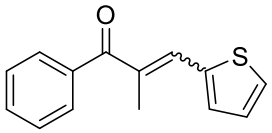
(*E*)-3-(3-fluorophenyl)-2-methyl-1-phenylprop-2-en-1-one (**4.1j**).[28] Purified by silica-gel column chromatography using ethyl acetate/hexane (0.5:99.5) mixture as an eluent. White solid. Yield (73 mg, 61%). IR (DCM): 742, 1296, 1455, 1610, 1671, 2945, 3051 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.67 (d, *J* = 7.8 Hz, 2H), 7.48 (t, *J* = 7.1 Hz, 1H), 7.39 (t, *J* = 7.4 Hz, 2H), 7.29 (dd, J_1 = 14.5, J_2 = 7.5 Hz, 1H), 7.07 (dd, J_1 = 20.1, J_2 = 9.7 Hz, 3H), 6.96 (t, *J* = 8.3 Hz, 1H), 2.18 (s, 3H), 2.10 (s, 1H). $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$): δ 199.3, 164.1, 140.4, 138.0, 132.0, 130.1, 130.0, 129.6, 128.4, 125.5, 116.4, 116.2, 115.6, 115.4, 14.6.



3-(Furan-2-yl)-2-methyl-1-phenylprop-2-en-1-one (**4.1k**).[29] Purified by silica-gel column chromatography using ethyl acetate/hexane (0.5:99.5) mixture as an eluent. Yellow oil. Yield (78 mg, 74%). IR (DCM): 739, 1172, 1297, 1473, 1602, 1663, 2844, 2945, 3135 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.99e7.95 (m, 1H), 7.69 (dd, J_1 = 5.2, J_2 = 3.3 Hz, 2H), 7.61-7.52 (m, 3H), 7.49-7.43 (m, 3H), 7.11 (d, *J* = 1.5 Hz, 1H), 7.02 (s, 1H), 6.67 (d, *J* = 3.5 Hz, 1H), 6.55 (dd, J_1 = 3.4, J_2 =1.8 Hz, 1H), 6.49 (d, *J* = 1.5 Hz, 1H), 6.24-6.11 (m, 1H), 2.36 (d, *J* = 1.0 Hz, 3H), 2.16 (d, *J* = 1.5 Hz, 2H). Mixture of both cis and trans isomers are present. $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$): δ 199.1, 151.8, 144.5, 142.6, 138.7, 133.6, 133.4, 131.5, 129.8, 129.3, 129.32, 128.7, 128.3, 117.7, 115.3, 112.5, 111.2, 109.7, 22.4, 14.26.

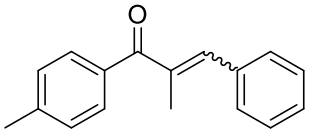


2-Methyl-1-phenyl-3-(thiophen-2-yl)prop-2-en-1-one (**4.1l**).[29] Purified by silica-gel column chromatography using ethyl acetate/hexane (0.5:99.5) mixture as an eluent. White solid. Yield (81 mg, 71%). IR (DCM): 735, 955, 1140 1195, 1455, 1595, 1660, 2931, 3049, 3079 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.89 (d, *J* = 7.8 Hz, 1H), 7.61 (d, *J* = 7.6 Hz, 2H), 7.47 (t, *J* = 7.0 Hz, 3H), 7.42-7.31 (m, 4H), 7.19-7.13 (m, 1H), 7.05 (t, *J* = 4.1 Hz, 1H), 6.98 (d, *J* = 5.0 Hz, 1H), 6.77-6.67 (m, 2H), 2.27 (s, 3H), 2.07 (s, 2H). Mixture of both cis and trans isomers are present. $^{13}C\{^{1}H\}$ NMR (101 MHz,

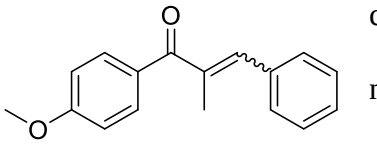


$CDCl_3$): δ 200.8, 198.9, 139.3, 138.8, 135.8, 133.8, 133.6, 132.2, 131.5, 130.1, 129.5, 129.4, 128.9, 128.3, 127.8, 127.6, 127.1, 126.1, 122.4, 22.6, 14.7.

2-Methyl-3-phenyl-1-(p-tolyl)prop-2-en-1-one (**4.1m**).[24] Purified by silica-gel column chromatography using hexane as an eluent. White solid. Yield (60 mg, 51%). IR (DCM): 731, 1012, 1224, 1482, 1598, 1664, 2944, 3063 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.73 (d, *J* = 8.1 Hz, 1H), 7.61 (d, *J* = 8.4 Hz, 2H), 7.34-7.27 (m, 4H), 7.19 (d, *J* = 7.2 Hz, 3H), 7.10-6.99 (m, 5H), 6.92 (s, 1H), 2.36 (s, 3H), 2.26 (s, 2H), 2.19 (s, 3H), 2.08 (s, 2H). Mixture of both cis and trans isomers are present. $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 199.4, 142.4, 141.4, 136.9, 129.8, 129.6, 129.5, 129.3, 128.9, 128.4, 128.3, 128.2, 127.3, 24.6, 21.6, 14.6.



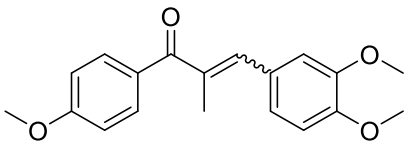
1-(4-Methoxyphenyl)-2-methyl-3-phenylprop-2-en-1-one (**4.1n**).[24] Purified by silica-gel column chromatography using ethyl acetate/hexane (1:99) mixture as an eluent. White solid. Yield (62 mg, 49%). IR (DCM): 748, 931, 1048, 1103, 1479, 1602, 1661, 2976, 3051, 3059 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.82-7.78 (m, 1H), 7.75-7.72 (m, 1H), 7.34-7.31 (m, 3H), 7.29-7.23 (m, 1H), 7.04 (dd, J_1 = 6.9, J_2 = 1.7 Hz, 2H), 6.91-6.85 (d, *J* = 8.8 Hz, 2H), 6.76-6.72 (d, *J* = 8.8 Hz, 1H), 3.80 (s, 3H), 3.73 (s, 3H), 2.18 (s, 3H), 2.08 (s, 3H). Both cis and trans isomers are present. $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 198.5, 162.9, 140.2, 137.5, 137.1, 136.1, 132.1, 131.9, 129.7, 128.6, 128.3, 114.0, 113.6, 55.6, 15.0.



1-(4-Methoxyphenyl)-2-methyl-3-(p-tolyl)prop-2-en-1-one (**4.1o**). Purified by silica-gel column chromatography using ethyl acetate/hexane (1:99) mixture as an eluent. White solid. Yield (71 mg, 53%). IR (DCM): 705, 741, 931, 1032, 1301, 1570, 1602, 1665, 2908, 2946 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.86-7.79 (m, 2H), 7.34 (t, *J* = 8.8 Hz, 1H), 7.25-7.17 (m, 2H), 7.12-7.08 (m, 1H), 6.98-6.95 (m, 2H), 3.90 (s, 3H) and 3.89 (s, 3H), 2.41 (s, 3H),

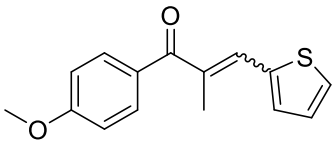
2.39 (s, 3H), 2.31 (s, 3H), 2.29 (s, 3H). Since mixture of cis and trans products are present, the -CH3 peaks corresponding to both cis and trans products are integrated together. $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$): δ 198.6, 162.8, 141.2, 140.6, 139.3, 138.6, 136.3, 135.6, 133.2, 132.2, 132.0, 131.0, 129.8, 129.4, 129.3, 128.2, 113.6, 113.6, 55.6, 21.4, 21.1, 15.0. Peaks for both cis and trans products are present.

