Catalysis by Iron and Manganese Pincer Complexes

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Suhas Shahaji Gawali

DECLARATION

I, hereby declare that the investigation presented in the thesis has been carried out by me. The work is original and has not been submitted earlier as a whole or in part for a degree / diploma at this or any other Institution / University.

Suhas Shahaji Gawali

List of publications arising from the thesis

Journal

1. "Iron-Catalyzed Regioselective Cyclotrimerization of Alkynes to Benzenes", **Gawali, S. S**.; Gunanathan, C., *J. Organomet. Chem.,* **2019,** *881*, 139-149. (Invited article)

2. "Manganese(I)-Catalyzed Cross-Coupling of Ketones and Secondary Alcohols with Primary Alcohols", **Gawali, S. S.**; Pandia, B. K; Pal, S. Gunanathan, C., *ACS Omega*., **2019**, *6*, 10741-10754. (Invited article)

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

Publication not included in thesis

4. "Iron-Catalyzed Selective Etherification and Transetherification Reactions Using Alcohols", †Sahoo, P. K.; †**Gawali, S. S**.; Gunanathan, C., *ACS Omega,* **2018**, *3*, 124-136. (Invited article)

(†Equal contribution)

<u>Conferences/ Symposium</u>

1. Gawali, S. S.; Gunanathan, C. Iron-Catalyzed Regioselective Cyclotrimerization of Alkynes to Benzenes. "Inter IISER and NISER Chemistry Meet (IINCM)", Dec 22-13, 2017. NISER, Bhubaneswar, India.

2. Gawali, S. S.; Pandia, B. K.; Gunanathan, C. Manganese(I)-Catalyzed α-Alkenylation of Ketones Using Primary Alcohols. "25th CRSI National Symposium in Chemistry", July 19-21, 2019. IIT, Kanpur, India.

Suhas Shahaji Gawali

To My Parents

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Chapter 5 Conclusions

Design, synthesis and characterization of new first row transition metal pincer complexes and finding their catalytic application in divers reactions are challenging. Highly selective catalytic transformations can be achieved by modifying the ligand steric and electronic properties of transition metal based pincer complexes. The work delineated in this thesis is attempted to uncover such catalytic applications of new and known pincer complexes.

Chapter 1 covered catalytic protocols based on the iron and manganese pincer complexes reported in the literature. Highly selective hydrogenation reactions (ketones, alkynes and carbonates), α-alkenylation (ketones and nitriles), α-Olefination (alkyl-substituted *N*-heteroarenes), N-alkylation (aromatic amines) and atom economical dimerizations (terminal alkynes) reactions have been described.

The chapter 2 revealed the regioselective synthesis of 1,2,4-trisubstituted and hexa-substituted benzene molecules from terminal aryl alkynes and internal aryl-alkyl alkynes, respectively. Mild reaction conditions, moderate loadings of catalysts and wide substrate scopes made these protocols highly efficient and practical. Aliphatic alkyne substrate containing different functional groups such as alkene, amines, silane protected alcohols and amines, which are sensitive, are well tolerated under the optimized reaction condition. However, aliphatic alkynes provided moderate regioselectivity (42% to 72%) for the 1,2,4-trisubstituted benzene products over 1,3,5-trisubstituted benzene molecules. Increased steric bulk on pincer ligands diminished the selectivity for cycloaddition reaction. EPR studies revealed that iron complex **2.1** shows spin crossover effect at low temperature (100 K).

These NNN iron(II) complexes might be used as promising catalyst for the synthesis of varieties of reactive unusual molecules such as metal hydrides, metal amides, diatomic molecule and low valent oxidation state complexes, which are further known to be used as catalyst. NNN ligand can be tuned with amide backbone and iron (II) complex can be synthesized.

Experiments performed in chapter 3 disclosed the catalytic protocol based on 4-phenyl-triazine substituted manganese pincer complex [(4-Ph)Tr(NHP(iPr$_2$))$_2$Mn(CO)$_2$Br] **3.1**. Manganese pincer **3.1** catalyzed efficient cross coupling of ketones and secondary alcohols with primary alcohols leading to the selective α-alkylation of ketones is demonstrated. Facile O-H bond activation of alcohols is described. This bond activation is further applied for developing an efficient protocol for the alkylation of ketones using alcohol as alkylating partner. Catalytic chemoselective manganese(I)-catalyzed cross-coupling of ketones and secondary alcohols with primary alcohols are achieved. Moreover, chemoselective catalytic C-alkylations of ketone and secondary alcohols over N-alkylation of aryl amine are attained. Mechanistic studies confirm the formation and progress of the reactions involving aldehyde, ketone and α,β-unsaturated ketone intermediates. The triazine backbone of catalyst further can be changed to other heteroaromatic backbone of neutral ligand systems to construct new manganese complexes and their catalytic applications can be explored. Such studies are underway in our laboratory.

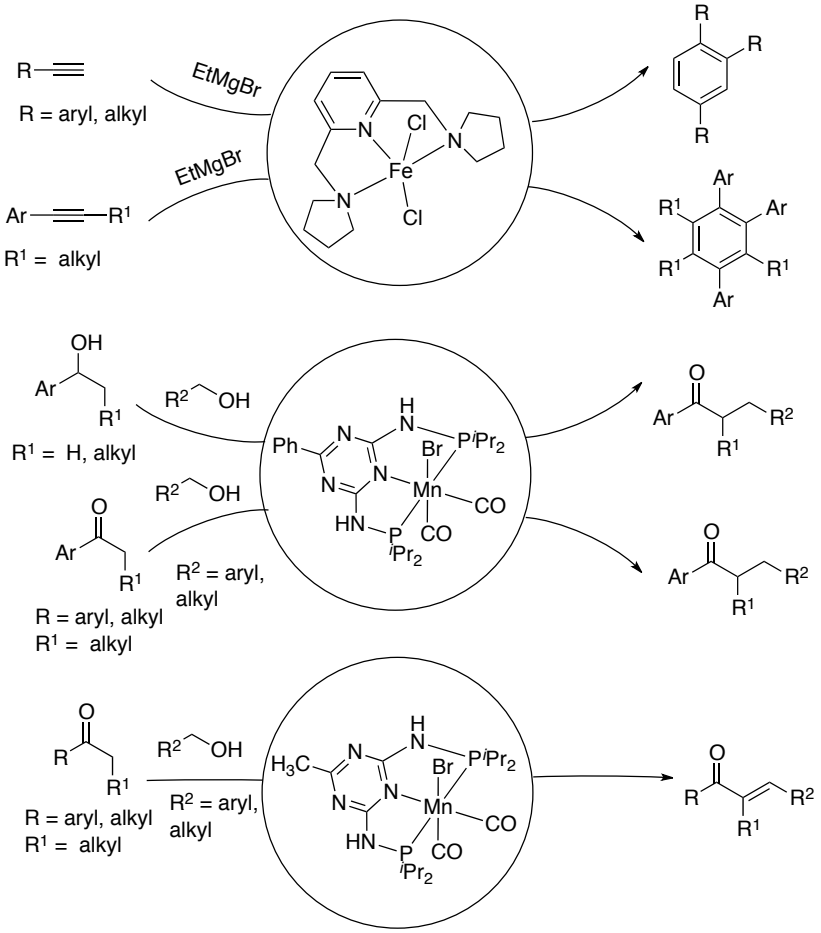
Chapter 4 disclosed the catalytic protocol based on 4-methyl-triazine substituted known manganese pincer complex [(4-Me)Tr(NHP(iPr$_2$))$_2$Mn(CO)$_2$Br] **4.1**. Highly efficient, catalytic, selective and atom economical α-alkenylation of ketones was demonstrated. Using minimal catalyst load, reaction of cyclic and acyclic benzylic

ketones with primary alcohols delivered the α-alkenylated ketone product in moderate to good yields. Remarkably, under these catalytic conditions, heteroaryl, aliphatic, and benzylic primary alcohols containing methoxy, thiomethyl, chloro, and bromo functionalities are well tolerated. Mechanistic studies confirm the involvement of an aldehyde intermediate and dearomatization-aromatization metal ligand cooperation. This catalytic protocol is highly efficient; water and molecular hydrogen are the only byproducts and thus can be employed for the synthesis of α,β-unsaturated ketones.

Overall by employing new iron and known manganese pincer complexes, simple, atom economical and important catalytic transformations were developed. Undoubtedly, this study will have broad impact to produce new and very exiting results such as synthesis of unsaturated bonds using alcohol as alkenylating source. This catalyst paves the way for the various catalytic reaction such as small bond activation, double alkylation studies, which are in progress in our research group.

The schematic summary of chapter 2-4 is presented in Scheme 5.1

Scheme 5.1 Catalysis Based on Iron and Manganese Pincer Complexes


R
R = aryl, alkyl
EtMgBr
Ar
R1
R1 = alkyl
EtMgBr
Cl
N
Fe
Cl
N
N
R
R
R
Ar
R1
Ar
R1
R1
Ar
OH
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R1
R1 = H, alkyl
R2
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iPr2
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R1

SUMMARY

This thesis emphasizes on the synthesis and characterization of simple di(aminomethyl)pyridine ligated iron-pincer complexes, which catalyzed the regioselective [2+2+2] cyclotrimerization of terminal aryl and alkyl alkynes to provide 1,2,4-trisubstituted benzene molecules. These complexes are characterized by FTIR, ^{1}H NMR, ^{13}C{^{1}H} NMR, ESI-mass spectra and single crystal X-ray diffraction analyses. Interestingly, internal alkynes also exhibited similar cyclization and resulted in hexa-substituted benzene compounds. Increased steric bulk on pincer ligands diminished the selectivity for cycloaddition. Cyclotrimerization reactions proceeded at room temperature upon activation of catalyst by a Grignard reagent. EPR studies indicated thermally induced spin crossover effect in catalyst.

Catalytic cross-coupling reactions by manganese-based pincer catalysts are developed using ketones and secondary alcohols with primary alcohols to afford α-alkylated ketones in good to excellent yields. Manganese catalyst (2 mol %) and catalytic use of a mild base (5− 10 mol %) are sufficient for efficient cross-coupling reactions. Various aryl and heteroaryl ketones are catalytically cross-coupled with diverse primary alcohols to provide the selective α-alkylated products. Challenging α-ethylation of ketones is also attained using ethanol as an alkylating reagent. Further, direct use of secondary alcohols in the reaction resulted in in-situ oxidation to provide the ketone intermediates, which underwent selective α-alkylation. The reaction proceeds via the borrowing hydrogen pathway. Notably either water or water and dihydrogen are the only byproducts in these environmentally benign catalytic processes. Mechanistic studies allowed inferring all of the intermediates involved. Dearomatization-aromatization metal-ligand cooperation in the catalyst facilitates the facile O−H bond activation of both primary and secondary alcohols, and the resultant

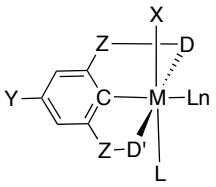
manganese alkoxide complexes produce corresponding carbonyl compounds, perhaps via *β*-hydride elimination. The manganese(I) hydride intermediate plays dual role as it hydrogenates *α,β*–saturated ketones and liberates molecular hydrogen to regenerate the catalytically active dearomatized intermediate. Metal-ligand cooperation allows all of the manganese intermediates to exist in same oxidation state (+1) and plays an important role in these catalytic cross-coupling reactions.

A simple protocol of manganese catalyzed selective *α*-alkenylation of ketones using primary alcohols have been reported. The reactions proceeded well with a low loading of catalyst (0.3 mol %). Various aryl and heteroaryl ketones are catalytically *α*-alkenylated with diverse primary alcohols to provide the selective *α,β*-unsaturated ketones products. The overall transformation operates through O−H bond activation of primary alcohols via dearomatization-aromatization metal-ligand cooperation in the catalyst to provide the corresponding aldehydes, which further undergo condensation with methylene ketones to deliver *α,β*-unsaturated ketones. This selective *α*-alkenylation proceeds with the release of water and liberation of molecular hydrogen.

Chapter 1. Introduction- Iron and Manganese Pincer Complexes

Activation of inert chemical bonds by a transition metal is utmost importance in the field of homogeneous catalysis. Efficient bond activation reactions can lead to successful design of catalytic cycles and provide greener and selective approach to synthetic processes of useful products. Pincer ligands are tridentate, which enforce meridional geometry upon complexation around the metal center and provide pincer complexes with unique stability and reactivity.[1] Highly distinct reactivity of the corresponding metal complexes can be achieved by modifying the ligand steric and electronic properties of transition metal based pincer complexes. In homogeneous catalysis, transition metal complexes particularly those from group eight precious metals occupy a central place. However, potential toxicity and high cost of precious metals make them less suitable for industrial and sustainable future applications. Thus, homogeneous catalysis using more abundant and environmentally benign first row transition metals has become a attractive research topic.[2] Pincer complexes consist of a central aryl ring (phenyl, pyridinyl, pyrazinyl, etc), which is 1,3-disubstituted with two chelating side arms. The majority of pincer complexes are palindromic (i.e., NNN, PNP, PCP, NCN etc) with having C_2 or C_{2v} symmetry but there is much more potential for variety in non-palindromic pincer (i.e., NNP, PNN etc) complexes.[3] Synthesis of NNN-pyridine containing diimines (PDI) pincer ligands and their iron complexes has shown catalytic applications in hydrogenation, polymerization, cycloaddition reactions and also in functionalization of ketones, alkynes, and alkene functionalities.[4] Reactivities of the pincer complexes can fine tuned by varying the electronic and steric properties of the pincer ligands (figure 1.1).

Figure 1.1 General structure of transition metal based pincer catalysis.

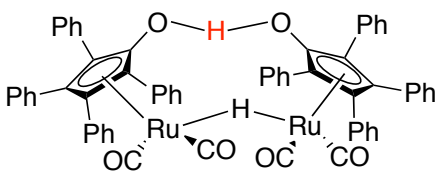


D = PR_2, NR_2, SR, OR, NHC
(modulation via donor atom)
Y = NR_1R_2 (remote electronic modulation)
C = C, N, S (modulation via donor atom)
M = Ru, Fe, Mn, Ir, Pd (transition metals)
Z = CH_2, NR, O

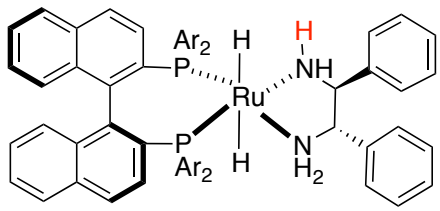
By modifying the ligand backbone, as well as, central and side donors, and its combinations can provides large number of pincer ligands with variety of steric and electronic properties.[2,5] Using these combinations of ligands and metals, systematic studies can provides diverse catalytic reactions in homogeneous catalysis.

In past decades, Shvo and Noyori were one of the discoverer and architect of metal-ligand bifunctional molecular catalysis concept, which relied on direct involvement of the chelating ligand in the catalytic reaction via a reversible proton (H+) transfer through cleavage/formation of one of its X-H bonds (X = O, N, C). (Scheme 1.1) Noyori and co-workers disclosed the efficiently catalyzed the hydrogenation of various polar unsaturated functionalized substrate upon hetrolytic activation of dihydrogen via metal-amine-amide cooperativity, which provided excellent reactivity and selectivity in the hydrogenation of carbonyl compounds.[6]

Scheme 1.1 Shvo and Noyori Catalyst of M/OH and M/NH Metal-Ligand Bifunctional Catalysis



Shvo, 1986

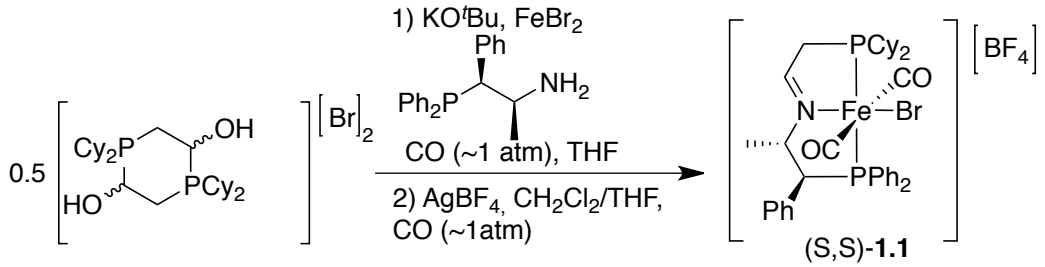


Noyori, 1995

In recent year, asymmetric hydrogenation and transfer hydrogenation of various polar

unsaturated substrate is having radical impact on the organic synthesis of chiral compounds in homogeneous catalysis.[7] In 2014, Morris and co-workers, synthesized the novel chiral iron (II) pincer complex (S,S)-[Fe(P−CH═N−P')$(CO)_2$(Br)][BF_4] [(P-CH=N-P') = Cy_2PCH_2CH═$NCH_2CH_2PPh_2$], (S,S)'-1.1 (Scheme-1.2), for asymmetric hydrogenation reaction of ketones and imines. Under mild condition, when cyclic phosphonium salt as a source of phosphine-aldehyde, $FeBr_2$, KO^{t}Bu, CO (~1atm) and chiral (S,S)-2-amino-1-phenylpropyldiphenylphosphine in THF followed by treatment with $AgBF_4$ and CO (~1atm) at room temperature generated chiral complex (S,S)-1.1. Complex (S,S) -1.1 has bulky Cy substituents on the ligand in the anticipation that it would enhanced enantiomeric interaction with the substrate during catalysis (Scheme 1.2)

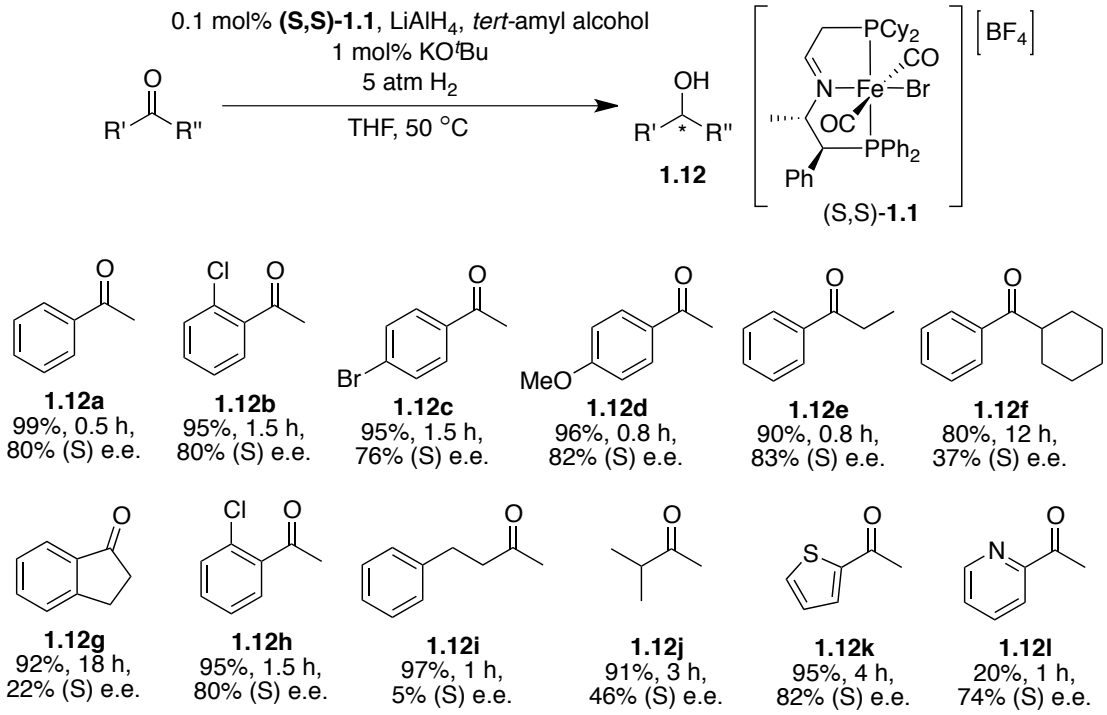
Scheme 1.2 Synthesis of the Chiral Iron Complex, [Fe(P−CH=N−P′)$(CO)_2$ (Br)][BF_4], (S,S)-1.1



Asymmetric hydrogenation of ketones to the alcohol with good enatioselectivity using an in situ-generated catalyst derived from chiral complex **(S,S)-1.1**. The reaction was performed using THF as solvent under pressurized H_2 (5 bar) atmosphere. An assortment of ketones were asymmetric hydrogenation reaction using an in situ - generated catalyst derived from (S,S)-1.1. Activated catalyst mixture prepared from

(S,S)-1.1 were found to give the efficient hydrogenation of the aryl-alkyl, hetro-aryl-alkyl ketones with enantiomeric excess upto 85% and dialkyl and cycloalkyl ketones with inferior enantioselectivity. (Scheme 1.3)

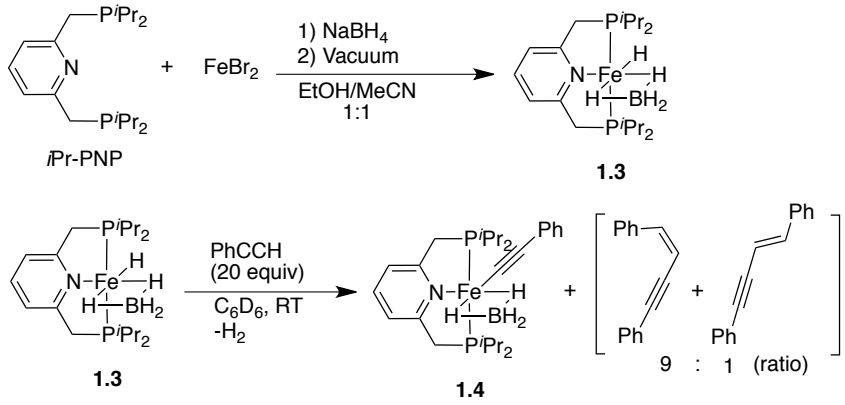
Scheme 1.3 Reactivity of Various Ketones in the Asymmetric Hydrogenation Reaction using an Insitu Generated Catalyst Derived from (S,S)-1.1



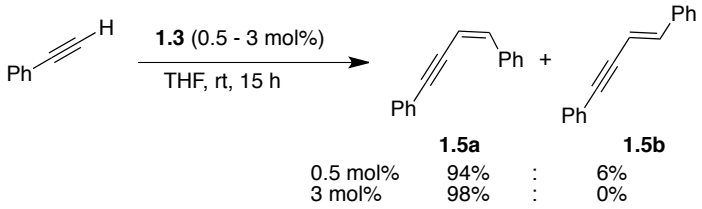
In recent years, one of the striking chemical transformation discover is direct hydroalkynylation across carbon carbon triple bond or alkyne dimerization reaction to synthesis conjugated 1,3-enyne building block in organic synthesis. This is a highly atom economical reaction.[8] Milstein and coworkers, disclosed a very interesting example of PNP iron hydride complexes for efficient Z-selective (cross) dimerization of terminal alkynes reaction under mild condition. The complexes can be prepared successfully by ligation of $FeBr_2$ by $PNP^{iPr}{}_2$ pincer ligand in presence of excess $NaBH_4$ to generate octahedral phosphine coordinated iron(II) complex **1.3**. Further, addition of excess phenylacetylene lead to the formation of saturated reactive

intermediate iron complex **1.4** (Scheme 1.4).[9] The catalyst (**1.3**; 0.5 mol%) reacted with phenylacetylene and provided excellent conversion and yield (94%) of Z-selective dimerized products with 94:6 (Z:E) selectivity for 1,4-diphenyl-1-buten-3-yne (Scheme 1.2). When similar experiment was carried out with increase in the catalyst load to 3 mol% resulted in complete conversion into the single Z-dimerized product, after 15 h (Scheme 1.5).