3-(3,4-Dimethoxyphenyl)-1-(4-methoxyphenyl)-2-methylprop-2-en-1-one and **3-(3,4-dimethoxyphenyl)-1-(4- methoxyphenyl)-2-methylpropan-1-one** (**4.1p**). Purified by silica-



gel column chromatography using ethyl acetate/hexane (5:95) mixture as an eluent. Yellow oil. Yield (101 mg, 65%). IR (DCM): 765, 971, 1257, 1326, 1464, 1605, 1658, 1684, 2841, 2936, 3000 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.90 (t, *J* = 5.9 Hz, 3H), 7.78 (d, *J* = 8.7 Hz, 2H), 7.10-7.04 (m, 2H), 6.97-6.94 (m, 2H), 6.91 (d, *J* = 8.7 Hz, 3H), 6.77-6.68 (m, 4H), 3.92 (s, 3H), 3.89 (s, 3H), 3.87 (s, 3H), 3.85 (s, 3H), 3.83 (s, 6H), 3.73-3.65 (m, 1H), 3.10 (dd, J_1 = 13.8, J_2 = 6.8 Hz, 1H), 2.65 (dd, J_1 = 13.8, J_2 = 7.3 Hz, 1H), 2.29 (s, 3H), 1.20 (d, *J* = 6.9 Hz, 3H). $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$): δ 202.5, 198.4, 163.4, 162.6, 149.4, 148.7, 148.7, 147.4, 140.7, 135.3, 132.8, 131.9, 130.5, 129.6, 128.8, 123.1, 121.0, 113.9, 113.8, 113.5, 112.9, 112.5, 111.2, 111.0, 56.0, 55.96, 55.91, 55.8, 55.4, 42.5, 39.3, 17.8, 15.0.

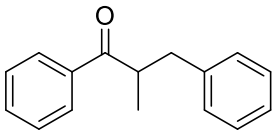
1-(4-Methoxyphenyl)-2-methyl-3-(thiophen-2-yl)prop-2-en-1-one (**4.1r**). Purified by silica-



gel column chromatography using ethyl acetate/hexane (0.5:99.5) mixture as an eluent. Yellow oil. Yield (75 mg, 58%). IR (DCM): 741, 955, 1140 1198, 1461, 1602, 1657, 2932, 3049, 3082 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.67-7.63 (m, 2H), 7.43 (d, *J* = 5.1 Hz, 1H), 7.26 (s, 1H), 7.13 (d, *J* = 3.5 Hz, 1H), 7.03 (dd, J_1 = 5.0 Hz, J_2 = 3.7 Hz, 1H), 6.86 (d, *J* = 8.8 Hz, 2H), 3.79 (s, 3H), 2.24 (s, 3H). $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$): δ 197.8, 162.7, 139.5, 133.9, 133.8, 131.8, 131.6, 130.9, 129.5, 127.5, 113.6, 55.5, 15.3.

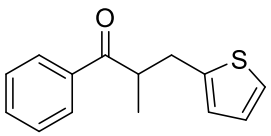
General Procedure for Cross-Coupling of Secondary Allylic Alcohols with Primary Alcohols (for Alkylation). To a Schlenk flask (25 mL) equipped with a stir bar, precatalyst **2** (2 mol %), KO^{t}Bu (50 mol %), α-vinylbenzyl alcohol (0.5 mmol), alcohol (0.6 mmol), and *tert*-amyl alcohol were added under nitrogen atmosphere in a glove box. The reaction mixture was taken out of the glove box, equipped with a condenser, and the solution was heated at 135 °C (oil bath temperature) with stirring in an open system under nitrogen flow for 24 h. After cooling, the reaction mixture was transferred to an RB flask. The solvent was removed under reduced pressure. The resultant residue was dissolved in chloroform, washed with water and brine. The collected organic layer was dried over anhydrous sodium sulfate and concentrated in a vacuum. The residue was purified by silica gel (100-200 mesh) column chromatography using ethyl acetate/hexane mixture as eluent. Yields were calculated for isolated products.

2-Methyl-1,3-diphenylpropan-1-one (**4.2a**).[30] Purified by silica-gel column chromatography



using hexane as an eluent. White solid. Yield (76 mg, 68%). IR (DCM): 697, 726, 1196, 1440, 1610, 1684, 2977, 3051 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.88-7.84 (m, 2H), 7.49-7.44 (m, 1H), 7.37 (m, 2H), 7.21-7.17 (m, 2H), 7.13-7.08 (m, 3H), 3.72-3.63 (m, 1H), 3.09 (dd, J_1 = 13.7, J_2 = 6.3 Hz, 1H), 2.62 (dd, J_1 =13.7, J_2 = 7.9 Hz, 1H), 1.13 (d, J = 6.9 Hz, 3H). ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ 203.9, 140.0, 136.5, 133.0, 129.2, 128.7, 128.5, 128.4, 126.3, 42.9, 39.4, 17.5.

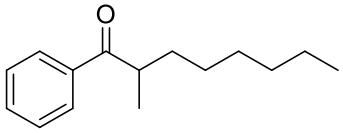
2-Methyl-1-phenyl-3-(thiophen-2-yl)propan-1-one (**4.2b**).[30] Purified by silica-gel column



chromatography using ethyl acetate/hexane (0.5:99.5) mixture as an eluent. White solid. Yield (73.6 mg, 64%). IR (DCM): 581, 695, 761, 1096, 1195, 1442, 1598, 1690, 3055, 3081 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.99-7.94 (m, 2H), 7.60-7.56 (m, 1H), 7.50-7.47 (m, 2H), 7.13 (dd, J_1 = 5.1, J_2 = 1.1 Hz, 1H), 6.91 (dd, J_1 = 5.1, J_2 = 3.4 Hz, 1H), 6.84-6.81 (m, 1H), 3.84-3.75 (m, 1H), 3.40 (dd, J_1 = 14.8, J_2 = 6.3 Hz,

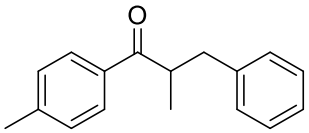
1H), 2.97 (dd, J_1 = 14.8, J_2 = 7.2 Hz, 1H), 1.28 (d, J = 7.0 Hz, 3H).$^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 203.4, 142.5, 136.4, 133.2, 128.8, 128.4, 126.9, 125.7, 123.7, 43.4, 33.4, 17.9.

2-Methyl-1-phenyloctan-1-one (**4.2c**).[31] Purified by silica-gel column chromatography using



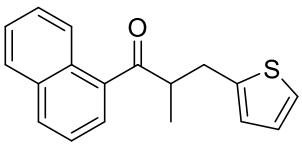
hexane as an eluent. White solid. Yield (56 mg, 51%). IR (DCM): 697, 743, 1198, 1596, 1686, 2977, 3051 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.89 (d, J = 7.3 Hz, 2H), 7.49 (t, J = 7.3 Hz, 1H), 7.40 (t, J = 7.5 Hz, 2H), 3.44-3.34 (m, 1H), 1.76-1.67 (m, 2H), 1.22-1.17 (m, 7H), 1.12 (d, J = 6.8 Hz, 3H), 0.82-0.77 (m, 4H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 204.7, 136.9, 132.9, 128.7, 128.3, 40.7, 33.8, 31.83, 29.5, 27.5, 22.7, 17.3, 14.2.