Scheme 1.4 Preparation of the [Fe(H)(BH_4)-(^{i}Pr-PNP)] (1.3) Catalyst and Formation of Iron-alkynyl Complex 1.4 (intermediate)



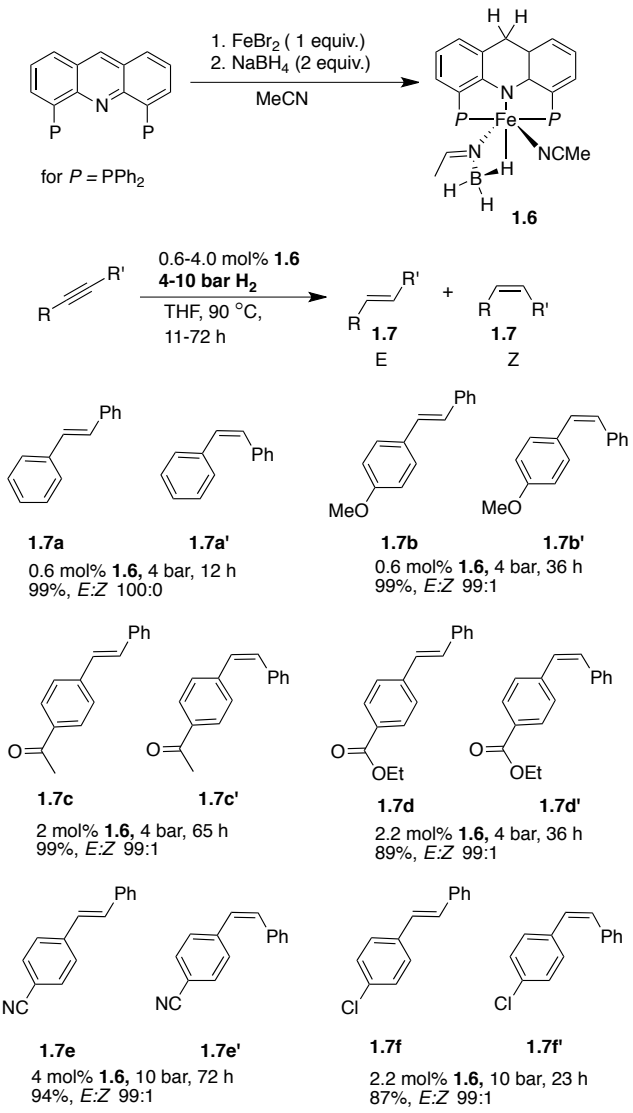
Scheme 1.5 Dimerization of Terminal Alkynes as Catalyzed by 1.3



The semihydrogenation of alkynes to alkenes is addition of hydrogen across a multiple bonds; a key transformation in organic synthesis to generate selective alkene compounds. Selective synthesis of olefin compounds finds utmost importance in biologically relevant compounds including pharmaceuticals, natural products and fragrances. C=C bonds often present in two defined configuration with E or Z

configurations. Practically, E-selective synthesis of alkenes from alkynes remains a challenge, as the methods commonly require stoichiometric amount of reagents and suffer from poor atom economy, i.e., Birch type reduction. Recently, an interesting example of E-selective semihydrogenation of alkynes in the presence of catalytic amounts of (5.5 mol%) [(Cp*)Ru(COD)Cl] (COD = 1,5-cyclooctadiene) and (5.0 mol%) AgOTf is reported by Fürstner and co-workers. The reactions have been carried out under a hydrogen (10 bar) pressure at room temperature.[10] Later, Milstein and co-worker indeed demonstrated practical and sustainable semihydrogenation of alkynes using the novel acridine-based PNP iron complex [(HACR PNP)Fe(CH_3CN)(κ^2-$CH_3CHCNBH_3$)] ((**3,** HACRPNP = 4,5-bis(diphenylphosphino)-9H-acridine-10-ide, Scheme 1.3). Under mild conditions, chemo and stereoselective semihydrogenation of various alkynes to E-selective alkenes in high yields have been achieved by iron complex **1.6** for the first time (Scheme 1.6). Under this catalytic condition aromatic dialkyne derivatives have been semihydrogenated with excellent conversion and selectivity.[11]

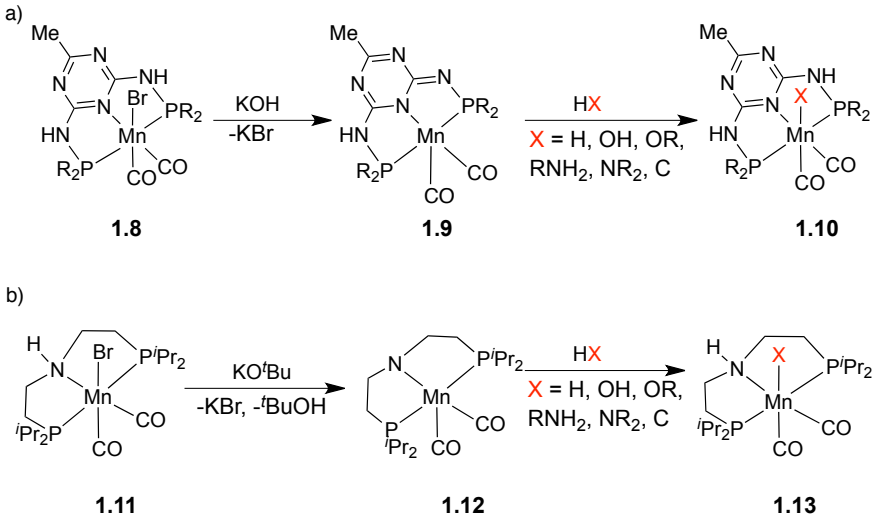
Scheme 1.6 E-Selective Semihydrogenation of Alkynes Catalyzed by 1.6



The unusual catalytic reactions of pincer complexes have been mainly derived from the metal-ligand cooperation (MLC). There are two major types of metal ligand co-operations operate in catalysis by pincer complexes; aromatization-de-aromatization MLC and amine-amide metal-ligand co-operation. MLC based on aromatization-dearomatization is described in Scheme 1.7a.[1] Typically, pyridine based pincer complexes of type **1.8** under basic condition undergo deprotonation at the pyridinyl-methylene carbon or amine to result in dearomatization of the heteroaromatic ring. The dearometized 16 electron five-coordinated pincer complexes of type **1.9** then react stoichiometrically with various small molecules (such as H-X; X = H, C, OH,

OR, NH_2, NR_2) and heterolytically cleave them in which the proton is accepted by the basic "methine carbon" or "imine nitrogen" and X-fragments (X-type ligands) occupy the vacant coordination site on metal center and generates 18 electron saturated complexes of type **1.10**. This mode of MLC based on the aromatization-dearomatization process of pyridine-based ligands and manganese pincer complexes have been reported by Kempe and coworkers.[12] MLC can also be operative in the metal complexes containing tridentate aliphatic PN^HP ligands consisting of a central "NH" donor. In presence of base, the complexes of type **1.11** undergo, deprotonation of coordinated amine functionality to provide a reactive and 16 electron unsaturated complexes of type **1.12**, which is also capable of activating unreactive bonds to generate a saturated 18 electron complexes of type **1.13**. In 2016, Beller and coworkers demonstrated reversible amine-amide MLC in manganese pincer complexes (Scheme 1.7b).[13]

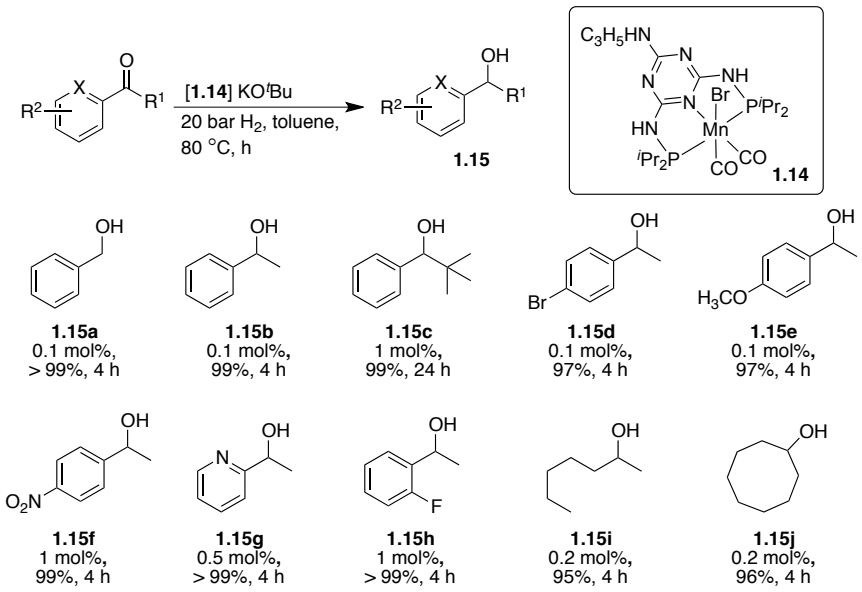
Scheme 1.7 (a) Metal-Ligand Cooperation via Dearomatization-aromatization Pathway. (b) Metal-Ligand Cooperation via Amine-amide Pathway



Recently, Kempe and coworkers disclosed the quantitative and selective

hydrogenation of ketones and aldehydes to alcohols catalyzed by complex **1.14**. The reaction was performed using toluene as solvent under pressurized H_2 (20 bar) atmosphere. An assortment of ketones and aldehydes was reduced with good conversion and selectivity in the presence of KO^{t}Bu. This catalytic method has a broad substrate scope. Catalyst **1.14** hydrogenated the aryl-alkyl, dialkyl and cycloalkyl ketones as well as aldehydes. Oxygen and nitrogen containing functional groups on aryl ring did not impact the activity of the catalyst. However, sterically hindered substrate required long reaction time (24 h, Scheme 1.8).[12a]

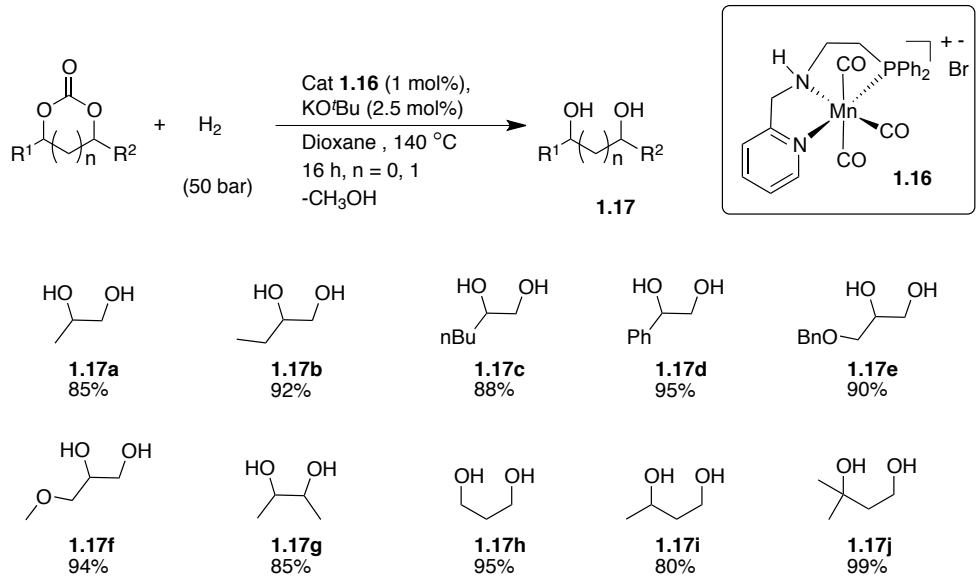
Scheme 1.8 Hydrogenolysis of Ketones and Aldehydes Catalyzed by Catalyst 1.12



Hydrogenation of cyclic organic carbonate to alcohols is one of the important chemical transformation in the green catalysis, as it provides methanol and value added diols. Generally, cyclic carbonates are synthesized from CO_2 and oxiranes. Using hydrogenation indirect conversion of CO_2 to methanol was achieved. Recently, Rueping and coworkers disclosed the first quantitative and selective hydrogenation of cyclic carbonates to vicinal diols and methanol catalyzed by manganese complex

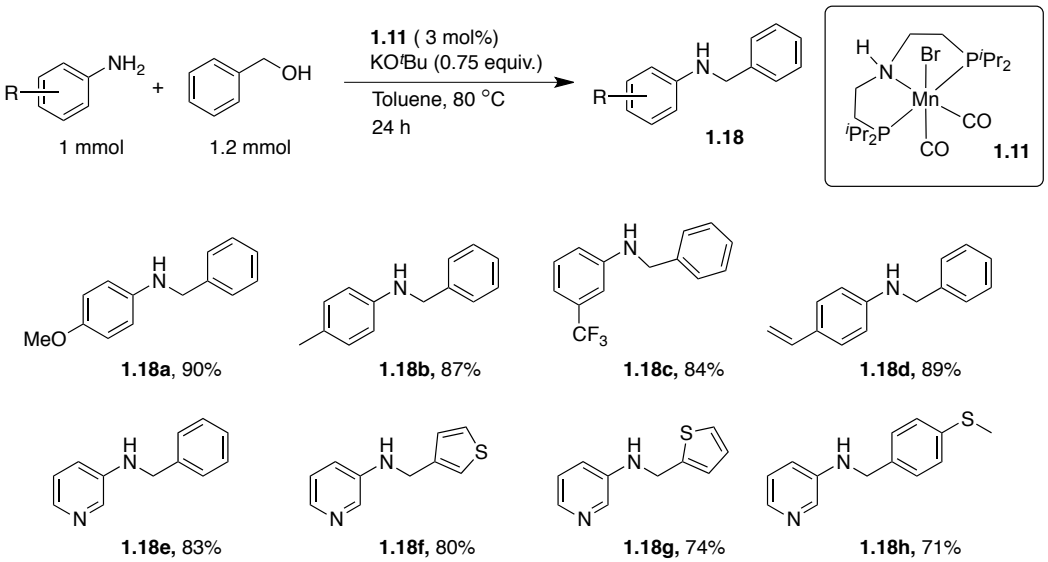
1.16. The reaction was performed using dioxane as solvent under pressurized H_2 (50 bar) atmosphere. A variety of five and six membered cyclic carbonate derivatives were successfully converted to vicinal diols and methanol with good to excellent yields (Scheme 1.9).[14]

Scheme 1.9 Selective Hydrogenation of Cyclic Carbonates to Vicinal Diols and Methanol Catalyzed by Complex 1.16



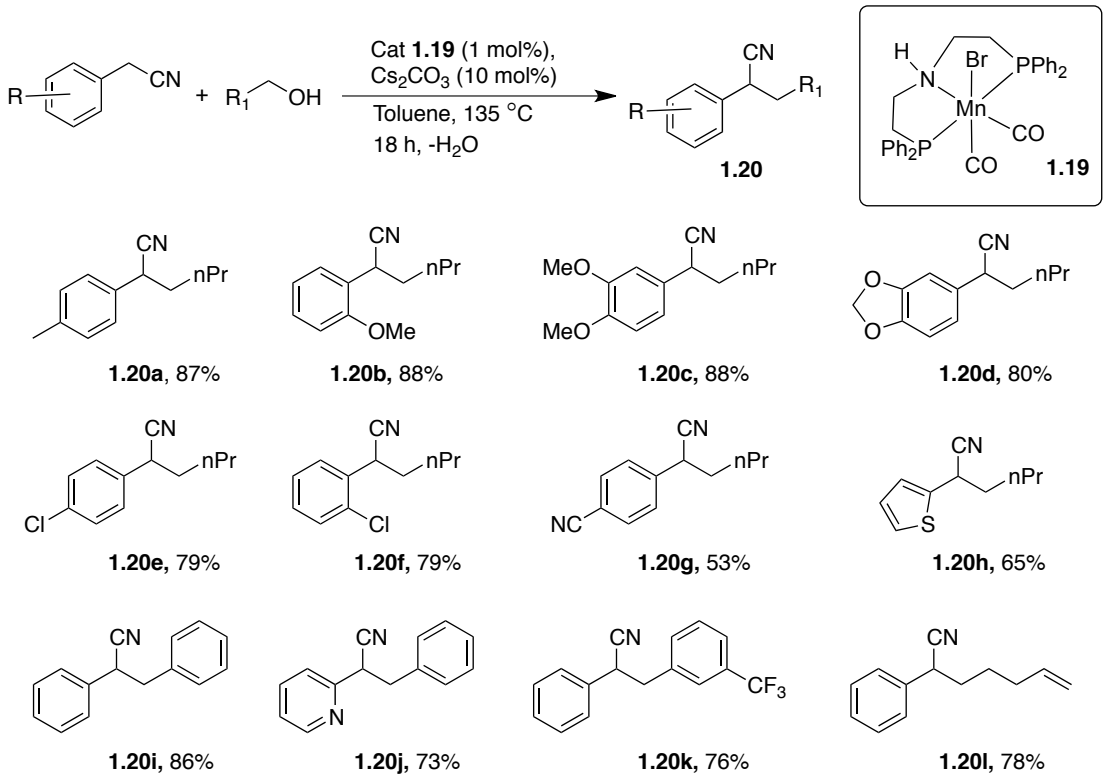
Manganese based catalysts for hydrogen transfer and borrowing hydrogen process have attracted much attention. In 2016, Beller and coworker disclosed very interesting example of synthesis of N-substituted amines by coupling of amines with alcohols catalyzed by complex **1.11**. The first catalytic dehydrogenation step of alcohols results in aldehydes. Subsequent, coupling reaction leads to aldimines and further hydrogenation provides *N*-alkylated amines, in the presence of 75 mol% KO^{t}Bu. The well-defined complex **1.11** displayed very efficient and selective alkylation using hetero aromatic alcohols and the reactions proceeded smoothly and furnished the desired alkylated products in most cases with moderate to excellent yields (up to 96%, Scheme 1.10). [13a]

Scheme 1.10 N-Alkylation of (Hetero)Aromatic Amines using (Hetero)Aromatic and Benzyl Alcohols Catalyzed by Complex 1.11



A biomass such as lignocellulose is abundantly available can be easily converted to alcohols. The development of reactions converting alcohols to fine and diverse bulk chemicals as a carbon source is an important topic in green chemistry. In that, alkylation of various functional groups using alcohol is a chemically important transformation in catalytic processes.[12d] In this direction, El-Sepelgy and coworkers introduced the C-alkylation of nitriles using alcohol as alkylating agent in 2019 catalyzed by complex **1.19**. The manganese complex **1.19** catalyzed dehydrogenation of alcohols followed by condensation of the *in-situ* generated aldehydes with nitriles under alkaline conditions occurs. Further, hydrogen liberated from alcohols used in reduction the unsaturated intermediate (e.g. α-alkenylnitriles) leads to the generation of the desired alkylated nitrile product and water as sole by-product. Using catalyst **1.19** under optimized reaction condition, wide range of functional groups are tolerated and efficiently provide useful chemoselective cyanoalkylated products in moderate to good yields (Scheme 1.11).[15]

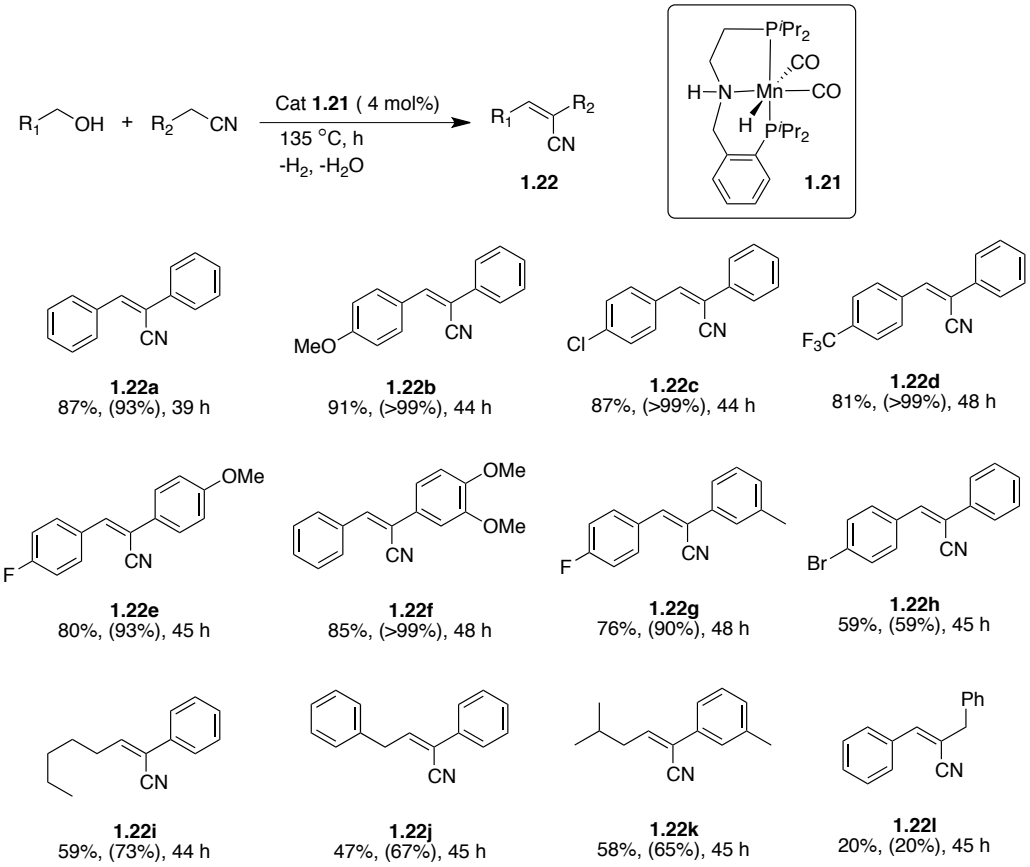
Scheme 1.11 Synthesis of α-Alkylated Nitrile using Nitriles and Alcohols Catalyzed by Complex 1.19