2-Methyl-3-phenyl-1-(p-tolyl)propan-1-one (**4.2d**).[30] Purified by silica-gel column



chromatography using hexane as an eluent. White solid. Yield (71 mg, 60%). IR (DCM): 698, 738, 1210, 1518,1610,1686, 2926, 3054 cm^{-1}. ^1H NMR (700 MHz, $CDCl_3$): δ 7.75 (d, J = 8.2 Hz, 1H), 7.57 (d, J = 8.2 Hz, 1H), 7.17 (dd, J_1 = 9.4, J_2 = 8.1 Hz, 3H), 7.13-7.10 (m, 3H), 7.06-7.04 (m, 1H), 3.64 (dd, J_1 = 14.2, J_2 = 6.9 Hz, 1H), 3.08 (dd, J_1 = 13.7, J_2 = 6.3 Hz, 1H), 2.60 (dd, J_1 = 13.7, J_2 = 7.9 Hz, 1H), 2.31 (s, 3H), 1.11 (d, J = 6.9 Hz, 3H).

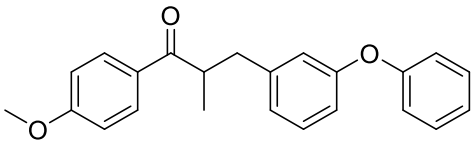
2-Methyl-1-(naphthalen-1-yl)-3-(thiophen-2-yl)propan-1-one (**4.2e**). Purified by silica-gel



column chromatography using ethyl acetate/hexane (0.5:99.5) mixture as an eluent. White solid. Yield (61 mg, 44%). IR (DCM): 731, 1120, 1198, 1516, 1609, 1684, 2981, 3057, 3085 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 8.25 (d, J = 8.5 Hz, 1H), 7.88 (d, J = 8.2 Hz, 1H), 7.79 (d, J = 8.0 Hz, 1H), 7.60 (d, J = 7.1 Hz, 1H), 7.49-7.43 (m, 2H), 7.38 (t, J = 7.7 Hz, 1H), 7.03 (d, J = 5.1 Hz, 1H), 6.82-6.80 (m, 1H), 6.76 (d, J = 2.4 Hz, 1H), 3.70-3.65 (m, 1H), 3.40 (dd, J_1 = 14.7, J_2 = 7.2 Hz, 1H), 2.92 (dd, J_1 = 14.7, J_2 = 6.8 Hz, 1H), 1.20 (d, J = 7.0 Hz, 3H). $^{13}C\{^1H\}$ NMR (101

MHz, $CDCl_3$): δ 207.4, 142.5, 136.6, 134.0, 132.3, 130.5, 128.4, 127.8, 127.5, 127.0, 126.9, 126.6, 126.6, 126.2, 125.9, 125.7, 124.5, 124.1, 123.8, 47.6, 33.3, 17.6.

1-(4-Methoxyphenyl)-2-methyl-3-(3-phenoxyphenyl) propan-1-one (**4.2f**) Purified by



silica-gel column chromatography using ethyl acetate/hexane (1:99) mixture as an eluent. White solid. Yield (98 mg, 62%). IR (DCM): 744, 1048, 1510, 1608, 1680, 2976, 3055, 3083 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.81 (d, *J* = 8.4 Hz, 2H), 7.22 (t, *J* = 7.5 Hz, 2H), 7.12 (t, *J* = 7.8 Hz, 1H), 6.99 (t, *J* = 7.4 Hz, 1H), 6.82 (dd, J_1 = 20.8, J_2 = 11.8 Hz, 6H), 6.72 (d, *J* = 8.1 Hz, 1H), 3.77 (s, 3H), 3.60 (dt, J_1 = 13.3, J_2 = 6.8 Hz, 1H), 3.03 (dd, J_1 = 13.6, J_2 = 6.6 Hz, 1H), 2.59 (dd, J_1 = 13.6, J_2 = 7.5 Hz, 1H), 1.11 (d, *J* = 6.8 Hz, 3H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 202.2, 163.5, 157.2, 142.3, 130.6, 129.8, 129.7, 129.5, 124.2, 123.1, 119.7, 118.7, 116.8, 113.9, 55.5, 42.2, 39.5, 17.7.

General Procedure for Mechanistic Studies.

Reaction of α-Vinylbenzyl Alcohol with Precatalyst 1. To a Schlenk flask (25 mL) equipped with a stir bar, precatalyst **1** (1.5 mol %), Cs_2CO_3 (8 mol %), α-vinylbenzyl alcohol (0.5 mmol), and *tert*-amyl alcohol were added under nitrogen atmosphere in a glove box. After completion of reaction, the solvent was removed, and the residue was purified by silica gel (100-200 mesh) column chromatography using ethyl acetate/hexane mixture as eluent. Yield was calculated for pure isolated product.

Reaction of α-Vinylbenzyl Alcohol with Benzaldehyde. To a Schlenk flask (25 mL) equipped with a stir bar, precatalyst **1** (1.5 mol %), Cs_2CO_3 (8 mol %), α-vinylbenzyl alcohol (0.5 mmol), benzaldehyde (0.6 mmol), and *tert*-amyl alcohol were added under nitrogen atmosphere in a glove box. After completion of reaction, the solvent was removed and the residue was purified by silica gel (100-200 mesh) column chromatography using ethyl acetate/hexane mixture as eluent. Yield was calculated for pure isolated product.

Reaction of Propiophenone with Benzaldehyde. To a Schlenk flask (25 mL) equipped with a stir bar, precatalyst **1** (1.5 mol %), Cs_2CO_3 (8 mol %), propiophenone (0.5 mmol), benzaldehyde (0.6 mmol) and *tert*-amyl alcohol were added under a nitrogen atmosphere in a glove box. After completion of the reaction, the solvent was removed, and the residue was purified by silica gel (100-200 mesh) column chromatography using ethyl acetate/hexane mixture as eluent. Yield was calculated for pure isolated product.

Reaction of α-Vinylbenzyl Alcohol with Benzyl Alcohol-d_3. To a Schlenk flask (25 mL) equipped with a stir bar, precatalyst **1** (1.5 mol %), Cs_2CO_3 (8 mol %), α-vinylbenzyl alcohol (0.5 mmol), benzyl alcohol-d_3 (0.6 mmol), and *tert*-amyl alcohol were added under nitrogen atmosphere in a glove box. After completion of the reaction, the solvent was removed, and the residue was purified by silica gel (100-200 mesh) column chromatography using ethyl acetate/hexane mixture as eluent. Yield was calculated for pure isolated product.

4.7. NOTES AND REFERENCES

(1) (a) Xing, Y.; Li, C.; Meng, J.; Zhang, Z.; Wang, X.; Wang, Z.; Ye, Y.; Sun, K. *Adv. Synth. Catal*. **2021**, *363*, 1-25. (b) Das, K.; Sarkar, K.; Maji, B. Manganese-Catalyzed Anti-Markovnikov Hydroamination of Allyl Alcohols via Hydrogen-Borrowing Catalysis. *ACS Catal*. **2021**, *11*, 7060-7069. (c) Zhang, J.; Liao, J.; Wei, Y. F.; Cheng, G.; Luo, R. Recent Advance of Allylic Alcohol Reagents in Organic Synthesis. *Mini rev. Org. Chem*. **2018**, *15*, 476-487. (d) Lumbroso, A.; Cooke, M. L.; Breit, B. Catalytic Asymmetric Synthesis of Allylic Alcohols and Derivatives and their Applications in Organic Synthesis. *Angew. Chem. Int*. **2013**, *52*, 1890-1932. (e) Kazmaier, U.; Lucas, S.; Klein, M. Syntheses and Synthetic Applications of Stannylated Allylic Alcohols. *J. Org. Chem*. **2006**, *71*, 2429-2433. (f) Radin, N. S. *Bioorg. Med. Chem*. **2003**, *11*, 2123-2142. (g) Krahling, L.; Krey, J.; Jakobson, G.; Grolig, J.; Miksche, L. Allyl compounds, in: *Ullmann's Encyclopedia of Industrial Chemistry*, Wiley, 2000.