Recently, Milstein and coworkers disclosed practical and an interesting example of an efficient catalytic α-olefination of nitriles using primary alcohol catalyzed by pincer complex **1.21**. This is the first report by transition metal catalyzed acceptorless dehydrogenative coupling of alcohols and nitriles. The method is highly beneficial for its application to synthesize α-alkenylnitriles from acceptorless dehydrogenative coupling of alcohols and nitriles. An assortment of benzyl nitriles was olefinated using aryl-alkyl alcohols with moderate to good conversion and selectivity in a base free condition. Electron withdrawing functional group at para position of benzyl alcohols did not impact its reactivity. However, acceptorless dehydrogenative coupling of aliphatic alcohols provided moderate yields of product when reacted with benzyl nitriles. Aliphatic nitriles also underwent dehydrogenative coupling of alcohol

to provide the corresponding α-alkenylnitrile products in low yield under mild reaction conditions (Scheme 1.12).[16]

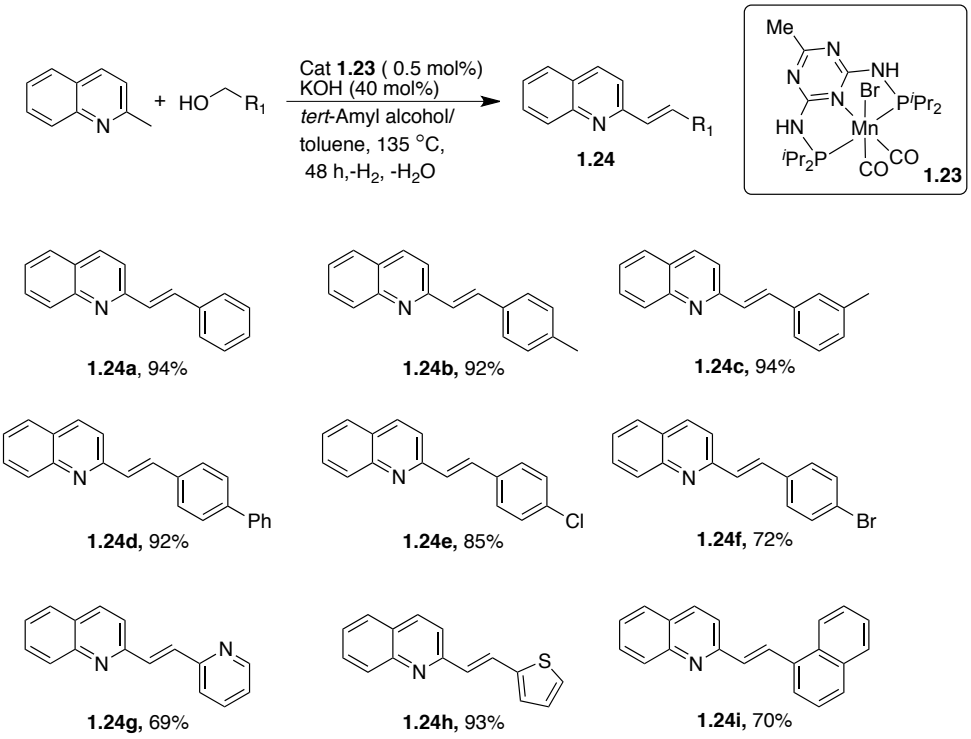
Scheme 1.12 Synthesis of α,β-unsaturated Nitrile using Nitriles and Alcohols Catalyzed by Complex 1.21



Aryl-substituted olefins find applications in agrochemicals and pharmaceuticals or as highly important intermediates in chemical synthesis. In this direction Kempe and coworkers disclosed the dehydrogenative alkylation or α-olefination of alkyl-substituted N-heteroarenes with alcohols catalyzed by complex **1.23**. The reactions were performed using tert-amyl alcohol and toluene as solvent under mild reaction condition for 48 h. An assortment of N-hetroarenes were olefinated with moderate to good yield in the presence of catalytic amount of KOH base. Benzylic and hetroaryl embedded alcohol were selectively olefinated under optimized reaction condition.

Electron withdrawing, electron donating and hetroarene functional group on alcohols did not impact their reactivity and provided the corresponding products in good to excellent yields (Scheme 1.13).[17]

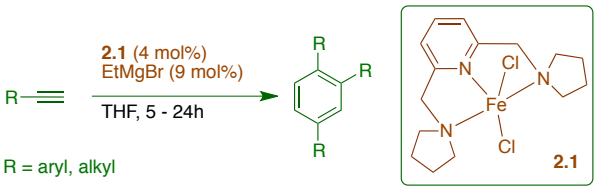
Scheme 1.13 Synthesis of *α*-Olefination of Alkyl-substituted N-Heteroarenes with Alcohols Catalyzed by Complex 1.23



CHAPTER 2

Iron-Catalyzed Regioselective Cyclotrimerization of Alkynes to Benzenes

2.1 ABSTRACT



We report the synthesis and characterization of simple di(aminomethyl)pyridine ligated iron-pincer complexes, which catalyzed the regioselective [2+2+2] cyclotrimerization of terminal aryl and alkyl alkynes to provide the 1,2,4-trisubstituted benzene molecules. Interestingly, internal alkynes also exhibited similar cyclization and resulted in hexa-substituted benzene compounds. Increased steric bulk on pincer ligands diminished the selectivity for cycloaddition. Cyclotrimerization reactions proceeded at room temperature upon activation of catalyst by a Grignard reagent. EPR studies indicated thermally induced spin crossover effect in catalyst.

2.2 INTRODUCTION

Synthesis of highly functionalized aromatic compounds finds utmost importance in pharmaceutical as well as material synthesis. In this direction, Reppe introduced a powerful and elegant approach for the synthesis of benzene compounds with multiple substitutions via [2+2+2] cyclotrimerization of alkynes[18]. Using various transition metals, number of procedures have been reported for the synthesis of arene compounds[18c,19,20]. However, selective construction of benzene rings remains a challenging task because of the poor regioselectivity, which depends on catalyst and substrates, initial formation of metallacyclopentadiene from alkyne-dimerization and subsequent cycloaddition of third alkyne[21]. As a result, such selective trimerization of

alkynes is realized using stoichiometric amounts of zirconium[22] and titanium complexes[18b,23]. Alternatively, the regioselectivity problem was addressed by introducing partially intermolecular reactions in which the use of tethered diynes provided the required geometric and entropic restrictions, and resulted in the selective formation of arenes[18a,23a,24].

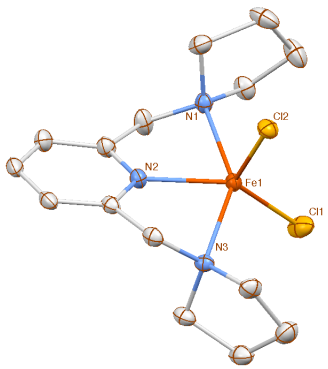
Homogeneous iron-catalysts have arguably started to challenge the dominance of noble transition metals[25]. Iron-catalyzed [2+2+2] cyclotrimerization[26] of alkynes to selective formation of benzene motifs is a challenge. In literature, different combination of iron complexes, ligands and activators have been shown to exhibit higher catalytic efficiency with wide substrate scope for 1,2,4-trisubstituted benzene derivatives. In addition to that, activator free and low oxidation state (0, +1) iron complexes have also been used[27]. However, in an intermolecular reaction, simple iron salts or even iron-carbene complexes predominantly dimerize the reactive terminal alkynes to provide a mixture (E, Z and geminal) of products[28] or self-coupled products[29]. Iron-catalyzed intermolecular cyclotrimerization of terminal alkynes remains rare with poor regioselectivity[30]. Thus, development of a defined and efficient iron catalyst for regioselective construction of 1,2,4- trisubstituted benzene compounds would be of high interest. Transition metal pincer complexes with planar backbone are efficient catalysts for numerous organic reactions. As the tridentate pincer ligands cover more than half of the metal coordination sphere, they offer better control over the metal coordination sites and enforce selectivity in catalytic processes. Using such iron pincer complexes, number of atom-economical transformations[11b] including the Z-selective dimerization of terminal alkynes[9] were reported recently. In this report, we disclose the syntheses and structure of new NNN iron-pincer

complexes and their catalytic applications in intermolecular regioselective [2+2+2] cycloaddition of both terminal and internal alkynes.

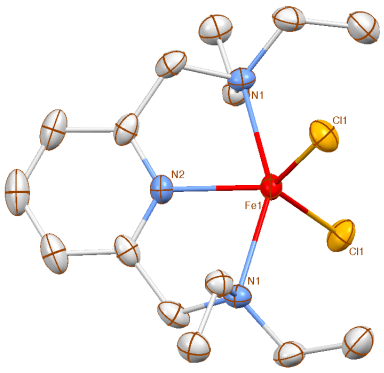
2.3 RESULTS AND DISCUSSIONS

Attempted cyclotrimerization of phenylacetylene with $FeCl_2$ (4 mol%) and ethylmagnesium bromide (9 mol%) as an activating reagent resulted in good conversion; but only to result in mixture of compounds, in which the cyclotrimerization products were found in low yields (entry 1, Table 2.1). Thus, we envisaged utilizing easily accessible and stable iron-pincer complexes for the catalytic cyclotrimerization of alkynes. The reaction of 2,6-bis(pyrrolidin-1- ylmethyl)pyridine (NNNpyr), N,N'-(pyridine-2,6-diylbis(methylene)) bis(N-ethylethanamine) (NNNEt), N,N'-(pyridine-2,6-diylbis (methylene))bis(N-isopropylpropan-2-amine) (NNN^{i}Pr), and 2,6- bis((di-tert-butylphosphino)methyl)pyridine (PNP^{t}Bu) ligands with anhydrous $FeCl_2$ provided the paramagnetic iron(II) pincer complexes **2.1-2.4**, respectively in very good yields (Scheme 2.1). The singlecrystal X-ray analyses of complexes [(NNNpyr)$FeCl_2$] **2.1** and [(NNNEt) $FeCl_2$] **2.2** revealed distorted square pyramidal geometry around the iron centers (Figure 2.1). We haven't attempted paramagnetic NMR Spectroscopy for Fe(II) complexes.

Figure 2.1 Single-crystal X-ray structures of NNN-iron pincer complexes **2.1** and **2.2** (ellipsoids are drawn at 30% probability)

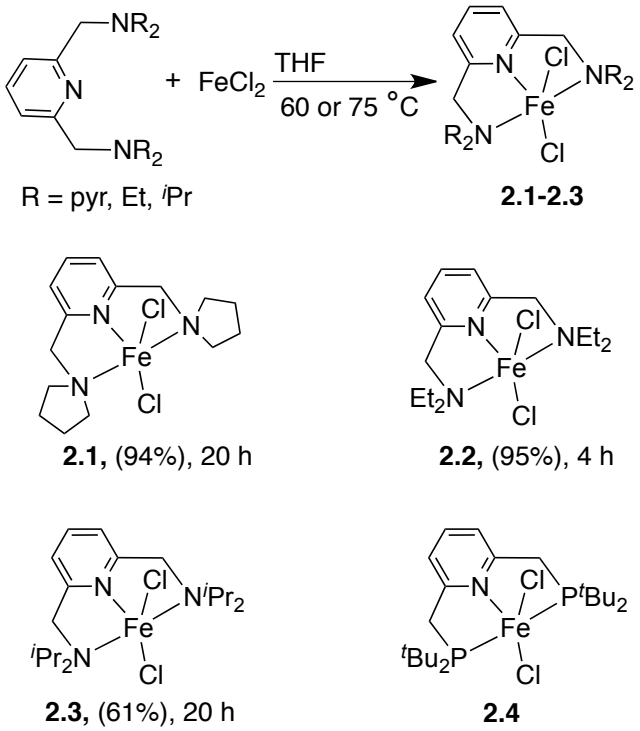


2.1



2.2

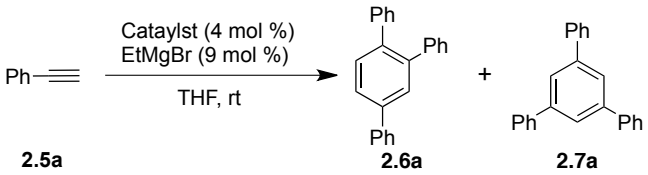
Scheme 2.1 NNN- and PNP-iron Complexes for Alkyne Trimerization.



Upon reaction of phenylacetylene and EtMgBr (9 mol%) with complex **2.1** (4 mol%) provided excellent conversion (97%), and 76% isolated yield of trisubstituted benzene products with 93:7 (2.6a:2.7a) selectivity for 1,2,4-triphenylbenzene and 1,3,5-triphenylbenzene (entry 2, Table 2.1). When similar experiment was carried out using only 4 mol% of EtMgBr (1 equiv. relative to catalyst), both conversion of alkyne and yield of the trimerization products decreased (entry 3, Table 2.1), indicating that two equivalents of activator (relative to catalyst) is essential for efficient catalysis. Notably, the sequence of addition of reagents (alkyne, catalyst, THF and finally activator EtMgBr) is important. When this addition sequence was altered and ethylmagnesium bromide was added before the addition of phenylacetylene, no desired product formation occurred (entry 4, Table 2.1). Use of iron-pincer [(NNNEt)$FeCl_2$] complex **2.2** as a catalyst provided similar results as that of catalyst

2.1 (entry 5, Table 2.1). However, when [(NNN^{i}Pr)$FeCl_2$] complex **2.3** was used as a catalyst (4 mol%) both conversion and yield of the corresponding benzene products were diminished (entry 6, Table 2.1). Further to test the role of stability and electronic influence of the catalyst in the cyclotrimerization reactions, the [(PNP^{t}Bu)$FeCl_2$] complex **2.4** was prepared[31]. Upon using **2.4** as a catalyst (4 mol%), although 94% conversion of phenylacetylene was observed, the desired products formed only in 72% yield. PNP ligated complex **2.4** having sterically hindered *tert*-butyl (^{t}Bu) substituted on donor phosphines. The reactivity of PNP pincer complex is only slightly lower than that of NNN iron pincer complex **2.1**. Perhaps, the higher steric hindrance somewhat disfavor the cylcoaddition and leads to other side reactions. When $FeCl_2$ was used as a catalyst, cyclotrimerization products were obtained in 47% yield. Moreover, synthesized Fe pincer complexes provided higher yield of the cyclotrimerization product (61%-76%). Synthesized NNN catalyst is relatively good catalyst than simple $FeCl_2$, which enhanced the reactivity. Footnote (f) indicates that the order of addition is important for the reaction outcome. Perhaps, some other active species might be forming when the order of addition is changed. Thus, iron-complex **2.1** was found to be a suitable catalyst for the selective [2+2+2] cycloaddition of terminal aryl alkynes to 1,2,4-trisubstituted benzenes. Further, using **2.1** as a catalyst cyclotrimerization of phenylacetylene in the presence of mercury (10 mol%) provided the products in 70% yield, indicating the involvement of soluble molecular catalyst in the reaction. These results confirm that by suitable modification of pincer ligands, both reactivity and selectivity in iron-catalyzed [2+2+2] cycloaddition of terminal aryl alkynes can be controlled. We didn't tried substrates other than phenylacetylene for $FeCl_2$ catalyzed cyclotrimerization reaction.

Table 2.1 Iron-catalyzed Cyclotrimerization of Phenylacetylene[a]



2.5a **2.6a** **2.7a**

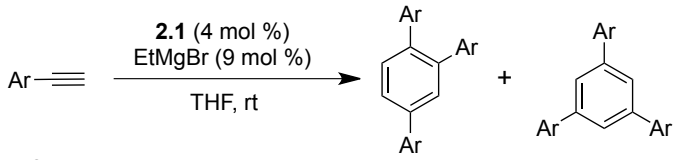
entry	catalyst	time (h)	conv. (%)[b]	yield (%)[c]	**2.6a/2.7a**[d]
1	$FeCl_2$	16	95	47	90/10
2	**2.1**	5	97	76	93/7
3[e]	**2.1**	16	85	54	93/7
4[f]	**2.1**	16	18	0	-
5	**2.2**	5	> 99	75	93/7
6	**2.3**	5	79	61	93/7
7	**2.4**	5	94	72	93/7

[a]Conditions: Phenylacetylene (0.5 mmol), catalyst (4 mol%), and THF (1 mL) were added in a scintillation vial and EtMgBr (9 mol%) was added at the end. [b]Conversion determined by GC using toluene (0.5 mmol) as an internal standard. [c]Yield of the products (**2.6a** and **2.7a**) after column chromatography. [d]Ratio determined by GC. [e]EtMgBr (4 mol%) was used. [f]EtMgBr, catalyst and THF (1 mL) was added prior to phenylacetylene.

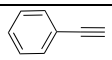
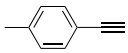
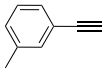
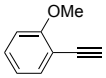
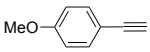
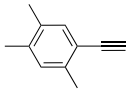
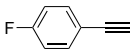
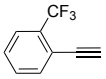
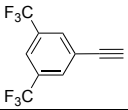
Next, we studied the cyclotrimerization of various substituted aryl terminal alkynes catalyzed by complex **2.1** and the results are summarized in Table 2.2. Arylacetylenes containing electrondonating substituents such as methyl, methoxy afforded the corresponding 1,2,4-trisubstituted benzenes in moderate yields with very high regioselectivity (entries 2-6). While phenylacetylenes containing methyl substituents underwent complete conversion in 3-5 h, the methoxy substituted phenylacetylenes required longer reaction time (14-16 h, entries 4 and 5). Arylacetylenes containing electron-withdrawing groups such as 4- fluro, 2-trifluromethyl and 3,5-di(trifluormethyl) substituents provided cyclotrimerization products with the

corresponding 1,2,4- trisubstituted benzenes in 58%, 51% and 67% yields, respectively at room temperature (entries 7-9).

Table 2.2 Iron-Catalyzed Cyclotrimerization of Aryl Terminal Alkynes[a]



2.5 **2.6** **2.7**

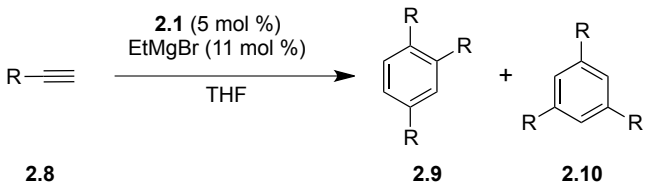
entry	substrate **2.5**		time (h)	conv (%)[b]	yield (%)[c]	ratio: **2.6/2.7**[d]
1		**a**	5	97	76	93/7
2		**b**	3	91	62	93/7
3		**c**	5	95	64	92/8
4		**d**	14	99	76	92/8
5		**e**	16	98	67	92/8
6		**f**	5	>99	64	92/8
7		**g**	16	99	58	94/6
8		**h**	5	92	51	92/8
9		**i**	14	96	67	97/3

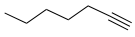
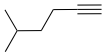
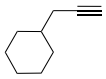
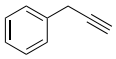
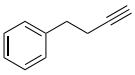
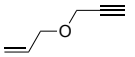
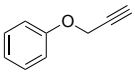
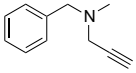
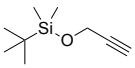
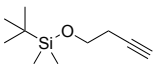
[a]Conditions: Arylacetylene (0.5 mmol), catalyst **2.1** (4 mol%), and THF (1 mL) were added in a scintillation vial and EtMgBr (9 mol%) was added at the end. [b]Conversion determined by GC using toluene (0.5 mmol) as an internal standard. [c]Yield of the products (**2.6** and **2.7**) after isolation from column chromatography.[d] Ratio determined by GC.

Remarkably, this iron-pincer catalyzed [2+2+2] cyclotrimerization is also applicable to aliphatic alkynes (Table 2.3). An assortment of linear, branched alkyl as well as aryl-alkyl substituted acetylenes underwent efficient cyclotrimerization to provide the

corresponding products in moderate yields (entries 1-8). Notably, wide range of functional groups such as alkenes, allyl, aryl and silyl ethers (tert-butyldimethylsilyl, TBDMS), and amines were well tolerated under these experimental conditions; however, these functionalized acetylenes required heating of the reaction mixture at 70 °C to obtain the moderate to quantitative conversions (entries 9-13). Further, we have also tested catalyst **2.1**-**2.4** for the cyclotrimerization reactions with aliphatic 4-(tert-butyldimethylsilyloxy)- 1-butyne at 70 °C, where complex **2.1** provided best yield (76%, entry 13, Table 3) compared to other catalysts **2.2**-**2.4** (68%, 56% and 60% yields, respectively) for the cyclotrimerized products (2.9m:2.10m). Unfortunately, all aliphatic alkynes used in Table 2.3 provided poor regioselectivity, and 1,3,5-trisubstituted benzenes were also formed in considerable amount together with the major isomer of 1,2,4-trisubstituted benzenes. Out of all the terminal alkynes tested only prop-2-yn-1-ylbenzene and but-3-yn-1- ylbenzene showed reversal of regioselectivity; 1,3,5-trisubstituted benzenes were found to be the major regioisomers with these two terminal alkynes (entries 7 and 8). When trimethylsilyl acetylene was employed for cyclotrimerization, efficient reaction occurred at room temperature and the trisubstituted benzenes were obtained in 80% yield with moderate regioselectivity (entry 14). Polymeric or complex mixture of side products were observed in all reactions in minor amount. However, electron deficient acetylene carboxylates such as methyl and ethyl propiolate failed to provide desired benzene products.

Table 2.3 Iron-Catalyzed Cyclotrimerization Aliphatic Terminal Alkynes[a]



entry	substrate **2.8**		time(h)	temp (°C)	conv. (%)[b]	yield (%)[c]	ratio: **2.9/2.10**[d]
1		**a**	9	rt	93	57	54/46
2		**b**	13	rt	>99	63	55/45
3		**c**	13	rt	>99	68	63/37
4		**d**	9	rt	86	51	50/50
5		**e**	13	rt	>99	66	56/44
6		**f**	5	rt	n.c	70	69/31
7		**g**	22	rt	>99	42	42/58
8		**h**	13	rt	99	53	45/55
9		**i**	15	70	>99	61	59/41
10		**j**	24	70	>99	36	50/50
11		**k**	22	70	73	50	59/41
12		**l**	9	70	96	72	72/28
13[e,]		**m**	18	70	99	76	60/40
14		**n**	3	rt	n.c	80	68/32

[a]Conditions: terminal alkyne (0.5 mmol), catalyst **2.1** (5 mol%), and THF (1 mL) were taken in a scintillation vial. EtMgBr (11 mol%) was added and reaction was carried out at room temperature. [b]Conversion was determined by GC using toluene (0.5 mmol) as an internal standard. [c]Yield of the products (**2.9** and **2.10**) after isolation from column chromatography. [d]Ratio determined by GC (for entries 1-8) and from ^{1}H NMR (for entries 9-14) after isolation. [e]Reactions were also carried out with catalyst **2.2** (68%), catalyst **2.3** (56%), catalyst **2.4** (60%). n.c: not calculated.

Further, cyclotrimerization of internal alkynes like 1-phenyl-1-propyne, 1-phenyl-1-butyne and 1-phenyl-1-hexyne was performed using catalyst **2.1**, which provided single regioisomer **2.12a**, **2.12b** and **2.12c** in 55%, 42% and 45% yields, respectively (See Scheme 2.2). Representative single-crystal structure of **2.6g** and **2.12a** further confirmed cyclotrimerization of terminal and internal alkynes (Figure. 2.1). Although, remarkable regioselectivity was observed with arylalkyl internal alkynes, use of

dialkyl and diaryl internal alkynes (4-octyne and diphenylacetylene, respectively) failed to provide cyclotrimerization reactions under this catalysis.

Scheme 2.2 Iron-Catalyzed Regioselective Cyclotrimerization Reaction of Internal Alkynes.

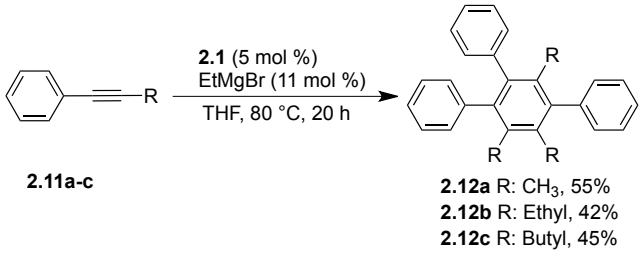
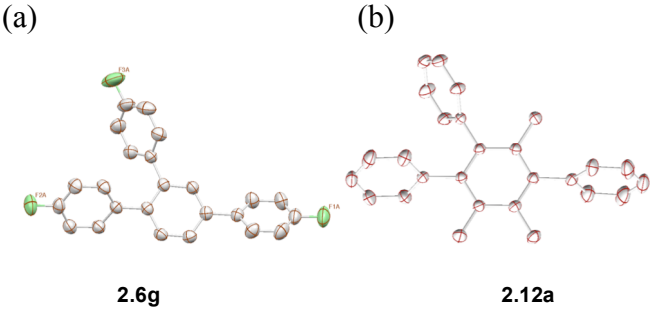
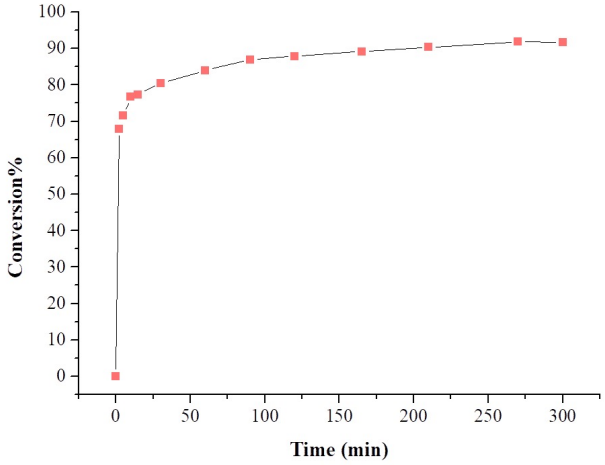


Figure 2.2 Single-crystal X-ray structures of compound **2.6g** and **2.12a** (ellipsoids are drawn at 30% probability)



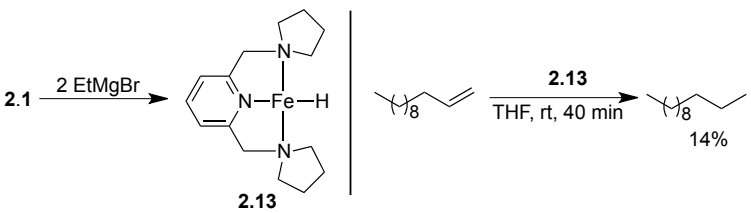
When the rate of cyclotrimerization of phenylacetylene catalyzed by iron-pincer complex **2.1** was monitored using GC, 93%. Conversion occurred in 5 h indicating the rapid reaction of alkynes (Figure 2.3).

Figure 2.3 Conversion of phenylacetylene in catalytic reaction with **2.1** and EtMgBr. Monitoring of the reaction progress using GC analysis.



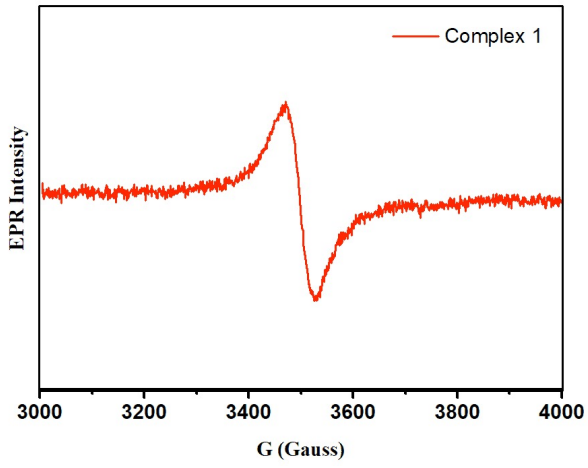
Upon reaction of complex **2.1** (0.05 mmol) with two equivalents of ethylmagnesium bromide (0.1 mmol) and stoichiometric amount of dodecene (0.05 mmol) in a closed vial under nitrogen atmosphere, immediate color change from yellow to brown was observed; however, after 10 min the reaction mixture turned turbid indicating the decomposition of active species. GC analysis of the reaction mixture after 40 min (using toluene as an internal standard) confirmed 14% formation of dodecane (Scheme 2.3), indicating the possible formation of an iron-hydride intermediate 2.13[30b]. Moreover, preliminary work reported in 2012 reveal that when iron salt reacts with ethylmagnesium bromide, it provides hydrogen source to diphenylacetylene. We have attempted to isolate the Fe-H intermediate or complex, which remains unsuccessful. Although, its is not exactly same complex but its a similar reaction condition as that $FeCl_2$ in Table 2.1, entry 1.[30d]

Scheme 2.3 Stoichiometric Reaction of Iron Complex 2.1 with Grignard Reagent and Alkene.



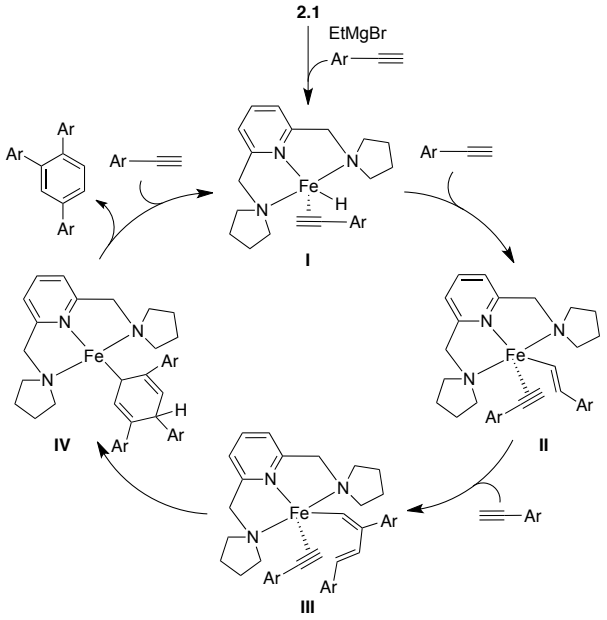
Electron paramagnetic resonance (EPR) measurements were carried out at 298 K in THF to investigate the spin state of complex **2.1**. Complex **2.1** shows a single EPR signal at room temperature, which is attributable to an S = 2 system (high spin-d^6-Fe^{II}, Figure 2.4). The g value (g = 2.01) of **1** is largely deviated from that (2.0023) of free electron. The width between extreme slopes (60 G) of this EPR signal is much broader than that of conventional organic radicals, and therefore, no hyperfine structure is observed. However, EPR analysis of complex **2.1** at 100 K revealed the disappearance of signal, observed at 298 K (low spin-d^6-Fe^{II}). This clearly indicates thermally induced spin crossover effect. Moreover, complex **2.1** has a solid-state magnetic moment of 5.2 μ_B at 298 K, indicating four unpaired electrons at the iron center. The measured magnetic moment is larger than spin-only value for an S = 2 spin state (4.89 μ_B), but still within the range of the reported high spin distorted square-pyramidal iron(II) compounds[31]. There is no evidence where change in spin state has any role in catalysis. However, if Fe(II) has low spin complex then we could have performed mechanistic study using NMR spectroscopy, which might have provided more insightful information to improve the catalysis.

Figure 2.4 X-band EPR of NNN-Fe catalyst **2.1** recorded at 298 K.



Although more studies are required, on the basis of experimental observations, a catalytic cycle for cyclotrimerization of alkynes involving Fe(I) intermediacy was proposed[32] as depicted in Scheme 2.4 Reaction of catalyst **2.1** with Grignard reagent and alkyne generates the Fe(I)-monohydride intermediate **I**. Upon insertion of coordinated alkyne into Fe-H bond and further preliminary interaction of another alkyne motif leads to the formation of II. Coordinated alkene and alkyne functionalities over the metal center further react to create a dienyl ligand and further coordination of third alkyne motif results in formation of intermediate **III**. On intermediate **III** the coordinated alkyne and dienyl ligands undergo [4+2] cylcoaddition leading to formation of cyclic hexadienyl coordinated intermediate **IV**. The addition of third alkyne probably directs the regioselectivity. After [4+2] cylcoaddition, A hydride elimination from coordinated intermediate **IV** liberate regioselective 1,2,4 triaryl benzene molecule and further reaction with alkyne can regenerate the intermediate **I**. to complete one loop of the catalytic cycle. When aliphatic alkynes were employed in the catalysis, perhaps the steric incompatibilities led to the formation of another regioisomer-1,3,5-trialkyl benzene in a considerable percentage. The intermolecular cycloaddition pathway of iron-coordinated dienyl ligand with alkynes may also be operative. Of course, this is only a proposed mechanism and further experiments are required to identify the intermediates involved in the reaction.

Scheme 2.4 Proposed Catalytic Cycle for Fe-catalyzed [2+2+2] Cycloaddition Reaction



2.4 CONCLUSIONS

In summary, we have described regioselective cyclotrimerization of aryl terminal alkynes and internal alkynes using simple and easily accessible NNN iron-pincer catalysts to provide the corresponding 1,2,4-trisubstituted and hexa-substituted benzene molecules. While arylalkynes provided up to 97% regioselective 1,2,4-trisubstituted isomers, aliphatic alkynes displayed poor regioselectivity perhaps due to the steric incompatibility on the metal coordination sphere. Notably, the arylalkyl internal alkynes provided hexasubstituted benzene compounds as single regioisomers. Mechanistic studies indicate the involvement of molecular catalyst and the reaction proceeds upon activation of iron dichloride to iron(I)-hydride intermediate by a Grignard reagent. Catalytic [2+2+2] cycloaddition is suggested to occur upon coordination of alkynes with Fe(I) intermediates in a stepwise reaction pathway.

2.5. EXPERIMENTAL SECTION

General experimental procedure:

All catalytic reactions were performed under nitrogen atmosphere in an MBraun

Glove-box. Chemicals were purchased from Acros, Sigma-Aldrich, Alfa-aesar and used without further purification. Dry solvents were prepared according to standard procedures.[31b] ^{1}H, ^{13}C, ^{29}Si, and ^{19}F NMR spectra were recorded using 400, 100.6, 79.5 and 376.5 MHz magnetic fields, respectively. ^{1}H and $^{13}C\{^{1}H\}$ NMR chemical shifts were reported in ppm downfield from tetramethylsilane. All NMR Spectra were recorded at 298K. Multiplicity is abbreviated as s, singlet; d, doublet; dd, doublet of doublet; t, triplet; q, quartet; dq, doublet of quartet; m, multiplet; br, broad. Mass spectra were recorded on a micro TOF-Q II spectrometer. Magnetic susceptibility was recorded on magnetic susceptibility balance. GC-FID measurements were performed with Shimadzu series instrument. The GC-FID instrument equipped with a capillary column coated with nonpolar stationary phase rtX was used for molecular weight determination and identification, which allowed the separation of hydrocarbons according to their boiling point differences.

Synthesis of 2,6-bis(bromomethyl)pyridine (2.13)[31]

To a 100 mL one neck round-bottomed flask equipped with a stirrer bar, guard tube and reflux condenser, pyridine-2,6- diyldimethanol (1 g, 7.05 mmol) and 60% HBr (7 mL) were added slowly. The reaction was heated at 125 °C for 7 h then cooled to room temperature. The resulting residue was dissolved in H_2O (25 mL) to give yellow solution. To this solution saturated $NaHCO_3$ was added to reach pH 8. The resulting aqueous solution was extracted with CH_2Cl_2 (4 x 25 mL), and the combined organic layers were dried over anhydrous sodium sulfate and filtered. The volatiles were evaporated under reduced pressure and the resulting residue was purified by flash column chromatography (10% ethyl acetate/hexane) to yield 2,6-bis(bromomethyl)pyridine (**2.13**) (1.6 g, 84%) as white solid. ^{1}H NMR($CDCl_3$): δ 7.70 (t, J = 8 Hz, 1H), 7.37 (d, J = 8 Hz, 2H), 4.54 (s, 4H). $^{13}C\{^{1}H\}$NMR ($CDCl_3$): δ

156.9, 138.3, 123.0, 33.6. HRMS (EI) m/z Calcd for $C_7H_8Br_2N$: $[M+H]^+$ 263.9018, found 263.9031.

Synthesis of 2,6, bis(pyrrolidine-1-ylmethyl)pyridine[34] (L1)

To a 50 mL two neck round-bottomed flask equipped with a stirrer bar, 2,6-bis(bromomethyl)pyridine (1 g, 3.8 mmol) was dissolved in dry acetonitrile (20 mL) under an argon atmosphere. The solution was cooled to 0 °C prior to the dropwise addition of pyrrolidine (1.09 g, 15.2 mmol) over a period of 5 min. The reaction was allowed to warm to room temperature (25 °C) and was stirred vigorously for a period of 24 h. The volatiles were removed under reduced pressure to give a pale yellow residue, which was diluted with 75 mL CH_2Cl_2 and neutralized with 1 M NaOH (1 x 30 mL) and washed with brine (1 x 30 mL). The organic layer was then dried over sodium sulfate, filtered, and concentrated under reduced pressure. The resulting reaction mixture was purified by alumina column chromatography (4% ethyl acetate/hexane) to yield 2,6- bis(pyrrolidine-1-ylmethyl)pyridine (0.69 g, 74%) as pale yellow oil. ^{1}H NMR ($CDCl_3$): δ 7.56 (t, J = 8 Hz, 1H), 7.24 (d, J = 8 Hz, 2H), 3.74 (s, 4H), 2.53-2.56 (m, 8H), 1.74-1.77 (m, 8H). $^{13}C\{^1H\}$ NMR ($CDCl_3$): δ 158.9, 136.7, 120.9, 62.4, 54.4, 23.6. HRMS (EI) m/z Calcd for $C_{15}H_{24}N_3$: $[M+H]^+$ 246.1965, found 246.1957.

Synthesis of *N,N'*-(pyridine-2,6-diylbis(methylene))bis(*N*-ethylethanamine)[35] (L2): To a 50 mL two neck round-bottomed flask equipped with a stirrer bar, 2,6-bis(bromomethyl)pyridine (0.5 g, 1.90 mmol), K_2CO_3 (1.05 g, 7.6 mmol) was dissolved in dry acetonitrile (10 mL) under an argon atmosphere. The solution was cooled to 0 °C prior to the dropwise addition of diethylamine (0.55 g, 7.6 mmol) over a period of 5 min. The reaction was allowed to warm to room temperature (25 °C) and was stirred vigorously for a period of 24 h. The reaction mixture was concentrated

under reduced pressure to give a pale yellow residue, which was diluted with 60 mL CH_2Cl_2 and neutralized with 1 M NaOH (1 x 30 mL) and washed with brine (1 x 20 mL). The organic layer was then dried over sodium sulfate, filtered and concentrated under reduced pressure. The resulting residue was purified by alumina column chromatography (4% ethyl acetate/hexane) to yield *N,N'*-(pyridine-2,6-diylbis(methylene))bis(N-ethylethanamine)(0.38 g, 80%) as pale yellow oil. ^{1}H NMR ($CDCl_3$): δ 7.55 (t, J = 8 Hz, 1H), 7.29 (d, J = 8 Hz, 2H), 3.67 (s, 4H), 2.53 (q, J = 8 Hz, 8H), 1.01 (t, J = 4 Hz, 12H). ^{13}C{^{1}H}NMR ($CDCl_3$): δ 159.8, 136.5, 120.6, 59.7, 47.3, 11.9. HRMS (EI) m/z Calcd for $C_{15}H_{28}N_3$: $[M + H]^+$ 250.2278, found 250.2279.

Synthesis of *N,N'*-(pyridine-2,6-diylbis(methylene))bis(*N*-isopropylpropan-2-amine)[35] (L3): To a 50 mL two neck round-bottomed flask equipped with a stirrer bar, 2,6-bis(bromomethyl)pyridine (0.5 g, 1.90 mmol), K_2CO_3 (1.05 g, 7.6 mmol) was dissolved in dry acetonitrile (10 mL) under an argon atmosphere. The solution was cooled to 0 °C prior to the dropwise addition of diisopropylamine (0.77 g, 7.6 mmol) over a period of 5 min. The reaction was allowed to warm to room temperature (25 °C) and was stirred vigorously for a period of 24 h. The volatiles were removed under reduced pressure to give a pale yellow residue, which was diluted with 60 mL CH_2Cl_2 and neutralized with 1 M NaOH (1 x 30 mL) and washed with brine (1 x 20 mL). The organic layer was then dried over anhydrous sodium sulfate, filtered and concentrated under reduced pressure. The resulting residue was purified by alumina column chromatography (4% ethyl acetate/hexane) to yield *N,N'*-(pyridine-2,6-diylbis(methylene))bis(*N*-isopropylpropan-2-amine) (0.42 g, 72%) as pale yellow oil. ^{1}H NMR ($CDCl_3$): δ 7.57 (t, J = 8 Hz, 1H), 7.44 (d, J = 8 Hz, 2H), 3.76 (s, 4H), 3.00 – 3.09 (m, 4H), 1.02 (d, J = 8 Hz, 24H). ^{13}C{^{1}H} NMR ($CDCl_3$) : δ 161.8, 135.5,

118.2, 50.6, 47.9, 19.9. HRMS (EI) m/z Calcd for $C_{19}H_{36}N_3$: $[M + H]^+$ 306.2904, found 306.2909.

Synthesis and Characterization of Complexes 2.1-2.4: $(NNN^{pyr})FeCl_2$ (2.1): To the suspension of $FeCl_2$ (127 mg, 1 mmol) in THF (15 mL) pyrrolidine-NNN ligand (245 mg, 1 mmol) was added. The reaction mixture was heated to 75 °C and vigorously stirred for a period of 20 h. The yellow solution was cooled to room temperature and filtered through 0.2 μm PTFE syringe filter. The filtrate was concentrated to 2 mL under vacuum. Hexane (15 mL) was added slowly to precipitate a bright yellow solid, which was isolated by filtration, washed with hexane (3 x 1 mL) and dried under vacuum yielding 352 mg (94% yield). The resulting complex is paramagnetic. Crystals suitable of X-ray quality were obtained by slow diffusion of hexane into a solution of **2.1** in CH_2Cl_2. IR (KBr): 3413, 2963, 2918, 2847, 1609, 1579, 1473, 1456, 1438, 1381, 1349, 1334, 1262, 1225, 1108, 1083, 1024, 863, 796, 757 cm^{-1}. HRMS (EI) m/z Calcd for $C_{15}H_{24}Cl_2FeN_3$: $[M +H]^+$ 372.0694, found 372.0664.

$(NNN^{Et})FeCl_2$ (2.2): To the pale yellow suspension of $FeCl_2$ (127 mg, 1 mmol) in THF (15 mL) NNN^{Et} ligand (249 mg, 1 mmol) was added. The reaction mixture was heated to 75 °C and vigorously stirred for a period of 4 h. The yellow solution was cooled to room temperature and filtered through 0.2 mm PTFE syringe filter. The filtrate was concentrated to 2 mL under vacuum. Hexane (15 mL) was added slowly to precipitate a bright yellow solid, which was isolated by filtration, washed with hexane (3 x 1 mL) and dried under vacuum yielding 357 mg (95% yield). The resulting complex is paramagnetic. Crystals suitable of X-ray quality were obtained by slow diffusion of Hexane into a solution of **2.2** in CH_2Cl_2. IR (KBr): 3408, 2983,

2855, 1605, 1579, 1464, 1402, 1380, 1360, 1262, 1168, 1150, 1133, 1035, 1025, 800, 762, 734.1 cm^{-1}. MS (EI) m/z Calcd for $C_{15}H_{28}Cl_2FeN_3$: $[M+H]^+$ 376.1, found 376.1

(NNN^{iPr})$FeCl_2$ (2.3): To the suspension of $FeCl_2$ (16.4 mg, 0.13mmol) in THF (4 mL) NNN^{iPr} ligand (40 mg, 0.13 mmol) was added. The reaction mixture was heated to 60 °C and vigorously stirred for a period of 20 h. The yellow solution was cooled to room temperature and filtered through 0.2 μm PTFE syringe filter. The filtrate was concentrated to 1 mL under vacuum. Hexane (4 mL) was added slowly to precipitate off-white solid, which was isolated by filtration, washed with hexane (2 x 1 mL) and dried under vacuum. The title compound was isolated as off-white solid (34 mg, 61%). The resulting complex is paramagnetic. Attempts made to crystallize the complex remain unsuccessful. IR (KBr): 3418, 2980, 1627, 1455, 1397, 1308, 1282, 1173, 1190, 1093, 983, 814 cm^{-1}. ESI m/z Calcd for $C_{19}H_{36}Cl_2FeN_3$: $[M+H]^+$ 432.1633, found 432.1568.