(2) Uma, R.; Crevisy, C.; Gree, R. Transposition of Allylic Alcohols into Carbonyl Compounds Mediated by Transition Metal Complexes. *Chem. Rev*. **2003**, *103*, 27-52.

(3) (a) Lorenzo-Luis, P.; Romerosa, A.; Serrano-Ruiz, M. Catalytic Isomerization of Allylic Alcohols in Water. *ACS Catal*. **2012**, *2*, 1079-1086. (b) Li, H.; Mazet, C. Iridium-Catalyzed Selective Isomerization of Primary Allylic Alcohols. *Acc. Chem. Res*. **2016**, *49*, 1232-1241. (c) Lee, D. Y.; Moon, C. W.; Jun, C. H. Synthesis of Aliphatic Ketones from Allylic Alcohols through Consecutive Isomerization and Chelation-Assisted Hydroacylation by a Rhodium Catalyst. *J. Org. Chem*. **2002**, *67*, 3945-3948. (d) Voronova, K.; Purgel, M.; Udvardy, A.; Benyei, A. C.; Katho, A.; Joo, F. Hydrogenation and Redox Isomerization of Allylic Alcohols Catalyzed by a New Water-Soluble Pd-tetrahydrosalen Complex. *Organometallics*. **2013**, *32*, 4391-4401. (e) Cadierno, V.; Garcıa-Garrido, S. E.; Gimeno, J.; Varela-Alvarez, A.; Sordo, J. A. Bis(allyl)−Ruthenium(IV) Complexes as Highly Efficient Catalysts for the Redox Isomerization of Allylic Alcohols into Carbonyl Compounds in Organic and Aqueous Media: Scope, Limitations, and Theoretical Analysis of the Mechanism. *J. Am. Chem. Soc*. **2006**, *128*, 1360-1370.

(4) (a) Xia, T.; Spiegelberg, B.; Wei, Z.; Jiao, H.; Tin, S.; Hinze, S.; de Vries, J. G. Manganese PNP-Pincer Catalyzed Isomerization of Allylic/Homo-Allylic Alcohols to Ketones-Activity, Selectivity, Efficiency. *Catal. Sci.Technol*. **2019**, *9*, 6327-6334. (b) Spiegelberg, B.; Dell'Acqua, A.; Xia, T.; Spannenberg, A.; Tin, S.; Hinze, S. Additive-Free Isomerization of Allylic Alcohols to Ketones with a Cobalt PNP Pincer Catalyst. *Chem. Eur J*. **2019**, *25*, 7820-7825 (c) Xia, T.; Wei, Z.; Spiegelberg, B.; Jiao, H.; Hinze, S.; de Vries, J. G. Isomerization of Allylic Alcohols to Ketones Catalyzed by Well-Defined Iron PNP Pincer Catalysts. *Chem. Eur J*. **2018**, *24*, 4043-4049. (d) Prasad, J.

V. N. V.; Samuelson, A. G.; Pillai, C. N. Isomerization of Allyl Alcohol In The Presence of Raney Nickel. *J. Catal*. **1982**, *75*, 1-6.

(5) (a) Suchand, B.; Satyanarayana, G. KO^{t}Bu-Mediated Domino Isomerization and Functionalization of Aromatic Allylic Alcohols. *Eur. J. Org. Chem*. **2017**, *26*, 3886-3895. (b) Martinez-Erro, S.; Sanz-Marco, A.; Gomez, A.B.; Vazquez-Romero, A.; Ahlquist, M. S. G.; Martín-Matute, B. Base-Catalyzed Stereospecific Isomerization of Electron-Deficient Allylic Alcohols and Ethers through Ion-Pairing. *J. Am. Chem. Soc*. **2016**, *138*, 13408-13414.

(6) (a) Zhang, S.; Neumann, H.; Beller, M. Synthesis of α,β-Unsaturated Carbonyl Compounds By Carbonylation Reactions. *Chem. Soc. Rev*. **2020**, *49*, 3187-3210. (b) Climent, M. J.; Corma, A.; Iborra, S.; Velty, A. Activated Hydrotalcites as Catalysts for The Synthesis Of Chalcones Of Pharmaceutical Interest. *J. Catal*. **2004**, *221*, 474-482. (c) Li, R.; Kenyon, G. L.; Cohen, F. E.; Chen, X.; Gong, B.; Dominguez, J. N.; Kurzban, E. D. G.; Miller, R. E.; Nuzman, E. O. In Vitro Antimalarial Activity of Chalcones and Their Derivatives. *J. Med. Chem*. **1995**, *38*, 5031-5037.

(7) (a) Smets, J.; Denutte, H. R. G.; Pintens, A.; Stanton, D. T.; Aken, K. V.; Laureyn, I. H. H.; Denolf, B.; Vrielynck, F. A. C. U.S. Pat, Appl. Publ, 2010. US 20100137178 A1 (b) Junzo, O. *Modern Carbonyl Chemistry*, Otera, J. (Eds.), Wiley-VCH, Weinheim, 2000.

(8) (a) Dhar, D.N. Chemistry of Chalcones and Related Compounds, Wiley, New York, **1981**. (b) Sinisterra, J. V.; Garcia-Raso, J. V.; Cabello, J. A.; Marinas, J. M. An Improved Procedure for the Claisen-Schmidt Reaction. *Synthesis*, **1984**, *6*, 502-504.

(9) (a) Reetz, M. T. Lewis Acid Induced α-Alkylation of Carbonyl Compounds. *Angew. Chem., Int. 21*, **1982**, 96-108. (b) Caine, D. in: Trost, B.M.; Fleming, I. (Eds.), Comprehensive Organic Synthesis, *3*, Pergamon, Oxford, **1991**, 1-63.

(10) (a) Das, J.; Singh, K.; Vellakkaran, M.; Banerjee, D. Nickel-Catalyzed Hydrogen-Borrowing Strategy for α-Alkylation of Ketones with Alcohols: A New Route to Branched gem-Bis(alkyl) Ketones. *Org. Lett*. **2018**, *20*, 5587-5591. (b) Schlepphorst, C.; Maji, B.; Glorius, F. Ruthenium-NHC Catalyzed α-Alkylation of Methylene Ketones Provides Branched Products through Borrowing Hydrogen Strategy. *ACS Catal*. **2016**, *6*, 4184-4188.

(11) Latham, D.E.; Polidano, K.; Williams, J. M. J.; Morrill, L. C. One-Pot Conversion of Allylic Alcohols to α-Methyl Ketones via Iron-Catalyzed Isomerization-Methylation. *Org. Lett*. **2019**, *21*, 7914-7918.

(12) (a) Crabtree, R.H. Homogeneous Transition Metal Catalysis of Acceptorless Dehydrogenative Alcohol Oxidation: Applications in Hydrogen Storage and to Heterocycle Synthesis. *Chem. Rev*. **2017**, *117*, 9228-9246. (b) Gunanathan, C.; Milstein, D. Applications of Acceptorless Dehydrogenation and Related Transformations in Chemical Synthesis. *Science*. **2013**, *341*, 1229712.

(13) (a) Yadav, V.; Landge, V. G.; Subaramanian, M.; Balaraman, E. Manganese-Catalyzed α-Olefination of Nitriles with Secondary Alcohols. *ACS Catal*. **2020**, *10*, 947-954. (b) Thiyagarajan, S.; Gunanathan, C. Ruthenium-Catalyzed α-Olefination of Nitriles Using Secondary Alcohols. *ACS Catal*. **2018**, *8*, 2473-2478. (c) Chakraborty, S.; Das, U. K.; Ben-David, Y.; Milstein, D. Manganese Catalyzed α-Olefination of Nitriles by Primary Alcohols. *J. Am. Chem. Soc*. **2017**, *139*, 11710-11713.

(14) (a) Penea-Lopez, M.; Piehl, P.; Elangovan, S.; Neumann, H.; Beller, M. Manganese-Catalyzed Hydrogen-Autotransfer C-C Bond Formation: α-Alkylation of Ketones with Primary Alcohols. *Angew. Chem., Int*. **2016**, *55*, 14967-14971. (b) Chakraborty, S.; Daw, P.; Ben-David, Y.; Milstein, D. Manganese-Catalyzed α-Alkylation of Ketones, Esters, and Amides Using Alcohols. *ACS Catal*. **2018**, *8*, 10300-10305. (c) Irrang, T.;

Kempe, R. 3d-Metal Catalyzed N- and C-Alkylation Reactions via Borrowing Hydrogen or Hydrogen Autotransfer. *Chem. Rev*. **2019**, *119*, 2524-2529.

(15) (a) Corma, A.; Navas, J.; Sabater, M. J. Advances in One-Pot Synthesis through Borrowing Hydrogen Catalysis. *Chem. Rev*. **2018**, *118*, 1410-1459. (b) Yang, Q.; Wang, Q.; Yu, Z. Substitution of Alcohols By N-Nucleophiles Via Transition Metal-Catalyzed Dehydrogenation. *Chem. Soc. Rev*. **2015**, *44*, 2305-2329. (c) Huang, F.; Liu, Z.; Yu, Z. C. C-Alkylation of Ketones and Related Compounds by Alcohols: Transition-Metal-Catalyzed Dehydrogenation. *Angew. Chem., Int*. **2016**, *55*, 862-875. (d) Mukherjee, A.; Milstein, D. Homogeneous Catalysis by Cobalt and Manganese Pincer Complexes. *ACS Catal*. **2018**, *8*, 11435-11469.

(16) (a) Sahoo, A. R.; Lalitha, G.; Murugesh, V.; Bruneau, C.; Sharma, G. V. M.; Suresh, S.; Achard, M. Ruthenium Phosphine-Pyridone Catalyzed Cross-Coupling of Alcohols to form α-Alkylated Ketones. *J. Org. Chem*. **2017**, *82*, 10727-10731. (b) Musa, S.; Ackermann, L.; Gelman, D. Dehydrogenative Cross-Coupling of Primary and Secondary Alcohols. *Adv. Synth. Catal*. **2013**, *355*, 3077-3080. (c) Gnanamgari, D.; Leung, C.H.; Schley, N.D.; Hilton, S.T.; Crabtree, R.H. Alcohol Cross-Coupling Reactions Catalyzed by Ru and Ir Terpyridine Complexes. *Org. Biomol*. **2008**, *6*, 4442-4445.

(17) (a) Thiyagarajan, S.; Gunanathan, C. Catalytic Cross-Coupling of Secondary Alcohols. *J. Am, Chem. Soc*. **2019**, *141*, 3822-3827. (b) Thiyagarajan, S.; Gunanathan, C. Ruthenium-Catalyzed Direct Cross-Coupling of Secondary Alcohols to β-Disubstituted Ketones. *Synlett*. **2019**, *30*, 2027-2034.

(18) (a) Gawali, S. S.; Pandia, B. K.; Pal, S.; Gunanathan, C. Manganese(I)-Catalyzed Cross-Coupling of Ketones and Secondary Alcohols with Primary Alcohols. *ACS Omega*. **2019**, *4*, 10741-10754 (b) Kallmeier, F.; Dudziec, B.; Irrang, T.; Kempe, R.

Manganese-Catalyzed Sustainable Synthesis of Pyrroles from Alcohols and Amino Alcohols. *Angew. Chem. Int. Ed.* **2017**, *56*, 7261-7265.

(19) (a) Gawali, S. S.; Pandia, B. K.; Gunanathan, C. Manganese(I)-Catalyzed α-Alkenylation of Ketones Using Primary Alcohols. *Org. Lett*. **2019**, *21*, 3842-3847. (b) Pandia, B. K.; Gunanathan, C. Manganese(I) Catalyzed α-Alkenylation of Amides Using Alcohols with Liberation of Hydrogen and Water. *J. Org. Chem*. **2021**, *86*, 9994-10005. (c) Pandia, B.K.; Pattanaik, S.; Gunanathan, C. Manganese(I) Catalyzed Alkenylation of Phosphine Oxides Using Alcohols with Liberation of Hydrogen and Water. *J. Org. Chem*. **2021**, *86*, 17848-17855.

(20) Kallmeier, F.; Irrgang, T.; Dietel, T.; Kempe, R. Highly Active and Selective Manganese C=O Bond Hydrogenation Catalysts: The Importance of the Multidentate Ligand, the Ancillary Ligands, and the Oxidation State. *Angew. Chem. Int*. **2016**, *55*, 11806-11809.

(21) Das, U. K.; Ben-David, Y.; Diskin-Posner, Y.; Milstein, D. N-Substituted Hydrazones by Manganese-Catalyzed Coupling of Alcohols with Hydrazine: Borrowing Hydrogen and Acceptorless Dehydrogenation in One System. *Angew. Chem. Int*. **2018**, *57*, 2179-2182.

(22) (a) Liu, T.; Wang, L.; Wu, K.; Yu, Z. Manganese-Catalyzed β-Alkylation of Secondary Alcohols with Primary Alcohols under Phosphine-Free Conditions. *ACS Catal*. **2018**, *8*, 7201-7207. (b) Fu, S.; Shao, Z.; Wang, Y.; Liu, Q. Manganese-Catalyzed Upgrading of Ethanol into 1-Butanol. *J. Am, Chem. Soc*. **2017**, *139*, 11941-11948.

(23) (a) Freitag, F.; Irrang, T.; Kempe, R. Mechanistic Studies of Hydride Transfer to Imines from a Highly Active and Chemoselective Manganate Catalyst. *J. Am. Chem. Soc*. **2019**, *141*, 11677-11685. (b) Fertig, R.; Irrang, T.; Freitag, F.; Zander, J.; Kempe, R. Manganese-Catalyzed and Base-Switchable Synthesis of Amines or Imines via

Borrowing Hydrogen or Dehydrogenative Condensation. *ACS Catal*. **2018**, *8*, 8525-8530.

(24) Wei, Y.; Tang, J.; Cong, X.; Zeng, X. Practical Metal-Free Synthesis of Chalcone Derivatives Via a Tandem Cross-Dehydrogenative-Coupling/Elimination Reaction. *Green Chem*. **2013**, *15*, 3165-3169.

(25) N. Axel, F. Werner, E. Karl, Ger. Offen, 1978. DE 2659293 A1 19780713.

(26) Ren, B. Z.; Ablise, M.; Yang, X. C.; Lio, B.; Yang, Z. Synthesis and Biological Evaluation of α-Methyl-Chalcone for Anti-Cervical Cancer Activity. *Med. Chem. Res*. **2017**, *26*, 1871-1883.

(27) Nagel, D. L.; Cromwell, N. H. The Synthesis and Chemistry of 2-Methyl-2-Benzoyl-3-Phenylaziridine and Some 1-Substituted Derivatives. *J. Heterocycl. Chem*. **1974**, *11*, 1093-1096.

(28) Viswanathan, G. S.; Li, C. J. A Highly Stereoselective, Novel Coupling Reaction Between Alkynes and Aldehydes. *Tetrahedron Lett*. **2002**, *43*, 1613-1615.

(29) Zvak, V.; Kovac, J.; Dandarova, M.; Gracza, T.; Kriz, M. Nucleophilic Substitution Reaction of Keto-Allylic Systems with a Heterocyclic Ring in γ-Position *Collect. Czech Chem. Commun*. **1984**, *49*, 1764-1773.

(30) Bettoni, L.; Seck, C.; Mbaye, M.D.; Gaillard, S.; Renaud, J.-L. Iron-Catalyzed Tandem Three-Component Alkylation: Access to α-Methylated Substituted Ketones. *Org. Lett*. **2019**, *21*, 3057-3061.