Complex **2.4** was prepared by following reported literature procedure.[31]

X-ray analyses and crystal data of 2.1, 2.2: Crystals suited for single crystal x-ray diffraction measurements were mounted on a glass fiber. Geometry and intensity data were collected with a Bruker SMART D8 goniometer equipped with an APEXCCD detector and with an Incoatecmicrosource (Mo-Kα radiation, λ = 0.71073 Å, multilayer optics). Temperature was controlled using an Oxford Cryostream 700 instrument. Intensities were integrated with SAINT+[36]and corrected for absorption with SADABS.[37] The structures were solved by direct methods and refined on $F^2$with SHELXL-97.[38,39]

Crystal data of complexes

(NNN^{pyr})$FeCl_2$(2.1): $C_{15}H_{23}Cl_2Fe\ N_3$, yellow block, crystal dimensions: 0.28 x 0.26 x 0.21 mm^{-1}, M = 372.11, Orthorhombic with space group Pbca, a = 12.9858(8)Å, b = 12.0845(8)Å, c = 21.5276(14)Å, α = 90°, β = 90° , γ = 90°, V = 3378.3(4) $Å^3$, Z = 8, F(000) = 1552.0, μ-(MoK_α) = 1.206 mm^{-1}, 2θmax = 59.318, ρ_{calcd} = 1.463 Mg/m^3, T = 100(2)K, min/max transmission factors = 0.5363/0.7459, 54540 Reflections collected, 4758 unique ($R1$ = 0.0269), $WR2$ = 0.0627(all data). Residual electron density max/min = 0.34/-0.39e.$Å^{-3}$.The structure has been deposited at the CCDC data center and can be retrieved using the deposit number 1823256.

(NNN^{Et})$FeCl_2$ (2.2): $C_{15}H_{23}Cl_2FeN_3$, yellow block, crystal dimensions: 0.18 x 0.14 x 0.12 mm^{-1}, M = 376.14, monoclinic with space group P2/n, a = 13.8250(14) Å, b = 9.3017(10) Å, c = 14.8050(15) Å, α = 90°, β = 97.27(7)°, γ = 90°, V = 1886.6(3) $Å^3$, Z = 4, F(000) = 792.0, μ-(MoK_α) = 1.080 mm^{-1}, 2θmax = 54.342, ρ_{calcd} = 1.324 Mg/m^3, T = 100(2)K, min/max transmission factors = 0.5356/0.7455, 15059 Reflections collected, 4150 unique ($R1$ = 0.0398), $WR2$ = 0.0929(all data). Residual electron density max/min = 0.28/-0.51e.$Å^{-3}$.The structure has been deposited at the CCDC data center and can be retrieved using the deposit number 1823257.

General procedure for catalytic cyclotrimerization of alkynes: To a stirred solution of catalyst **2**.**1** in THF (1 mL), alkyne (0.5 mmol) and then EtMgBr (11 mol%, 1 M in THF) was charged in PTFE screw-capped reaction vial equipped with a stirrer bar inside the glovebox. Then, the reaction mixture was brought outside and stirred at room temperature. Progress of the reaction was monitored by GC, which indicated the completion of the reaction in specified time. The reaction mixture was quenched by exposing it to the open atmosphere. The solvent was evaporated under

reduced pressure and the residue was purified by column chromatography to provide cyclotrimerized product.

Kinetic studies on cylotrimerization of phenylacetylene catalyzed by 2.1: The conversion of phenylacetylene versus time was monitored by GC. Within 2 minute 70% conversion was observed by GC, for remaining 23% it has taken ~ 5 h (Figure 3). Thus, these NNN iron pincer catalyst species were found to be highly active precursor catalysts for the phenylacetylene cyclotrimerization with an initial TOF of 1.05 s−1 (measured at 15 min).

4'-Phenyl-1,1':2',1''-terphenyl and 5'-phenyl-1,1':3',1''-terphenyl (2.6a and 2.7a): 2.6a:2.7a = 93:7; determined by GC analysis, this product was isolated by flash column chromatography on silica gel (Hexane). Yield 39 mg (76%), White solid; IR (DCM): 3057 (w), 3025 (w), 1472, 1441, 1264, 1241, 1074, 1028, 836, 754, 739, 694, 629 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 7.81 (s), 7.67-7.71 (m, 4H), 7.54 (d, 8 Hz, 1H), 7.46-7.50 (m, 2H), 7.37-7.41 (m, 1H), 7.21-7.26 (m, 10H). $^{13}C\{^{1}H\}$ NMR ($CDCl_3$): δ 141.6, 141.3, 141.1, 140.7, 140.5, 139.7, 131.2, 130.1, 130.0, 129.6, 129.0, 128.1, 128.0, 127.6, 127.3, 126.7, 126.7, 126.3. HRMS (EI) m/z Calcd for $C_{24}H_{19}$: $[M + H]^+$ 307.1481, found 307.1470.

4,4''-Dimethyl-4'-(p-tolyl)-1,1':2',1''-terphenyl and 4,4''-dimethyl-5'-(p-tolyl)-1,1':3',1''-terphenyl (2.6b and 2.7b): 2.6b:2.7b = 92:8; determined by GC analysis, this product was isolated by flash column chromatography on silica gel (hexane). Yield 36 mg (62%), White solid; IR (DCM): 3022 (w), 2919 (w), 2860 (w), 1512, 1479, 1451, 1239, 1110, 1019, 1006, 841, 805, 759, 737 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 7.78 (s), 7.60-7.67 (m), 7.49-7.51 (m), 7.26-7.33 (m), 7.07-7.16 (m), 2.46 (s, 3H), 2.44 (s, 3H), 2.36 (s, 6H). $^{13}C\{^{1}H\}$ NMR ($CDCl_3$): δ 142.3, 141.5, 140.9, 140.2,

139.3, 138.9, 138.55, 138.50, 137.9, 137.4, 137.3, 136.2, 136.1, 134.3, 131.2, 129.9, 129.8, 129.7, 129.4, 128.82, 128.79, 127.3, 127.1, 125.8, 124.7, 29.8, 21.3. HRMS (EI) m/z Calcd for $C_{27}H_{25}$: $[M + H]^+$ 349.1951, found 349.1957.

3,3''-Dimethyl-4'-(m-tolyl)-1,1':2',1''-terphenyl and 3,3''-dimethyl-5'-(m-tolyl)-1,1':3',1''-terphenyl (2.6c and 2.7c): 2.6c:2.7c = 93:7; determined by GC analysis, this product was isolated by flash column chromatography on silica gel (hexane). Yield 37 mg (64%), white solid; IR (DCM): 3049 (w), 2923 (w), 2853 (w), 1583, 1551, 1264, 1243, 1045, 834, 782, 733, 701, 637cm^{-1}. ^1H NMR ($CDCl_3$): δ 7.67 (s), 7.52-7.56 (m), 7.38-7.42 (m), 7.23-7.27 (m), 7.07-7.12 (m), 6.82-6.86 (m), 2.36 (s, 3H), 2.34 (s, 3H), 2.19 (s, 3H), 2.18 (s, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$): δ 142.5, 141.7, 141.4, 141.3, 141.2, 140.8, 140.4, 139.7, 138.55, 138.51, 137.55, 137.49, 131.1, 130.70, 130.68, 129.5, 128.9, 128.3, 128.1, 127.78, 127.76, 127.4, 127.3, 127.24, 127.20, 126.1, 124.6, 124.4, 29.9, 21.7, 21.5. HRMS (EI) m/z Calcd for $C_{27}H_{25}$: $[M + H]^+$ 349.1951, found 349.1980.

2,2''-Dimethoxy-4'-(2-methoxyphenyl)-1,1':2',1''-terphenyl and 2,2''-dimethoxy-4'-(2-methoxyphenyl)-1,1':2',1''-terphenyl (2.6d and 2.7d): 2.6d:2.7d = 92:8; determined by GC analysis, this product was isolated by flash column chromatography on silica gel (EtOAc/hexane – 1/30). Yield 50 mg (76%), yellow gel; IR (DCM): 2998 (w), 2923 (w), 2836 (w), 1528, 1515, 1478, 1462, 1287, 1243, 1173, 1115, 1031, 819, 798, 637cm^{-1}.^1H NMR ($CDCl_3$): δ 7.73 (s), 7.63-7.65 (m), 7.47-7.49 (m), 7.33-7.37 (m), 7.18-7.20 (m), 7.08-7.16 (m), 7.02-7.07 (m), 6.85 (t, 8 Hz), 6.75 (t, 8 Hz), 3.87 (s, 3H), 3. 86 (s, 3H), 3.53 (s, 3H), 3.50 (s, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$): δ 156.7, 156.4, 137.2, 131.7, 131.6, 131.3, 131.2, 130.6, 128.5, 128.4, 128.1,

120.9, 119.9, 111.2, 110.34, 110.33, 55.7, 55.6, 55.05, 55.03. HRMS (EI) m/z Calcd for $C_{27}H_{25}O_3$: $[M + H]^+$ 397.1798, found 397.1775.

4,4''-Dimethoxy-4'-(4-methoxyphenyl)-1,1':2',1''-terphenyl and 4,4''-dimethoxy-5'-(4-methoxyphenyl)-1,1':3',1''-terphenyl (2.6e and 2.7e): 2.6e:2.7e = 92 :8; determined by GC analysis, this product was isolated by flash column chromatography on silica gel (EtOAc/hexane – 1/30). Yield 44 mg (67%), yellow gel; IR (DCM): 2998 (w), 2929 (w), 2834 (w), 1606, 1522, 1509, 1478, 1462, 1286, 1236, 1173, 1108, 1031, 819, 799, 734, 641 cm^{-1}. ^1H NMR ($CDCl_3$): δ 7.57-7.69 (m), 7.46 (d, 8H), 7.11-7.16 (m), 7.00-7.04 (m), 6.79-6.83 (m), 3.88 (s, 3H), 3.87 (s, 3H), 3.81 (s, 3H), 3.81 (s, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$): δ 159.3, 158.5, 158.4, 140.5, 139.7, 134.3, 133.9, 133.3, 131.1, 131.05, 131.01, 129.0, 128.2, 125.5, 114.4, 113.6, 113.5, 55.49, 55.47, 55.30, 55.29. HRMS (EI) m/z Calcd for $C_{27}H_{25}O_3$: $[M + H]^+$ 397.1798, found 397.1768.

2,2'',4,4'',5,5''-Hexamethyl-4'-(2,4,5-trimethylphenyl)-1,1':2',1''-terphenyl and 2,2'',4,4'',5,5''-hexamethyl-5'-(2,4,5-trimethylphenyl)-1,1':3',1''-terphenyl (2.6f and 2.7f): 2.6f:2.7f = 92:8; determined by GC analysis, this product was isolated by flash column chromatography on silica gel (hexane). Yield 46 mg (64%), yellow solid; IR (DCM): 2966 (w), 2918 (w), 2861 (w), 1479, 1451, 878, 842, 738, 705 cm^{-1}. ^1H NMR ($CDCl_3$): δ 7.14-7.21 (m), 7.04 (s), 6.97 (s), 6.74-6.75 (m), 2.23 (s, 4H), 2.18-2.19 (m, 7H), 2.08 (s, 3H), 2.06 (s, 3H), 2.02 (s, 3H), 1.99 (s, 3H), 1.94 (s, 6H). $^{13}C\{^1H\}$ NMR ($CDCl_3$): δ 141.4, 140.1, 139.2, 135.5, 134.7, 133.9, 132.9, 132.8, 132.7, 132.6, 131.9, 131.7, 131.4, 131.1, 130.5, 128.6, 127.5, 20.2, 19.4, 19.3, 19.2, 19.1. HRMS (EI) m/z Calcd for $C_{33}H_{37}$: $[M + H]^+$ 433.2890, found 433.2904.

4,4''-Difluoro-4'-(4-fluorophenyl)-1,1':2',1''-terphenyl and 4,4''-difluoro-5'-(4-fluorophenyl)-1,1':3',1''-terphenyl (2.6g and 2.7g): 2.6g:2.7g = 94:6; determined by GC analysis, this product was isolated by flash column chromatography on silica gel (hexane). Yield 35 mg (58%), white solid; IR (DCM): 3046 (w), 1603, 1522, 1509, 1480, 1222, 1158, 835, 820, 739 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 7.68 (s), 7.58-7.65 (m), 7.47 (d, J = 8 Hz, 1H), 7.11-7.19 (m), 6.93-6.98 (m). $^{13}C\{^{1}H\}$ NMR ($CDCl_3$): δ 164.0, 163.25, 163.21, 161.5, 160.80, 160.76, 141.7, 139.8, 131.55, 131.51, 131.47, 131.4, 131.2, 129.3, 128.85, 128.77, 126.3, 116.0, 115.8, 115.31, 115.27, 115.09, 115.06. ^{19}F NMR ($CDCl_3$): δ -115.5, -115.4, -115.0, -114.8. (ESI-MS) m/z Calcd for $C_{24}H_{16}F_3$: $[M + H]^+$ 361.1, found 361.1.

2,2''-Bis(trifluoromethyl)-4'-(2-(trifluoromethyl)phenyl)-1,1':2',1''-terphenyl and 2,2''-bis(trifluoromethyl)-5'-(2-(trifluoromethyl)phenyl)-1,1':3',1''-terphenyl (2.6h and 2.7h): 2.6h:2.7h = 92:8; determined by GC analysis, This product was isolated by flash column chromatography on silica gel (hexane). Yield 44 mg (51%), white solid; IR (DCM): 3067 (w), 1473, 1309, 1264, 1163, 1102, 1007, 765, 755, 656, 632 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 7.67 (d, J = 8 Hz, 2H), 7.54-7.59 (m), 7.47-7.50 (m), 7.29-7.41 (m), 7.18-7.25 (m), 7.01-7.16 (m), 6.99 (t, J = 6 Hz, 2H). $^{13}C\{^{1}H\}$ NMR ($CDCl_3$): δ 140.7, 139.3, 139.0, 137.5, 137.3, 132.2, 132.0, 131.4, 131.1, 130.7, 129.64, 129.62, 129.3, 129.0, 128.7, 127.9, 127.7, 127.3, 126.3, 126.25, 126.20, 125.9, 125.8, 125.6, 123.2, 123.1, 122.9. ^{19}F NMR ($CDCl_3$): δ -57.92, -57.91, -57.19, -57.18, -57.13. HRMS (EI) m/z Calcd for $C_{27}H_{16}F_9$: $[M + H]^+$ 511.1103, found 511.1116.

4'-(3,5-Bis(trifluoromethyl)phenyl)-3,3'',5,5''-tetrakis(trifluoromethyl)-1,1':2',1''-terphenyl and 5'-(3,5-bis(trifluoromethyl)phenyl)-3,3'',5,5''-

tetrakis(trifluoromethyl)-1,1':3',1''-terphenyl (2.6i and 2.7i): 2.6i:2.7i = 97:3; determined by GC analysis, this product was isolated by flash column chromatography on silica gel (hexane). Yield 80 mg (67%), white solid; IR (DCM): 1371, 1273, 1171, 1126, 1079, 893, 833, 740, 706 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 8.10 (s, 2H), 7.96 (s, 1H), 7.82-7.86 (m, 2H), 7.80 (s, 1H), 7.76 (d, J = 2 Hz), 7.70-7.72 (m, 1H), 7.60 (s, 2H), 7.57 (s, 2H). $^{13}C\{^{1}H\}$ NMR ($CDCl_3$): δ 141.8, 141.7, 141.6, 141.4, 141.3, 139.7, 139.6, 139.2, 139.0, 138.5, 138.3, 132.2, 131.3, 131.2, 129.8, 129.1, 129.0, 128.23, 128.16, 127.3, 126.9, 124.6, 124.2, 121.8, 121.5, 121.2, 118.8. ^{19}F NMR ($CDCl_3$): δ -64.34, -64.30, -63.8.

1,2,4-Tripentylbenzene and1,3,5-tripentylbenzene (2.9a and 2.10a): 2.9a:2.10a = 60:40; determined by ^{1}H NMR, this product was isolated by flash column chromatography on silica gel (hexane). Yield 28 mg (57%), yellow oil; IR (DCM): 2954, 2925, 2859, 1497, 1459, 1375, 829, 729 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 7.05 (d, J = 8 Hz, 1H), 6.93-6.95 (m, 2H), 6.82 (s, 3H), 2.53-2.59 (m), 1.57-1.62 (m), 1.33-1.37 (m), 0.88-0.93 (m). $^{13}C\{^{1}H\}$ NMR ($CDCl_3$): δ 142.9, 140.5, 140.3, 137.8, 129.4, 129.1, 126.0, 125.8, 36.1, 35.7, 32.9, 32.4, 32.20, 32.19, 31.83, 31.81, 31.45, 31.43, 31.2, 22.75, 22.72, 14.2. HRMS (EI) m/z Calcd for $C_{21}H_{35}$: $[M - H]^{+}$ 287.2733, found 287.2728.

1,2,4-Triisopentylbenzene and 1,3,5-triisopentylbenzene (2.9b and 2.10b): 2.9b:2.10b = 60:40; determined by GC analysis, this product was isolated by flash column chromatography on silica gel (hexane). Yield 48 mg (63%), yellow oil; IR (DCM): 2954, 2929, 2869, 1466, 1383, 1367, 736, 704cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 7.04 (d, J = 8Hz, 1H), 6.93-6.95 (m, 2H), 6.82 (s, 3H), 2.53-2.57 (m), 1.46-1.56 (m), 0.93-0.98 (m). $^{13}C\{^{1}H\}$ NMR ($CDCl_3$): δ 143.1, 140.7, 140.5, 137.9, 129.3, 129.2, 125.8,

41.12, 41.08, 34.0, 33.5, 30.8, 30.3, 28.6, 28.5, 28.0, 22.8, 22.7. (ESI-MS) m/z Calcd for $C_{21}H_{37}$: $[M + H]^+$ 289.2, found 289.2.

1,2,4-Triisobutylbenzene and 1,3,5-triisobutylbenzene (2.9c and 2.10c): 2.9c:2.10c = 63:37; determined by GC analysis, this product was isolated by flash column chromatography on silica gel (hexane). Yield 28 mg (68%), yellow oil; IR (DCM): 2954, 2927, 2869, 1735, 1464, 1383, 1367, 1264, 1243, 737, 721cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 7.01 (d, J = 8 Hz, 1H), 6.88-6.91 (m, 2H), 6.75 (s, 3H), 2.46 (dd, J_1 = 7 Hz, J_2 = 2 Hz), 2.42 (d, J = 7 Hz), 1.81-1.86 (m, J = 7 Hz), 0.93 (d, J = 7 Hz), 0.90 (d, J = 7 Hz). ^{13}C{^{1}H} NMR ($CDCl_3$): δ 141.1, 139.4, 138.7, 137.0, 131.0, 129.8, 127.5, 126.4, 45.6, 45.3, 42.2, 41.7, 30.50, 30.46, 30.0, 22.8, 22.6. HRMS (EI) m/z Calcd for $C_{18}H_{29}$: $[M - H]^+$ 245.2264, found 245.2232.

1,2,4-Tricyclopentylbenzene and 1,3,5-tricyclopentylbenzene (2.9d and 2.10d): 2.9d:2.10d = 50:50; determined by ^{1}H NMR, this product was isolated by flash column chromatography on silica gel (hexane). Yield 24 mg (51%), yellow oil; IR (DCM): 2947, 2866, 1496, 1451, 1301, 1184, 1046, 886, 868, 712 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 7.20 (d, J = 8 Hz, 1H), 7.15 (d, 2 Hz, 1H), 7.05 (dd, J_1 = 8 Hz, J_2 = 2 Hz), 6.96 (s, 3H), 3.25-3.36 (m), 2.96 (pent, J = 8 Hz), 2.03-2.08 (m), 1.80-1.82 (m), 1.61-1.70 (m). ^{13}C{^{1}H} NMR ($CDCl_3$): δ 146.3, 143.8, 143.6, 141.4, 125.7, 124.7, 124.5, 123.6, 46.3, 46.0, 41.3, 41.0, 35.12, 35.09, 34.84, 34.77, 25.69. HRMS (EI) m/z Calcd for $C_{21}H_{29}$: $[M - H]^+$ 281.2264, found 281.2243.

(Benzene-1,2,4-triyltris(methylene))tricyclohexane and 1,3,5-tris(cyclohexylmethyl)benzene (2.9e and 2.10e): 2.9e:2.10e = 56:44; determined by GC analysis, this product was isolated by flash column chromatography on silica gel (hexane). Yield 40 mg (66%), yellow gel; IR (DCM): 2918, 2848, 1447, 1372, 1262,

1239, 1046, 737 cm^{-1}. ^1H NMR ($CDCl_3$): δ 6.99 (d, J = 8 Hz, 1H), 6.86-6.88 (m, 2H), 6.73 (s, 3H), 2.41-2.45 (m), 1.48-1.69 (m), 1.16-1.18 (m), 0.89-0.98 (m). $^{13}C\{^1H\}$ NMR ($CDCl_3$): δ 140.7, 139.0, 138.2, 136.6, 131.2, 129.9, 127.6, 126.2, 44.3, 43.9, 40.9, 40.5, 40.0, 39.9, 39.6, 33.7, 33.4, 26.8, 26.6, 26.5. ESI-MS m/z Calcd for $C_{27}H_{41}$ $[M - H]^+$: 365.3 found 365.3.