(31) Chakrabarti, K.; Maji, M.; Panja, D.; Paul, B.; Shee, S.; Das, G.K.; Kundu S. Utilization of MeOH as a C1 Building Block in Tandem Three-Component Coupling Reaction. *Org.Lett*. **2017**, *19*, 4750-4753.

^{1}H, ^{13}C NMR Spectra of the Products:

Figure 4.1. ^{1}H NMR Spectrum of (*E)*-3-(benzo[d][1,3]dioxol-5-yl)-2-methyl-1-phenylprop-2-en-1-one (**4.1e**, 400 MHz, $CDCl_3$):

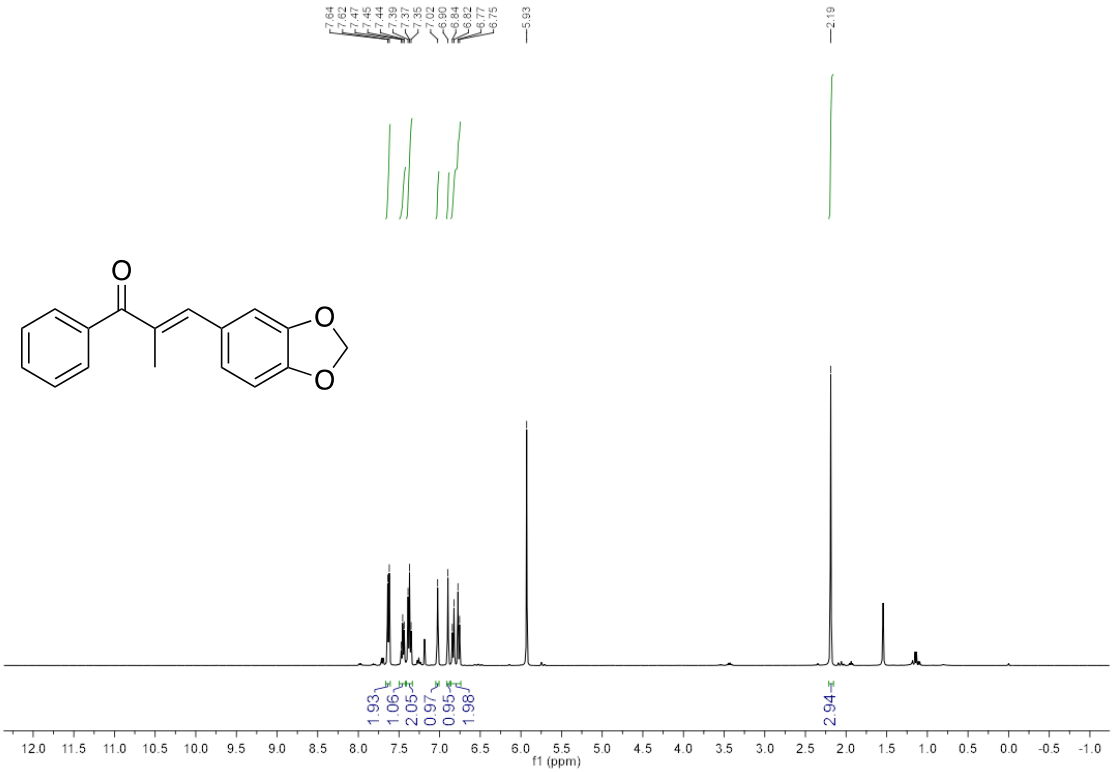


Figure 4.2. ^{13}C NMR Spectrum of (*E)*-3-(benzo[d][1,3]dioxol-5-yl)-2-methyl-1-phenylprop-2-en-1-one (**4.1e**, 101 MHz, $CDCl_3$):

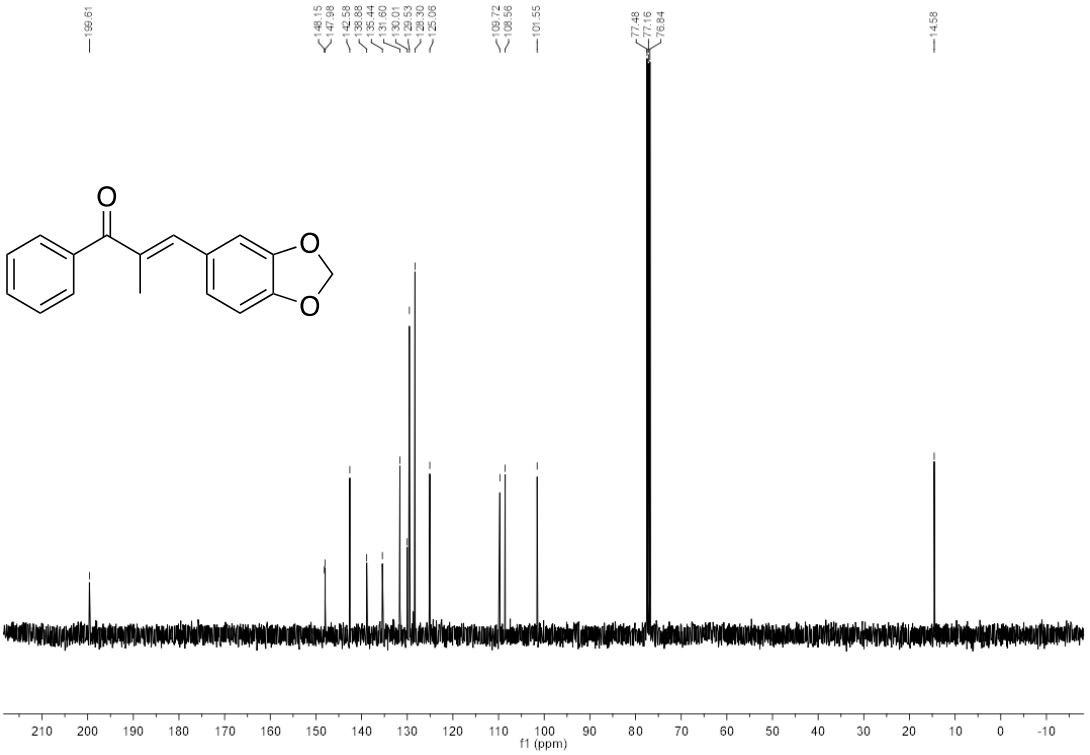


Figure 4.3. ^{1}H NMR Spectrum of 2-methyl-1-phenyl-3-(thiophen-2-yl)prop-2-en-1-one (**4.1l**, 400 MHz, $CDCl_3$):

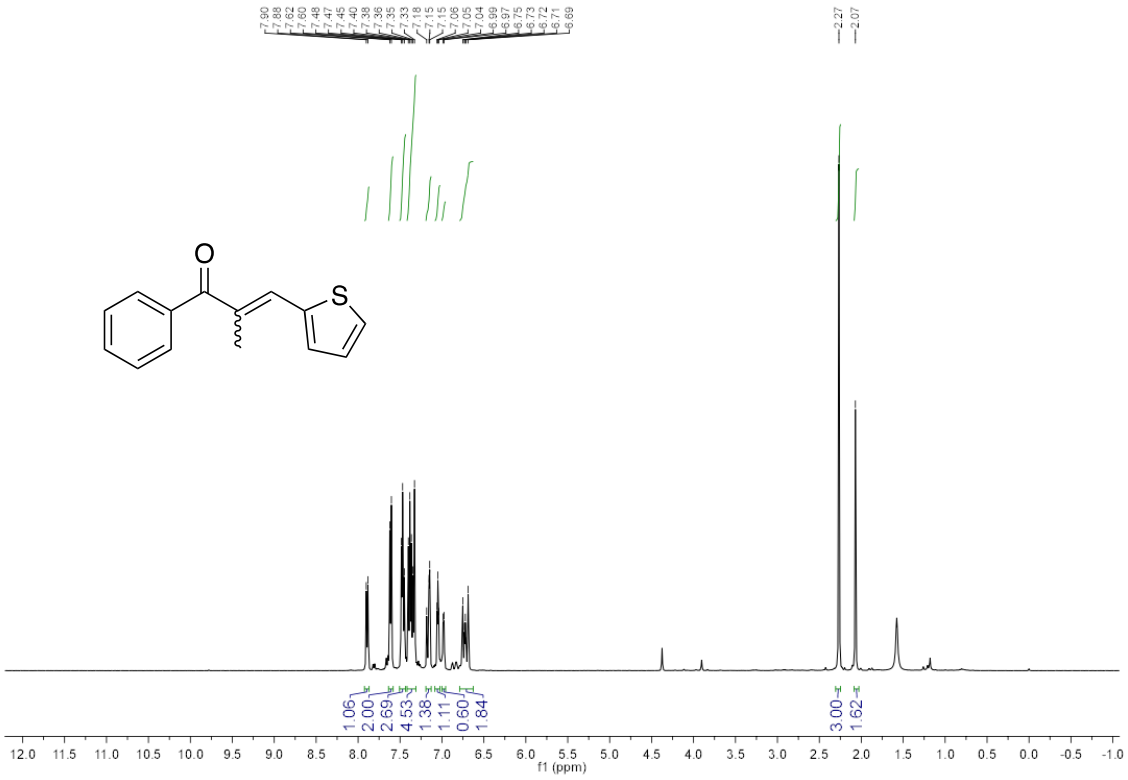


Figure 4.4. ^{13}C NMR Spectrum of 2-methyl-1-phenyl-3-(thiophen-2-yl)prop-2-en-1-one (**4.1l**, 101 MHz, $CDCl_3$):

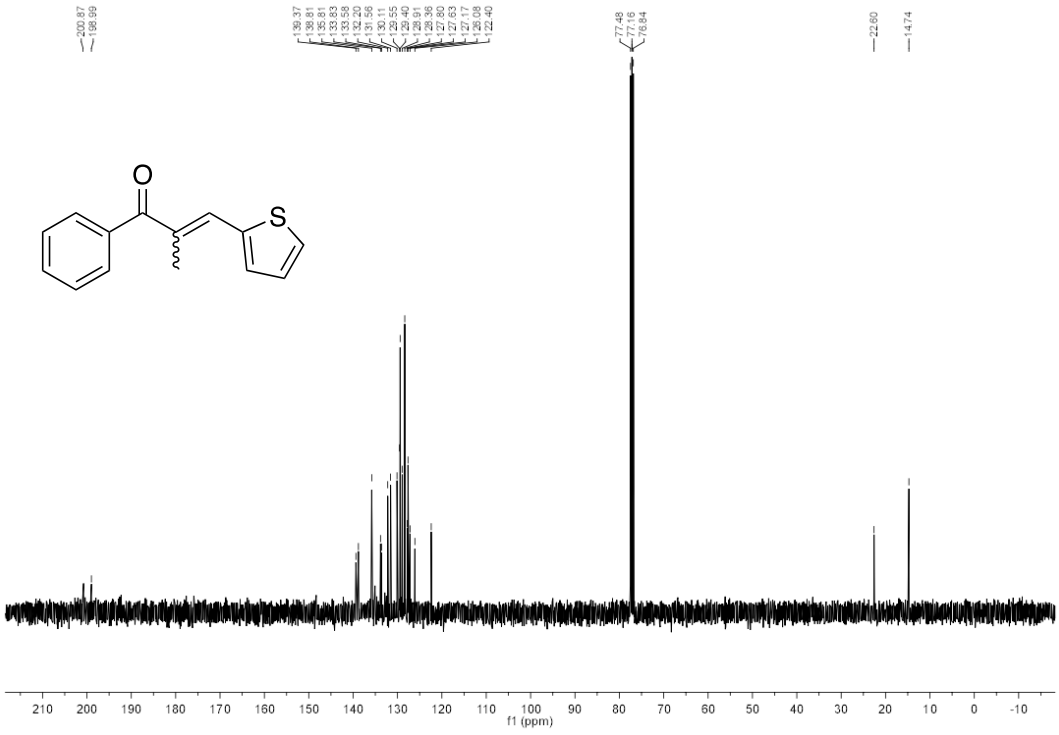


Figure 4.5. ^{1}H NMR Spectrum of 2-methyl-1,3-diphenylpropan-1-one (**4.2a**, 400 MHz, $CDCl_3$):

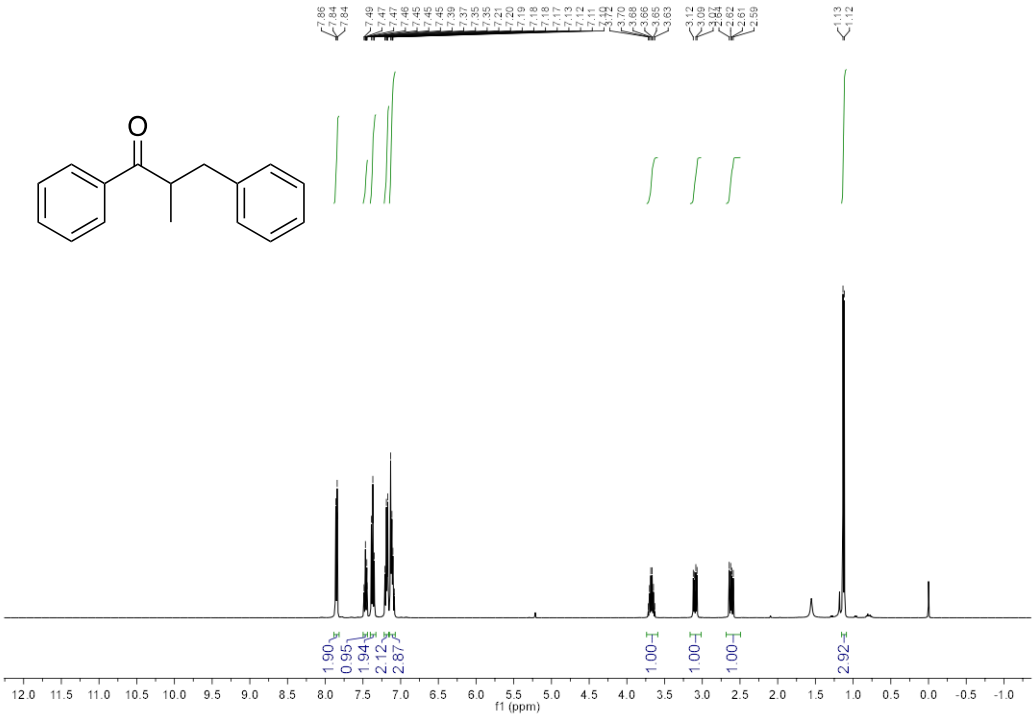
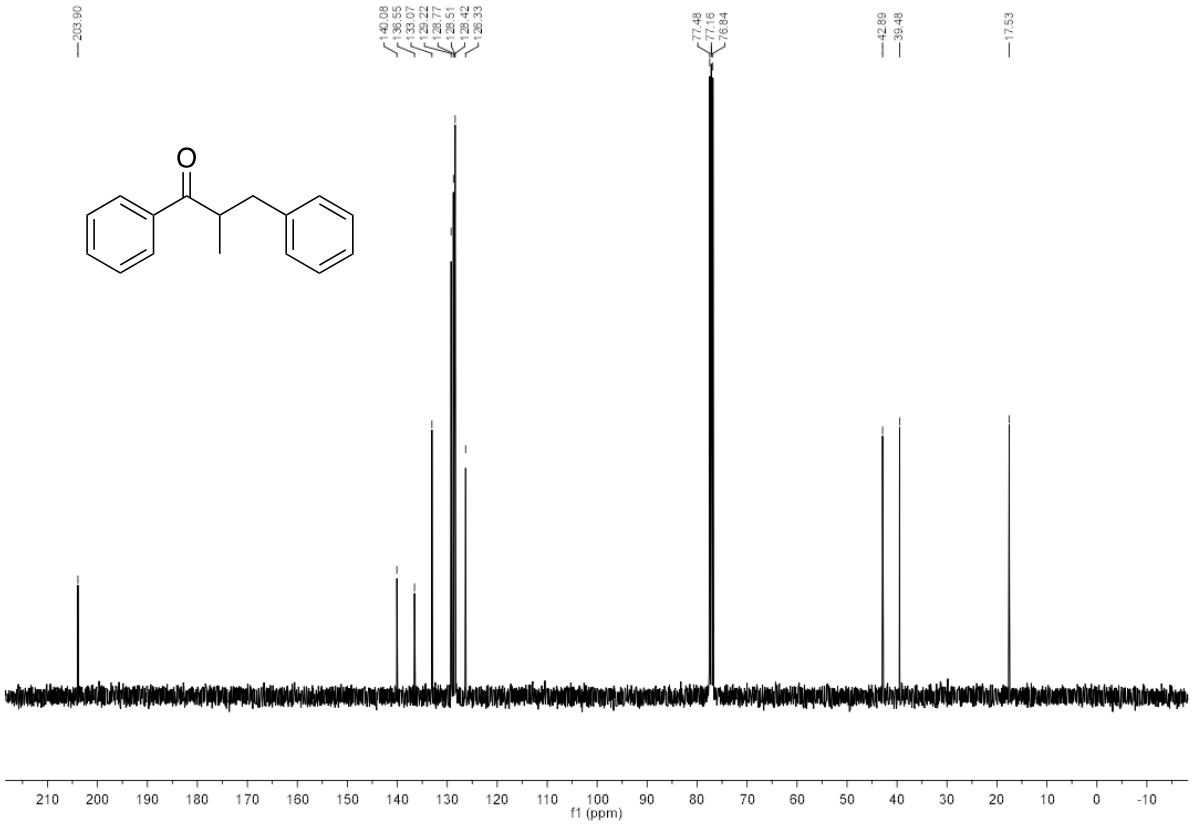