1,2,4-Tri-tert-butylbenzene and 1,3,5-tri-tert-butylbenzene (2.9f and 2.10f): 2.9f:2.10f = 69:31; determined by GC analysis, this product was isolated by flash column chromatography on silica gel (hexane). Yield 29 mg (70%), yellow oil; IR (DCM): 2956, 2868, 1470, 1391, 1362, 1259, 1201, 893, 737 cm^{-1}. ^1H NMR ($CDCl_3$): δ 7.62 (d, J = 8 Hz, 1H), 7.50 (d, J = 8 Hz, 1H), 7.25 (s, 3H), 7.12 (dd, J_1 = 8 Hz, J_2 = 2 Hz), 1.56 (s), 1.54 (s), 1.33 (s), 1.31 (s). $^{13}C\{^1H\}$ NMR ($CDCl_3$): δ 150.1, 147.5, 145.7, 129.3, 126.9, 122.4, 121.7, 119.6, 37.4, 35.1, 35.01, 34.97, 32.7, 32.3, 31.7, 31.5. ESI-MS m/z Calcd for $C_{18}H_{31}$: $[M + H]^+$ 247.2, found 247.2.

(Benzene-1,2,4-triyltris(methylene))tribenzene and 1,3,5-tribenzylbenzene (2.9g and 2.10g): 2.9g:2.10g = 58:42; determined by GC analysis, this product was isolated by flash column chromatography on silica gel (hexane). Yield 34 mg (53%), yellow oil; IR (DCM): 3058, 3025, 2918, 1599, 1493, 1449, 1073, 1029, 726, 699 cm^{-1}. ^1H NMR ($CDCl_3$): δ 7.23-7.30 (m), 7.14-7.20 (m), 7.06 (d, J = 8 Hz), 6.88 (s, 3H), 3.93 (d, J = 8 Hz), 3.90 (s). $^{13}C\{^1H\}$ NMR ($CDCl_3$): δ 141.4, 141.35, 141.29, 140.74, 140.68, 139.4, 139.0, 137.0, 131.5, 130.8, 129.02, 128.98, 128.9, 128.8, 128.54, 128.51, 128.49, 127.6, 127.3, 126.1, 126.1, 126.0, 41.9, 41.6, 39.2, 38.7. HRMS (EI) m/z Calcd for $C_{27}H_{25}$: $[M + H]^+$ 349.1951, found 349.1936.

(Benzene-1,2,4-triyltris(ethane-2,1-diyl))tribenzene and 1,3,5-triphenethylbenzene (2.9h and 2.10h): 2.9h:2.10h = 45:55; determined by GC

analysis, this product was isolated by flash column chromatography on silica gel (hexane). Yield 34 mg (53%), yellow oil; IR (DCM): 3025, 2927, 2857, 1602, 1495, 1452, 1074, 1029, 746, 699 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 7.35-7.36 (m), 7.26-7.27 (m), 7.03-7.08 (m), 6.90 (s, 1H), 2.94 (s). $^{13}C\{^{1}H\}$ NMR ($CDCl_3$): δ 142.1, 141.9, 139.7, 139.5, 137.1, 129.7, 129.4, 128.6, 128.5, 128.4, 126.5, 126.4, 126.1, 126.0, 38.22, 38.17, 38.09, 37.9, 37.7, 35.0, 34.6. HRMS (EI) m/z Calcd for $C_{30}H_{31}$: $[M + H]^+$ 391.2420, found 391.2401.

1,2,4-Tris((allyloxy)methyl)benzene and 1,3,5-tris((allyloxy)methyl)benzene (2.9i and 2.10i): 2.9i:2.10i = 60:40; determined by GC analysis, this product was isolated by flash column chromatography on silica gel (hexane). Yield 37 mg (64%), colorless oil; IR (DCM): 2919, 2857, 1720, 1697, 1354, 1157, 1068, 990, 925, 835 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 7.34-7.36 (m, 3H), 7.24 (s, 3H), 5.89-5.96 (m), 5.26-5.30 (m), 5.17-5.19 (m), 4.56-4.57 (m), 4.50 (s), 3.99-4.02 (m). $^{13}C\{^{1}H\}$ NMR ($CDCl_3$): δ 138.8, 138.0, 136.7, 135.9, 134.84, 134.81, 129.0, 128.3, 127.1, 126.4, 117.32, 117.29, 117.2, 72.0, 71.9, 71.44, 71.37, 71.3, 71.2, 69.8, 69.6. HRMS (EI) m/z Calcd for $C_{18}H_{23}O_3$: $[M - H]^+$ 287.1647, found 287.1645.

((Benzene-1,2,4-triyltris(methylene))tris(oxy))tribenzene and 1,3,5-tris(phenoxymethyl)benzene (2.9j and 2.10j): 2.9j:2.10j = 60:40; determined by ^{1}H NMR, this product was isolated by flash column chromatography on silica gel (hexane). Yield 24 mg (36%), yellow oil; IR (DCM): 3068, 2923, 1594, 1493, 1234, 1172, 1076, 1036, 743, 696 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 7.63 (s, 1H), 7.56 (d, J = 8 Hz, 1H), 7.50 (s), 7.46 (d, J = 8 Hz, 1H), 7.28-7.33 (m), 6.97-7.01 (m), 5.19 (s), 5.11 (s), 5.10 (s). $^{13}C\{^{1}H\}$ NMR ($CDCl_3$): δ 158.8, 158.7, 138.1, 137.5, 135.0, 129.67, 129.65, 129.64, 129.3, 128.1, 127.5, 126.1, 121.30, 121.27, 121.20, 121.16, 115.0, 114.99,

114.97, 114.96, 69.8, 69.6, 68.0, 67.8. HRMS (EI) m/z Calcd for $C_{27}H_{24}NaO_3$: $[M + Na]^+$ 419.1618, found 419.1608.

***N,N′,N′′*-(Benzene-1,2,4-triyltris(methylene))tris(*N*-methyl-1-phenylmethanamine) and *N,N′,N′′*-(benzene-1,3,5-triyltris(methylene))tris(*N*-methyl-1-phenylmethanamine) (2.9k and 2.10k):** 2.9k:2.10k = 59:41; determined by GC analysis, this product was isolated by flash column chromatography on silica gel (hexane). Yield 40 mg (50%), yellow oil; IR (DCM): 3059, 3028, 2931, 2783, 1493, 1452, 1363, 1129, 1026, 738, 700 cm^{-1}. ^1H NMR ($CDCl_3$): δ 7.22-7.42 (m), 3.64 (d, J = 8 Hz), 3.53 (m), 3.49 (s), 2.18-2.20 (m), 2.12 (s), 2.11 (s). $^{13}C\{^1H\}$ NMR ($CDCl_3$): δ 139.7, 139.4, 139.1, 138.1, 137.6, 137.0, 131.0, 130.3, 129.2, 129.13, 129.10, 128.5, 128.33, 128.28, 127.5, 127.03, 127.00, 126.98, 62.49, 62.46, 62.0, 61.93, 61.86, 61.8, 59.5, 59.2, 42.40, 42.37, 42.3. HRMS (EI) m/z Calcd for $C_{33}H_{40}N_3$: $[M + H]^+$ 478.3217, found 478.3208.

((Benzene-1,2,4-triyltris(methylene))tris(oxy))tris(tert-butyldimethylsilane) and 1,3,5-tris(((tert-butyldimethylsilyl)oxy)methyl)benzene (2.9l and 2.10l): 2.9l:2.10l = 69:31; determined by GC analysis, this product was isolated by flash column chromatography on silica gel (hexane). Yield 61 mg (72%), Yellow oil; IR (DCM): 3068, 2923, 1594, 1493, 1234, 1172, 1076, 1036, 743, 696 cm^{-1}. ^1H NMR ($CDCl_3$): δ 7.40 (s), 7.36 (d, J = 8 Hz, 1H), 7.20 (d, J = 8 Hz, 1H), 7.16 (s, 3H), 4.76 (s), 4.73 (s), 0.94 (s), 0.93 (s), 0.10 (s), 0.09 (s). $^{13}C\{^1H\}$ NMR ($CDCl_3$): δ 141.5, 126.7, 124.7, 124.6, 122.5, 65.2, 63.0, 29.8, 26.15, 26.13, 26.09, 18.6, -5.08, -5.15. (ESI-MS) m/z Calcd for $C_{27}H_{54}NaO_3Si_3$: $[M + Na]^+$ 533.3, found 533.3.

((Benzene-1,2,4-triyltris(ethane-2,1-diyl))tris(oxy))tris(tert-butyldimethylsilane) and 1,3,5-tris(2-((tert-butyldimethylsilyl)oxy)ethyl)benzene (2.9m and 2.10m):

2.9m:2.10m = 60:40; determined by GC analysis, this product was isolated by flash column chromatography on silica gel (hexane). Yield 37 mg (64%), yellow oil; IR (DCM): 2931, 2891, 2858, 1466, 1385, 1253, 1092, 834, 775, 731, cm^{-1}.^{1}H NMR ($CDCl_3$): δ 7.07 (d, J = 8 Hz, 1H), 6.97-7.00 (m, 2H), 6.88 (s), 3.75-3.80 (m), 2.85 (t, J = 8 Hz), 2.77 (t, J = 8 Hz), 0.88 (s), 0-0.01 (m). $^{13}C\{^1H\}$ NMR ($CDCl_3$): δ 139.0, 137.1, 135.0, 131.1, 130.2, 128.0, 127.2, 64.8, 64.5, 64.4, 39.7, 39.4, 36.5, 36.2, 26.1, 18.5, -5.2. HRMS (EI) m/z Calcd for $C_{30}H_{61}O_3Si_3$: $[M + H]^+$ 553.3923, found 553.3940.

(Benzene-1,2,4-triyltris(trimethylsilane) and 1,3,5-tris(trimethylsilyl)benzene (2.9n and 2.10n): 2.9n:2.10n = 60:40; determined by GC analysis, this product was isolated by flash column chromatography on silica gel (hexane). Yield 40 mg (80%), yellow oil; IR (DCM): 2955 (w), 2899 (w), 1250, 1147, 836, 750, 691 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 7.85 (s, 3H), 7.66-7.70 (m, 1H), 7.50-7.52 (m, 1H), 0.38 (d, J = 4 Hz), 0.28 (s). $^{13}C\{^1H\}$ NMR ($CDCl_3$): δ 146.7, 145.0, 140.1, 139.5, 134.5, 132.9, 2.1, 2.0, -1.1. (ESI-MS) m/z Calcd for $C_{15}H_{31}Si_3$: $[M + H]^+$ 295.1, found 295.1.

3',4',6'-Trimethyl-5'-phenyl-1,1':2',1''-terphenyl[40] **(2.12a):** This product was isolated by flash column chromatography on silica gel (hexane). Yield 32 mg (55%), white solid; IR (DCM): 3021 (w), 2963 (w), 2930 (w), 2874 (w), 1444, 1373, 1076, 1049, 1047, 734, 698 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 7.47-7.50 (m, 2H), 7.37-7.41 (m, 1H), 7.28-7.31 (m, 2H), 7.00-7.18 (m, 10H), 2.09 (overlapped singlet, 2x3H), 1.76 (s, 3H). $^{13}C\{^1H\}$ NMR ($CDCl_3$): δ 142.6, 141.8, 141.7, 141.6, 140.8, 139.4, 134.1, 132.0, 131.4, 130.4, 129.5, 128.6, 127.5, 127.4, 126.6, 125.9, 125.8, 19.6, 18.4, 18.2. (ESI-MS) m/z Calcd for $C_{27}H_{25}$: $[M +H]^+$ 349.1, found 349.1.

3',4',6'-Triethyl-5'-phenyl-1,1':2',1''-terphenyl[41] **(2.12b):** This product was isolated by flash column chromatography on silica gel (hexane). Yield 27 mg (42%), white solid; IR (DCM): 3022 (w), 2968 (w), 2931 (w), 2872 (w), 1440, 1371, 1071, 1047, 1042, 735, 697 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 7.42-7.46 (m, 2H), 7.35-7.39 (m, 3H), 7.02-7.14 (m, 10H), 2.44-2.53 (m, 4H), 2.10-2.18 (m, 2H), 0.96-1.04 (m, 6H), 0.65 (t, J = 8 Hz, 3H). $^{13}C\{^{1}H\}$ NMR ($CDCl_3$): δ 141.7, 141.6, 141.5, 141.4, 141.3, 139.5, 139.4, 137.8, 137.4, 130.7, 130.6, 130.2, 127.9, 127.10, 127.07, 126.6, 125.75, 125.69, 24.7, 23.7, 23.6, 15.8, 15.4. HRMS (EI) m/z Calcd for $C_{30}H_{31}$: $[M+H]^+$ 391.2420, found 391.2401.

3',4',6'-Tributyl-5'-phenyl-1,1':2',1''-terphenyl[41] **(2.12c):** This product was isolated by flash column chromatography on silica gel (hexane). Yield 36 mg (45%), white solid; IR (DCM): 3021 (w), 2955 (w), 2926 (w), 2870 (w), 1459, 1378, 1071, 1026, 1042, 749, 699 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 7.40-7.44 (m, 2H), 7.32-7.36 (m, 3H), 7.01-7.13 (m, 10H), 2.37-2.44 (m, 4H), 2.04-2.08 (m, 2H), 1.36-1.45 (m, 4H), 1.05-1.17 (m, 6H), 0.68-0.75 (m, 8H), 0.38 (t, 3H). $^{13}C\{^{1}H\}$ NMR ($CDCl_3$): δ 141.73, 141.67, 141.42, 141.36, 139.4, 138.5, 136.7, 136.4, 130.8, 130.6, 130.2, 127.8, 127.04, 127.00, 126.5, 125.7, 125.6, 33.6, 33.0, 31.2, 30.6, 30.4, 23.3, 22.8, 13.7, 13.6, 13.2. HRMS (EI) m/z Calcd for $C_{36}H_{43}$: $[M+H]^+$ 475.3359, found 475.3321.

Determination of the Molecular Structures of4,4''-difluoro-4'-(4-fluorophenyl)-1,1':2',1''-terphenyl (2.6g), 4'-(3,5-bis(trifluoromethyl)phenyl)-3,3'',5,5''-tetrakis(trifluoromethyl)-1,1':2',1''-terphenyl (2.6i) and 3',4',6'-trimethyl-5'-phenyl-1,1':2',1''-terphenyl (2.12a) in the Solid State by Single Crystal X-ray Diffraction: Single crystals of complexes **2.6g, 2.6i** and **2.12a** suitable for X-ray analysis was obtained from solutions of hexane-dichloromethane and hot hexane,

respectively. Crystals suited for single crystal x-ray diffraction measurements were mounted on a glass fiber. Geometry and intensity data were collected with a Bruker SMART D8 goniometer equipped with an APEX CCD detector and with an Incoatecmicrosource (Mo-Kα radiation, λ = 0.71073 Å, multilayeroptics). Temperature was controlled using an Oxford Cryostream 700 instrument. Intensities were integrated with SAINT+[36]and corrected for absorption with SADABS.[37] The structures were solved by direct methods and refined on $F^2$with SHELXL-97.[38,39]

Crystal Data of 2.6g, 2.6i and 2.12a

4,4''-Difluoro-4'-(4-fluorophenyl)-1,1':2',1''-terphenyl (2.6g): $C_{24}H_{15}F_3$, colorless block, crystal dimensions: 0.18 x 0.15 x 0.12 mm^3, *M* =360.36, Monoclinic with space group $P2_1/c$, *a* = 12.3035(8)Å, *b* = 9.5708(7)Å, *c* = 30.749(2)Å, *α* = 90°, *β* = 96.009°, *γ* = 90°,*V* = 3600.9(4) $Å^3$, *Z* = 8,*F*(000) = 1488.0, μ-(MoK_α) = 0.098 mm^{-1}, 2θmax = 57.346, ρ_{calcd} = 1.329 Mg/m^3, T = 296(2)K, min/max transmission factors = 0.6390/0.7458, 31818 Reflections collected, 9254 unique (*R1* = 0.0554), *WR2* = 0.1260 (all data). Residual electron density max/min = 0.16/-0.25e.$Å^{-3}$.The structure has been deposited at the CCDC data center and can be retrieved using the deposit number 1823258.

4'-(3,5-bis(trifluoromethyl)phenyl)-3,3'',5,5''-tetrakis(trifluoromethyl)-1,1':2',1''-terphenyl (2.6i) $C_{30}H_{12}F_{18}$, colorless block, crystal dimensions: 0.14 x 0.13 x 0.11 mm^3, *M* = 714.40, Monoclinic with space group P21/c, *a* = 11.2394(5)Å, *b* = 16.1180(6)Å, *c* = 15.2720(5)Å, *β* = 91.835(2)°, V = 2765.21(18)$Å^3$, Z = 4, T = 296.15 K, μ(MoKα) = 0.185 mm-1, min/max transmission factors = 0.6108/0.7456, ρ_{calcd} = 1.716 g/cm3, 40456 Reflections collected, 6367 unique (*R1* = 0.0709), 2θmax = 55.282°, *WR2* = 0.2108 (all data). Residual electron density max/min = 1.28 -1.07e.$Å^-$

^{3}. The structure has been deposited at the CCDC data center and can be retrieved using the deposit number 1858249.

3',4',6'-Trimethyl-5'-phenyl-1,1':2',1''-terphenyl (2.12a): $C_{27}H_{24}$, colorless block, crystal dimensions: 0.19 x 0.17 x 0.12 mm^3, M =348.46, Monoclinic with space group P1 21/c 1, a = 11.5979(8)Å, b = 11.2436(7)Å, c = 15.6132(10)Å, α = 90°, β = 99.630(4)°, γ = 90°, V = 2007.3(2) $Å^3$, Z = 4, F(000) = 744, μ-(MoK_α) = 0.065 mm^{-1}, 2θmax = 56.772, ρ_{calcd} = 1.153 Mg/m^3, T = 298(2)K, min/max transmission factors = 0.5722/0.7457, 17427 Reflections collected, 5006 unique (*R1* = 0.0522), *WR2* = 0.1501 (all data). Residual electron density max/min = 0.199/ -0.169e.$Å^{-3}$. The structure has been deposited at the CCDC data center and can be retrieved using the deposit number 1823259.

EPR Studies

EPR measurement parameters

Frequency = 9.45 GHz, modulation amplitude = 4 G, receiver gain = 2 X 10^2, modulation frequency = 100 KHz, conversion time = 20 msec, sweep width = 1000 G, center field = 3400 G, Power = 5.35 e^{-1} mW.

^{1}H and ^{13}C NMR spectra of cyclotrimerized products:

Figure 2.5 ^{1}H NMR spectrum of 4'-phenyl-1,1':2',1"-terphenyl and 5'-phenyl-1,1':3',1"-terphenyl (**2.6a** and **2.7a**) (400 MHz, $CDCl_3$):

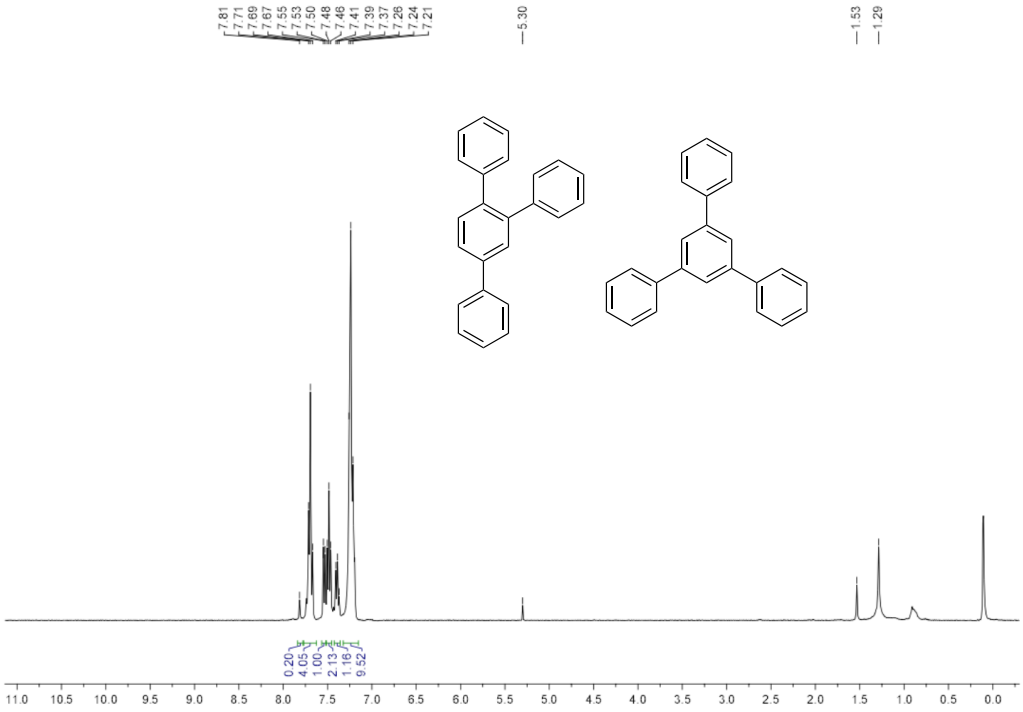


Figure 2.5 ^{13}C NMR spectrum of 4'-phenyl-1,1':2',1"-terphenyl and 5'-phenyl-1,1':3',1"-terphenyl (**2.6a:2.7a**) (100.6 MHz, $CDCl_3$):