Figure 4.6. ^{13}C NMR Spectrum of 2-methyl-1,3-diphenylpropan-1-one (**4.2a**, 101 MHz, $CDCl_3$):



Chapter 5

Conclusions

Classical methods to construct C–C bond make use of organohalides and other organometallic reagents, which generates stoichiometric amount of waste. To overcome drawbacks associated with conventional synthesis, transition metal-based catalysis has emerged as an alternative, which promotes the principles of "green-chemistry". In the last two decades study of synthesis of pincer-complexes and their reactivity has been a topic of interest as they have played a key role in developing greener protocols for valuable chemical transformations. Pincer complexes possess unique balance of stability and reactivity. They can withstand high temperature, hence making them useful in homogeneous catalysis. Manganese being the third most abundant transition metal, synthesis and reactivity of the corresponding pincer complexes has been studied extensively. This thesis attempts to delineate important C–C bond forming reactions with particular focus on alkenylation and alkylation reactions.

Chapter 1 describes the importance of pincer complexes in general and the unusual reactivity present in them namely, "metal-ligand cooperation". The acceptorless dehydrogenative coupling (ADC) and borrowing hydrogen (BH) strategies are discussed as well, which help in construction of new C–C and C–N bonds. Following these pathways, important literature reports based on manganese-pincer complex are discussed, which include hydrogenation, deuteration, alkenylation, and alkylation reactions.

Chapter 2 describes the facile α-alkenylation of amides with primary alcohols using 4-methyl-triazine substituted manganese pincer complex [(4-Me)Tr(NHP(^{i}Pr$_2$)$_2$Mn(CO)$_2$Br)] **1**. Selective α-alkenylation of amides was attained by using sodium *tert*-butoxide (1 equiv), and catalytic amount of a manganese pincer complex **1**. Using an assortment of primary alcohols

and amides bearing electron withdrawing as well as electron donating group, α,β-unsaturated amides were synthesized following this catalytic protocol. When tertiary amides were employed, formation of mixture of alkenylation and alkylation products was observed. Reaction of 2-fluoroacetanilide, and benzyl alcohol provided 2-methoxy substituted α,β-unsaturated amides, which resulted from further reaction of the alkenylation product with methanol. This reaction proceeded via S_NAr pathway. Mechanistic studies confirmed that the alkenylation reaction proceeds via in-situ oxidation of alcohol to aldehyde. Mechanistic studies also confirmed the definite role of manganese catalyst in the aldol condensation step. A series of reaction with deuterated substrates under the catalytic conditions established that when deuterated amide substrate was used, the deuterium scrambling occurred at both α and β positions. Overall, the reaction is facilitated by dearomatization-aromatization metal ligand cooperation operative in the catalyst and accordingly a catalytic cycle was proposed. This catalytic protocol is environmentally benign and proceeds via acceptorless dehydrogenative coupling (ADC) pathway in which water and molecular hydrogen are the only byproducts.

In chapter 3, direct α-alkenylation of methyldiphenylphosphine oxide with primary alcohols is demonstrated. Methyldiphenylphosphine oxide was reacted with primary benzyl alcohols to furnish selectively *E*-alkenylphosphine oxides using catalyst **1**. Suitable reaction condition was carefully established by use of different bases, temperature, solvent, and reaction time. An assortment of primary alcohols bearing electron withdrawing and donating groups were used as alkenylation reagents and the corresponding alkenylphosphine oxide compounds were synthesized in good to moderate yields. Polyaromatic alcohols such as anthracene methanol, pyrene methanol and ferrocene methanol also furnished the products in moderate yields. Mechanistic studies confirmed that the dearomatization-aromatization metal ligand cooperation promotes oxidation of alcohols to aldehydes. The aldol condensation between methyldiphenylphosphine oxide and aldehyde is facilitated by the manganese pincer catalyst

and base. This catalytic protocol also proceeds via the ADC strategy in which water and molecular hydrogen are the only byproducts. A greener synthesis of alkenylphosphine oxide is attained.

Chapter 4 demonstrates the cross-coupling of allylic secondary alcohols and primary alcohols to corresponding α-alkenyl or alkylation products. Alkenylation was attained by a 4-methyl substituted manganese pincer catalyst **1,** and a weak base, cesium carbonate. The alkylation was attained by use of a 4-phenyl substituted manganese pincer complex **2,** and a strong base, potassium *tert*-butoxide and the reactions proceeded via the borrowing hydrogen (BH) strategy. Both the reactions proceeded by redox isomerization of secondary allylic alcohols, followed by condensation with the in-situ generated aldehydes.

Overall, efficient catalytic protocols for alkenylation and alkylation are developed, which are atom economical and environmentally benign. Readily available alcohols are used as alkenylation or alkylation reagents to replace waste generating methods. In all the reactions described in the thesis, water and/or molecular hydrogen are the only byproducts, thereby promoting sustainable and green chemistry (**Scheme 5**). We believe that manganese pincer complexes can be a suitable alternative to their precious transition metal counterparts to promote new C-C bond forming reactions using alcohols as coupling partners. Typically, presence of phosphine ligands results in expensive, and moisture sensitive complexes. Therefore, designing of phosphine free pincer ligands, especially NNN pincer ligands and their corresponding pincer complexes using manganese precursors containing ancillary ligands other than carbonyl (e.g.- $MnCl_2$, $Mn(OTf)_2$) will be undertaken. Exploring the reactivity of such complexes will be useful in studying activation of small molecules, and solving other synthetic challenges.

Scheme 5. Alkenylation and Alkylation Reactions Developed Using Manganese Pincer Catalysts