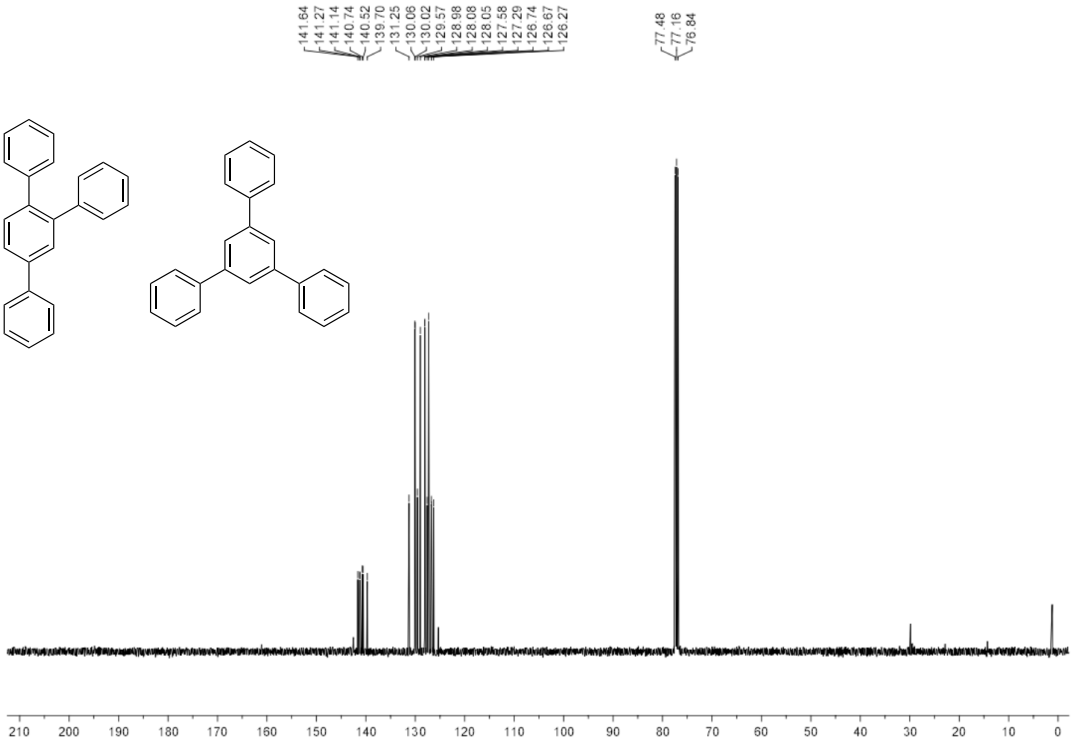


Figure 2.6 ^{1}H NMR spectrum of 4'-phenyl-1,1':2',1"-terphenyl and 5'-phenyl-1,1':3',1"-terphenyl (**2.6a** and **2.7a**) (400 MHz, $CDCl_3$):

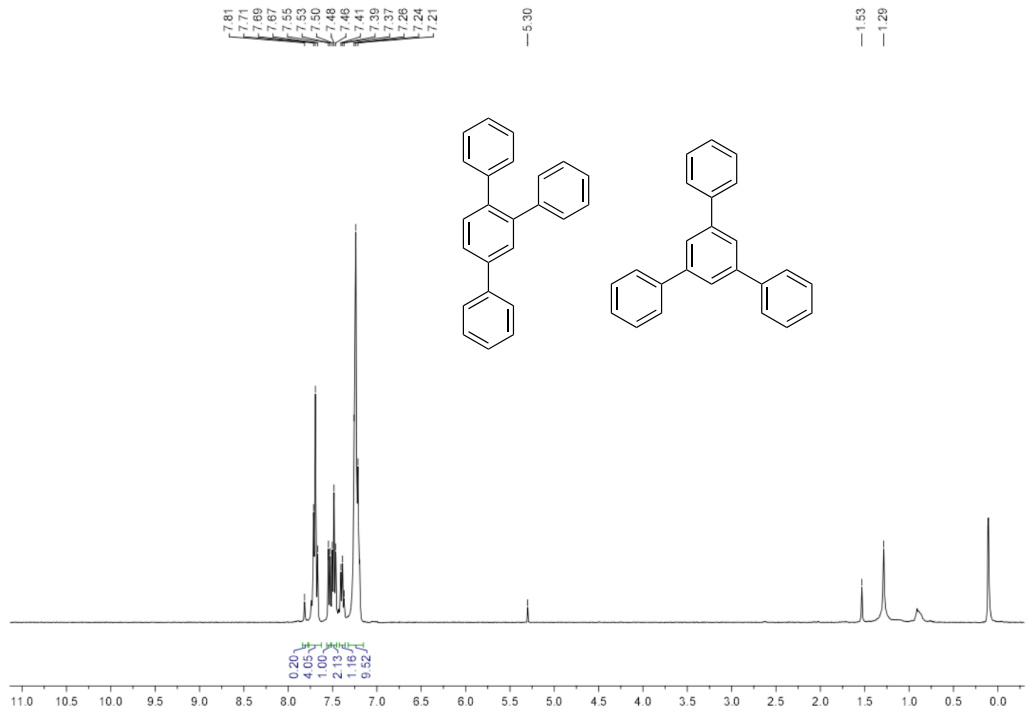


Figure 2.6 ^{13}C NMR spectrum of 4'-phenyl-1,1':2',1"-terphenyl and 5'-phenyl-1,1':3',1"-terphenyl (**2.6a:2.7a**) (100.6 MHz, $CDCl_3$):

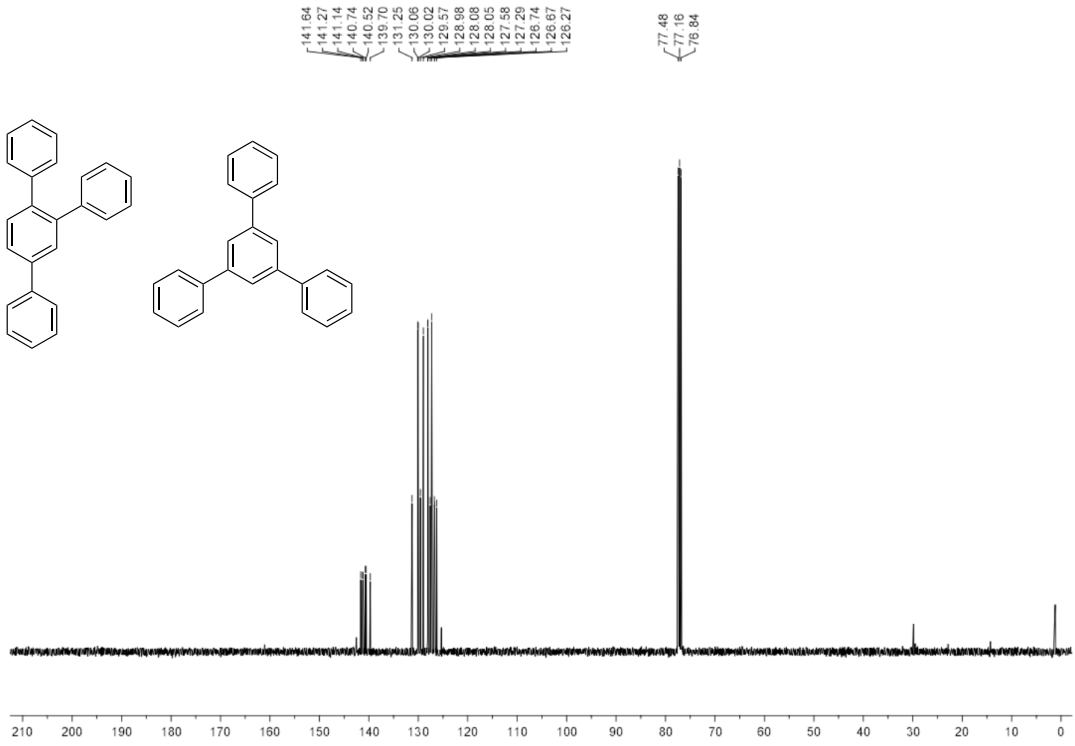


Figure 2.7 ^{1}H NMR spectrum of 1,2,4-tripentylbenzene and 1,3,5-tripentylbenzene (**2.9a:2.10a**) (400 MHz, $CDCl_3$):

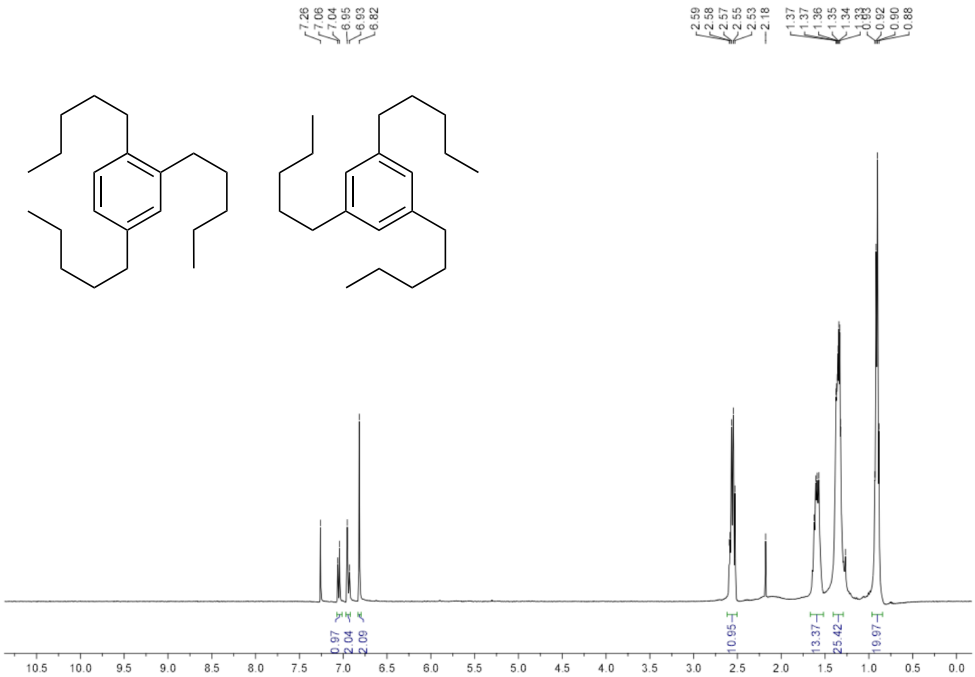


Figure 2.7 ^{13}C NMR spectrum of 1,2,4-tripentylbenzene and 1,3,5-tripentylbenzene (**2.9a:2.10a**) (100.6 MHz, $CDCl_3$):

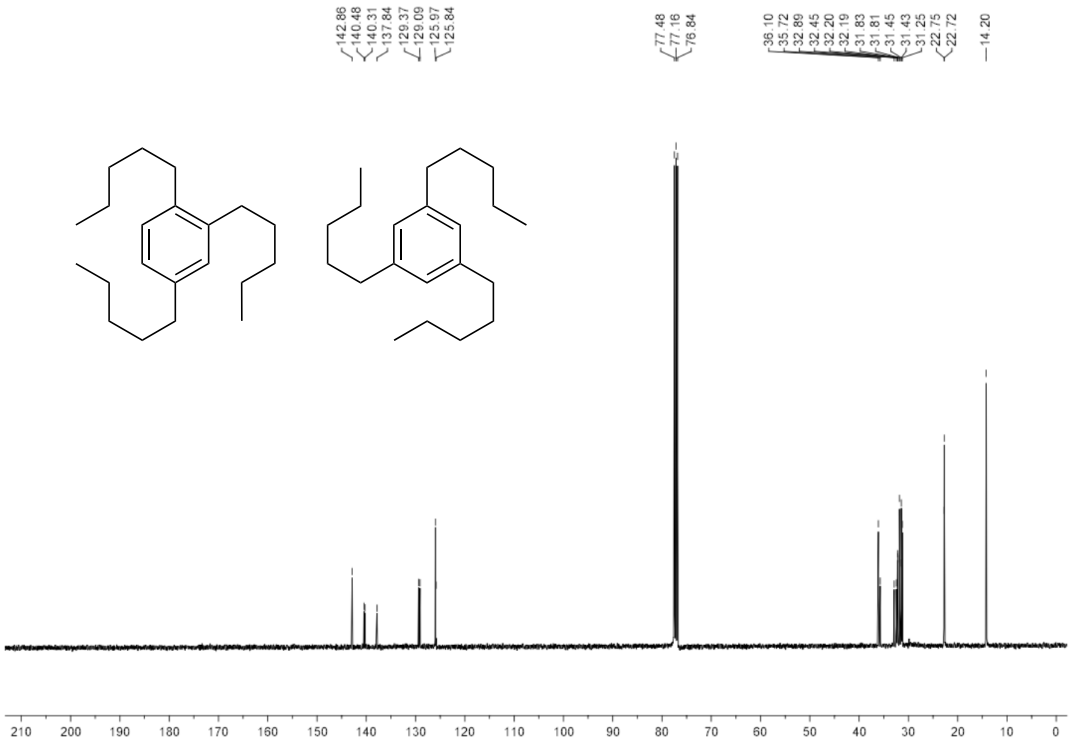


Figure 2.8 ^{1}H NMR spectrum of 3',4',6'-triethyl-5'-phenyl-1,1':2',1"-terphenyl **(2.12c)** (400 MHz, $CDCl_3$):

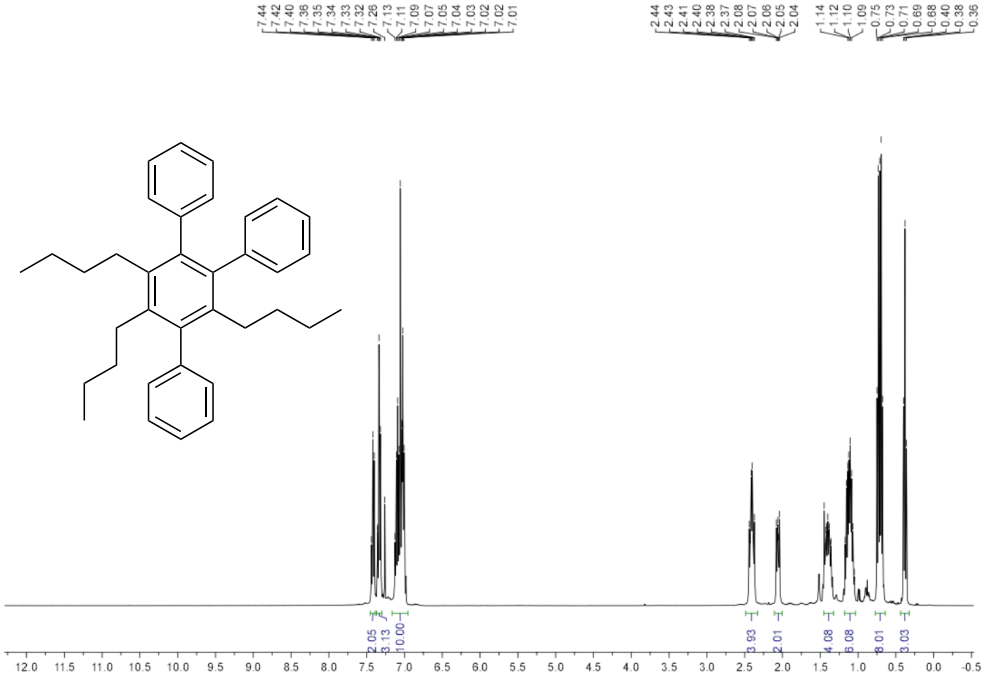
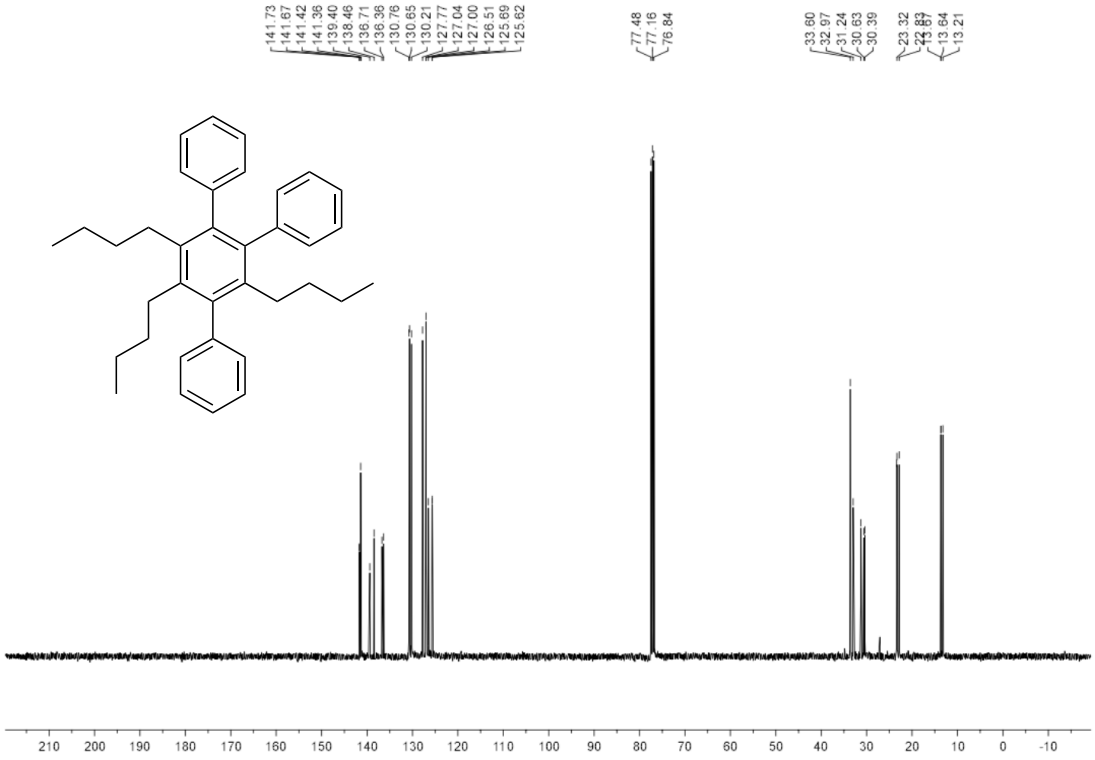


Figure 2.8 ^{13}C NMR spectrum of 3',4',6'-tributyl-5'-phenyl-1,1':2',1"-terphenyl **(2.12c)** (100.6 MHz, $CDCl_3$):



CHAPTER 3

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

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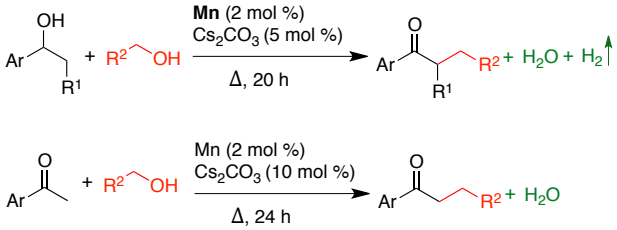
3.1 ABSTRACT



Catalytic cross-coupling of ketones and secondary alcohols with primary alcohols is reported. An abundant manganese based pincer catalyst catalyzes the reactions. Catalyst load (2 mol %) and catalytic use of a mild base (5-10 mol %) are sufficient for efficient cross-coupling. Various aryl and heteroaryl ketones are catalytically cross-coupled with primary alcohols to provide the selective α-alkylated products. Challenging α-ethylation of ketones is also attained using ethanol as an alkylating reagent. Further, direct use of secondary alcohols in the reaction results in in situ oxidation to provide the ketone intermediates, which undergo selective α-alkylation. The reaction proceeds via the borrowing hydrogen pathway. The catalyst oxidizes the primary alcohols to aldehydes, which undergo subsequent aldol condensation with ketones, promoted by catalytic amount of Cs_2CO_3, to provide the α,β–unsaturated ketone intermediates. The hydrogen liberated from oxidation of alcohols is used for hydrogenation of α,β–unsaturated ketone intermediates. Notably either water or water and dihydrogen are the only byproducts in these environmentally benign catalytic processes. Mechanistic studies allowed inferring all the intermediates involved. Dearomatization-aromatization metal-ligand cooperation in the catalyst

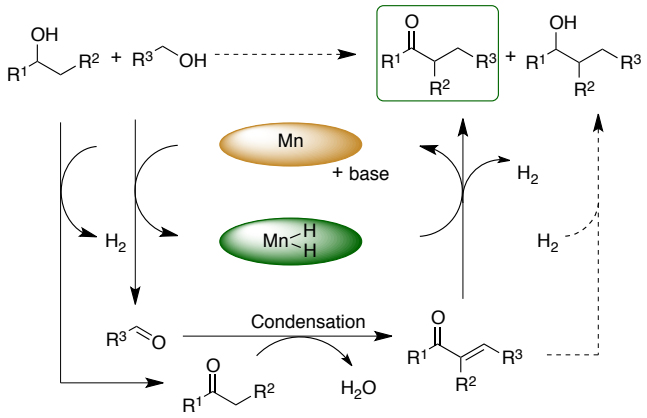
facilitates the facile O–H bond activation of both primary and secondary alcohols and the resultant manganese alkoxide complexes produce corresponding carbonyl compounds, perhaps via β-hydride elimination. The manganese(I) hydride intermediate plays dual role as it hydrogenates α,β–unsaturated ketones and liberates molecular hydrogen to regenerate the catalytically active dearomatized intermediate. Metal-ligand cooperation allows all the manganese intermediate to exist in same oxidation state (+1) and plays an important role in these catalytic cross-coupling reactions.

3.2 INTRODUCTION

Efficient and catalytic construction of C−C bond is an important transformation in organic synthesis. Among C−C bond formation methods, *α*-alkylation of ketones is one of the pivotal routes for the synthesis of several biologically active, heterocyclic compounds and natural product building blocks.[42] Conventional methods involved use of reactive alkyl halides as alkylating reagents in the presence of stoichiometric amount of base that resulted in generation of toxic waste, which limited their sustainable applications.[43] Advancement in catalysis, in particular introduction of "borrowing hydrogen" or "hydrogen autotransfer" methods allowed to overcome these drawbacks. In recent years, borrowing hydrogen strategy for C−C bond formation has received significant attention for the construction of functionalized organic molecules.[44] Typical borrowing hydrogen method involves catalytic dehydrogenation of alcohol to aldehyde and ketones, followed by base mediated aldol reaction, which generates the corresponding *α,β*–unsaturated ketone intermediate with elimination of water. Further, catalytic and selective transfer hydrogenation of the enone intermediates using the hydrogen obtained from the oxidation of alcohols

affords α-alkylated ketones with high atom efficiency. Liberated molecular hydrogen and water are the only byproducts from this transformation (Scheme 1).[45]

Scheme 3.1 Selective Catalytic Dehydrogenative Cross-Coupling of Ketones and Secondary Alcohols with Primary Alcohols Enabled by Borrowing Hydrogen Concept



In general, this catalytic alkylation of ketones using alcohols is implemented using noble metals such as ruthenium[46], palladium[47], osmium[48], iridium[49] etc. Accordingly non-precious first row transition metals[50] have drawn much attention. Recently, Beller and co-workers reported an aliphatic electron rich PNP tridentate manganese(I) catalyst, for alkylation of ketones.[51] More recently, α-alkylated ketones have been synthesized by direct dehydrogenative coupling of readily available and cheap secondary alcohols with primary alcohols.[51b,c] Dehydrogenative cross coupling of secondary alcohols and primary alcohols using Rh, Ru and Ir catalysts have been reported.[46,49b,52] Thus, earth-abundant, inexpensive, more eco-friendly base metals like Mn, Fe, and Co catalyzed cross coupling of primary and secondary alcohols to α-alkylated ketones is desirable. In this direction, recently, Lang and coworkers have reported ligand-controlled copper(I) catalyzed cross-coupling of secondary and primary alcohols.[52b]

Eminent research groups have designed and developed various manganese pincer catalysts, which catalyzed an assortment of organic transformations.[13b,53-60] Manganese pincer based catalysis have become more attractive because of new selectivity patterns in known reactions; just by altering different base provides different product.[61] Recently, Yu and co-workers[62] have reported manganese catalyzed cross-coupling of secondary alcohols with primary alcohols, which provided the Guerbet *β*-alkylated secondary alcohol products in good yields. Kempe and co-workers[53c] reported the multicomponent synthesis of pyrimidines from alcohols and amidines that proceeded via *β*-alkylation of alcohols. Using ruthenium pincer catalyst, we have reported the cross coupling of secondary alcohols.[63a] Selective *α*-alkylation and *α*-olefination of nitriles compounds with primary alcohols and secondary alcohols, respectively were also reported using ruthenium catalyst.[63b-c] Very recently, we have also reported manganese catalyzed selective *α*-alkenylation of ketones using primary alcohols.[63d] In continuation of our quest to devise and develop atom economical and sustainable catalytic transformations, herein we report the selective cross-coupling of ketones and secondary alcohols with primary alcohols, which provided the *α*-alkylated ketone products in good to excellent yields. These dehydrogenative and dehydrative cross-coupling reactions are catalyzed by the manganese(I) triazine pincer based Kempe catalyst **[(4-Ph)Tr(NHP(iPr)$_2$)$_2$Mn(CO)$_2$Br]** (**3.1**) together with catalytic amount of a mild base.

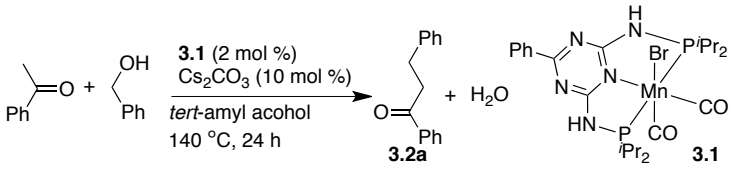
3.3. RESULTS AND DISCUSSIONS

During the development of selective *a*-alkenylation of ketones using primary alcohols, we have found that catalyst **3.1** with phenyl substituent in the catalyst backbone favorably produced the *a*-alkylated ketone products, while similar catalyst with 4-methyl substitution promoted the selective *a*-olefination reaction.[63d] Thus,

catalytic α-alkylation of ketones by primary alcohols using manganese pincer catalyst **3.1** was investigated (Table 3.1). At the outset of our studies, acetophenone and benzyl alcohol were chosen as benchmark substrates to find the optimal reaction conditions for the PN_5P triazine based manganese catalyst **3.1** and the results are presented in Table 3.1 Reaction of acetophenone and benzyl alcohol (each 0.5 mmol), was performed in presence of 2 mol % of catalyst **3.1** and 5 mol % of Cs_2CO_3 as base in *tert*-amyl alcohol solvent, which delivered the desired alkylated product in 63% yield (entry 1). Upon increase of base load to 10 mol %, alkylated product **3.2a** was isolated in 75% yield (entry 2). When amount of alcohol was increased from 1 to 1.2 equiv, the outcome was optimal, where the desired **3.2a** was isolated in 86% yield with more than 99% conversion of acetophenone (entry 3). Further, lowering the catalyst load to 1 mol % resulted in diminished yield of the product (entry 4). Use of different solvents like 1,4-dioxane and toluene provided the alkylated product **3.2a** in 84% and 51% yield, respectively (entries 5 and 6). Reactions were tested with different bases. Upon use of sodium carbonate, product **3.2a** was isolated in 11% yield (entry 7). Although use of potassium carbonate as a base provided 97% conversion of acetophenone, the desired product **3.2a** was isolated in 47% yield (entry 8). Further, use of strong base sodium *tert*-butoxide provided the moderate conversion (80%) and yield (71%, entry 9). When reaction was carried out in the absence of catalyst **3.1** and in presence of base alone, the product was obtained in 20% yield along with other undesired side products (entry 10). When alkylation reactions were carried out with catalyst **3.1** in the absence of base and in the absence of both catalyst and base (entries 11 and 12), no product was observed, implying that catalyst and base are essential for the alkylation of ketones using alcohols. Control experiment without Mn complex and only base were carried out under inert atmosphere. Catalyst

3.1 was stable at 140 °C, reaction performed in the presence of mercury metal provided the comparable yield respective to optimized reaction condition. This experiment indicates that reaction proceeded through homogenous pathway (with catalyst integrity remain intact).

Table 3.1 Optimization of the Reaction Conditions for the α-Alkylation of Ketones[a]

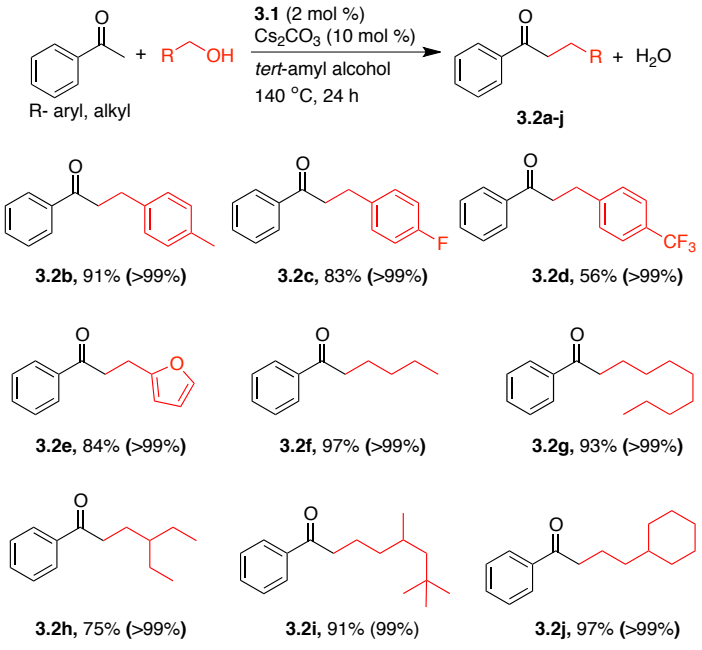


entry	**3.1** (mol %)	base (mol %)	alcohol (equiv)	conv. (%)	yield (%)
1	2	Cs_2CO_3 (5)	1	> 99	63
2	2	Cs_2CO_3 (10)	1	> 99	75
3	2	Cs_2CO_3 (10)	1.2	> 99	86
4	1	Cs_2CO_3 (10)	1.2	> 99	71
5[b]	2	Cs_2CO_3 (10)	1.2	> 99	84
6[c]	2	Cs_2CO_3 (10)	1.2	98	51
7	2	Na_2CO_3 (10)	1.2	33	11
8	2	K_2CO_3 (10)	1.2	97	47
9	2	NaO^{t}Bu (10)	1.2	80	71
10	-	Cs_2CO_3 (10)	1.2	75	20
11	2	-	1.2	-	-
12	-	-	1.2	-	-

[a]Reaction conditions: acetophenone (0.5 mmol), benzyl alcohol, catalyst **3.1** (0.02 mmol), and the base in *tert*-amyl alcohol were heated at 140 °C for 24 h. [b]dioxane was used as solvent. [c]toluene was used as solvent.

Following the optimized experimental conditions, a wide range of alcohols was subjected to manganese-catalyzed **3.1** α-alkylation reaction of acetophenone, which offered moderate to excellent yields of alkylated ketones (Table 3.2). In general, complete conversion of acetophenone was observed in all reactions. Upon using 4-methylbenzyl alcohol, the corresponding alkylated product **3.2b** was isolated in 91% yield. While 4-fluorobenzyl alcohol provided the corresponding alkylated product **3.2c** in 83% yield, 4-(trifluoromethyl)benzyl alcohol gave **3.2d** only in 56% yield. A heteroaryl alcohol, 2-furanylmethanol provided 84% of the alkylated product **3.2e**. Further, a series of aliphatic primary alcohols such as 1-butanol, 1-octanol, 3,5,5-trimethylhexanol, 2-cyclohexylethanol were investigated as alkylating partners and in all these experiments excellent yields (91-97%) were obtained (**3.2f, 3.2g, 3.2i, 3.2j**). However, 2-ethyl-butanol provided 75% of the alkylated product **3.2h**, perhaps due to steric hindrance in proximity to alcohol functionality.

Table 3.2 Manganese-Catalyzed α-Alkylation of Acetophenone Using Primary Alcohols[a]

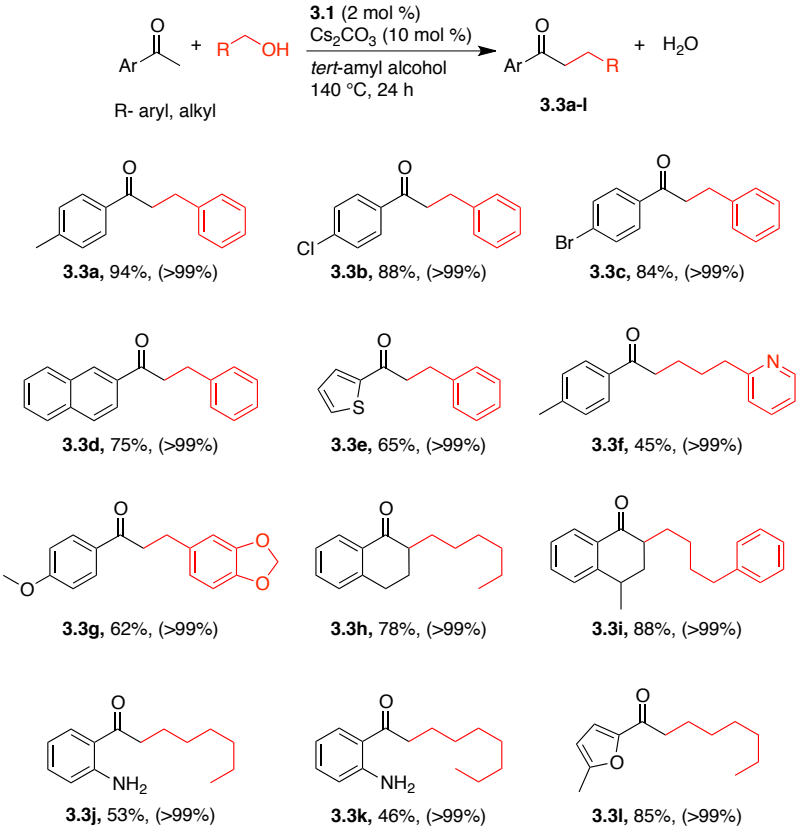


[a]Reaction conditions: ketone (0.5 mmol), alcohol (0.6 mmol), *tert*-amyl alcohol (2 mL), catalyst **3.1** (2 mol %), and Cs_2CO_3 (10 mol %) were heated at 140 °C under open condition with an argon flow. Yields were calculated for isolated products after column chromatography. Conversion of ketones was determined by GC analysis using toluene as an internal standard and given within parentheses.

Then, we explored the scope of different aryl ketones in the catalytic *α*-alkylation reactions using various primary alcohols (Table 3.3). Initially, different acetophenone derivatives bearing electron withdrawing and electron donating substituents were subjected to alkylation with benzyl alcohol. 4-Methylacetophenone provided the desired alkylated product **3.3a** in 94% isolated yield. In general, aryl ketones having poor electron-aryl motifs provided the corresponding alkylated products in lower yields (**3.3b-3.3e**) than compared to electron rich aryl ketones. Gratifyingly, heteroaryl ketone, 2-acetylthiophene was transformed to the desired alkylated product. Upon reaction with benzyl alcohol, 65% of the alkylated product **3.3e** was isolated. Despite that 3-(pyridin-2-yl)propan-1-ol provided good conversion, its catalytic *α*-alkylation with 4-methylacetophenone resulted in 45% of **3.3f**. With piperonyl alcohol as alkylating partner, 4-methoxyacetophenone yielded 62% of the corresponding alkylated product **3.3g**. 1-Tetralone and 4-methyl-1-tetralone were converted quantitatively to the *α*-alkylated products **3.3h** and **3.3i** in 78% and 88% yields, respectively. Remarkably, this manganese catalyzed *α*-alkylation reaction is highly chemoselective. Even in the presence of amine functionality, alkylation occurred exclusively on a carbon *α*-to carbonyl group. Upon catalytic *α*-alkylation of 2'-aminoacetophenone with 1-hexanol and 1-heptanol, the corresponding alkylated products were obtained in 53% and 46% yield (**3.3j, 3.3k**). Notably, the *N*-alkylated product was not observed in this condition, which indicates the chemoselective C-alkylation over N-alkylation. Chemoselectivity has been observed with the amino-

acetophenone substrate. Moreover, isolated yield and conversion having difference of 50% the undesired product. The observed undesired product spectrum shows complex mixture. GC-FID reaction mixture spectrum showed that there is only one C-alkylated product. Retention time for C-alkylated product was observed 19.53 min. However, GC-FID didn't show the complex mixture.

Table 3.3 Manganese-Catalyzed *α*-Alkylation of Ketones Using Alcohols[a]

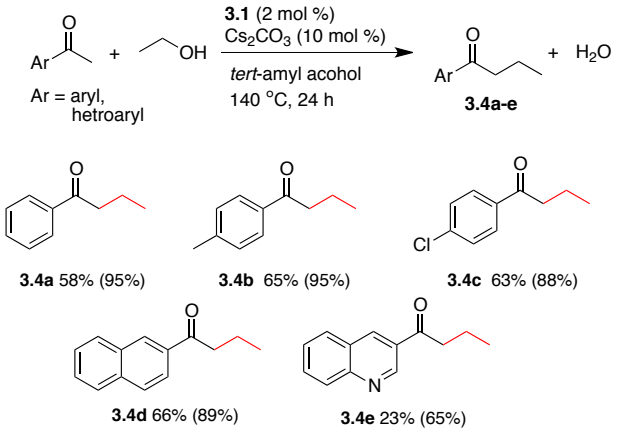


[a]Reaction conditions: same as in footnote of Table 3.2.

To further explore the scope of manganese catalyzed *α*-alkylation of ketones with primary alcohols, alkylation using ethanol is demonstrated (Table 3.4). Acetophenone and ethanol under the optimized catalytic conditions yielded 58% of the ethylated product **3.4a**. 4'-Methylacetophenone and 4'-chloroacetophenone provided 65% and 63% of the corresponding ethylated product **3.4b, 3.4c**, respectively. *β*-Napthyl methyl ketone provided the ethylated product **3.4d** in 66% yield. However, when 3-

acetyl quinoline was examined under standard experimental conditions, only 23% of the ethylated product **3.4e** was isolated. Similar catalytic results were obtained by previously reported manganese, iron and cobalt catalyzed *α*-alkylation of ketones using primary alcohols.[50, 51a]

Table 3.4 Manganese-Catalyzed *α*-Alkylation of Ketones Using Ethanol[a]

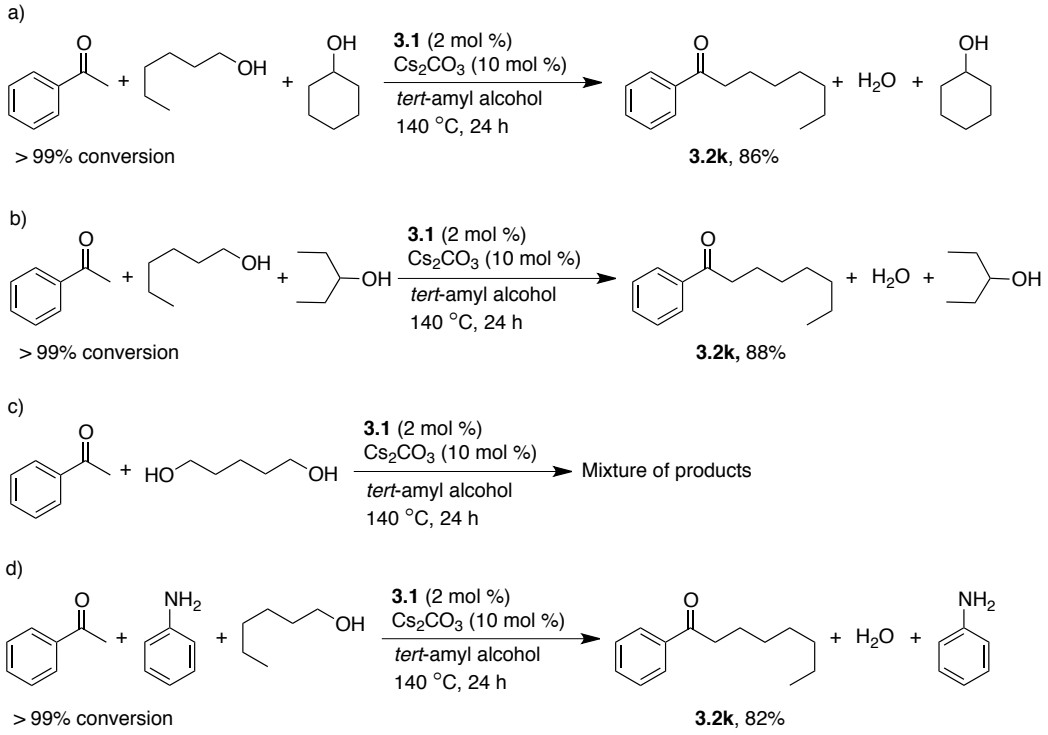


[a]Reaction conditions: ketone (0.5 mmol), ethanol (1 mL), *tert*-amyl alcohol (1 mL), catalyst **3.1** (2 mol %), and Cs_2CO_3 (10 mol %) were heated at 140 °C in a sealed tube. Yields were calculated for isolated products after column chromatography. Conversion of ketones was determined by GC analysis using toluene as an internal standard and given within parentheses.

Exclusive chemoselectivity of primary alcohols over secondary alcohols on alkylation of ketone was investigated. Acetophenone (1 equiv) with cyclohexanol and 1-hexanol (each 1.2 equiv) was quantitatively converted to the *α*-alkylated product in the presence of catalyst **3.1** (2 mol %) and Cs_2CO_3 (10 mol %) to form 1-phenyloctan-1-one (**3.2k**, 86% isolated yield, Scheme 3.2a). Similar experiment using 3-pentanol also provided almost identical result (**3.2k**, 88% isolated yield Scheme 3.2b). Reaction of diols such as 1,5-hexanediol with acetophenone in the presence of catalyst **3.1** provided a mixture of products (Scheme 3.2c). Remarkably, when acetophenone (1 equiv) was reacted with 1-hexanol (1.2 equiv) and aniline (1 equiv) in the presence of catalyst **3.1** (2 mol %) and Cs_2CO_3 (10 mol %), quantitative

conversion of ketone was observed to provide 1-phenyloctan-1-one (**3.2k**, 82% isolated yield, Scheme 3.2d).

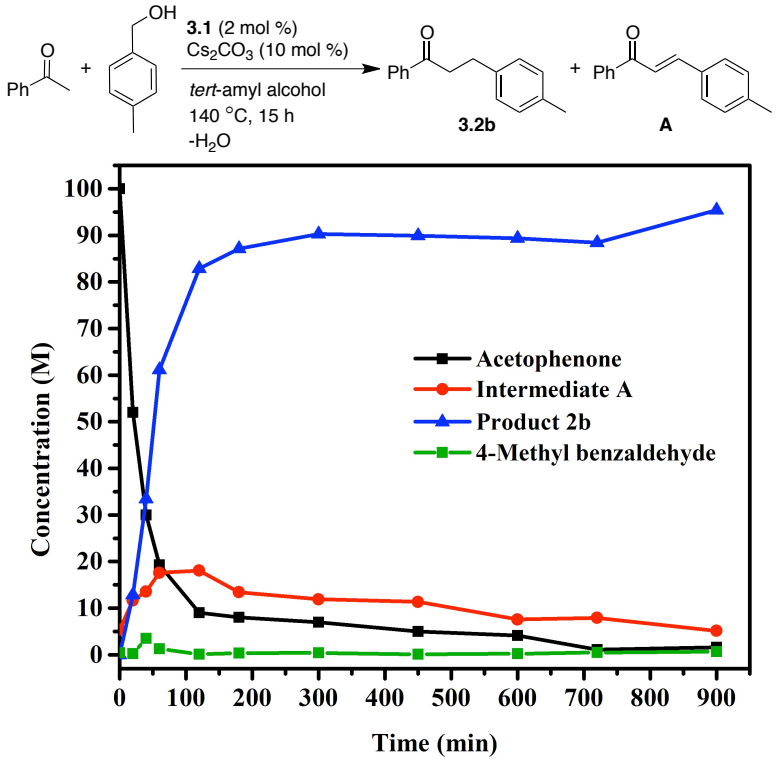
Scheme 3.2 Manganese-Catalyzed Chemoselective *α*-Alkylation of Acetophenone



In situ monitoring of the reaction progress by GC on the catalytic *α*-alkylation reaction of acetophenone using 4-methylbenzyl alcohol catalyzed by **3.1** allowed to infer the intermediates involved. As reaction proceeded, decrease in concentration of acetophenone (black line) can be corroborated with increasing concentration of product **3.2b** (blue line). Notably, upon oxidation of 4-methylbenzyl alcohol, the *in situ* formed intermediate 4-methylbenzylaldehyde (green line) was only short-lived as it undergoes rapid condensation with acetophenone to provide intermediate **A** (*α,β*-unsaturated ketones, red line). Reaction kinetics also indicated that hydrogenation of *α,β*-unsaturated ketone intermediate **A** to the corresponding alkylated product was rapid at the outset of the reaction and became slower over the time 4-phenyl substituted triazine base manganese catalyst is capable of doing the dehydrogenation of alcohol. Catalyst 3.1 provided some alkenylated (enone) product with shorter

reaction time. But prolonged reaction time provides selective *α*-alkylated product. This alkenyl intermediate is observed during monitoring of the reaction progress in *α*-alkylation (Figure 3.1). As we have observed in figure 3.1, acetophenone concentration decrease (8%-1%), whereas, enone intermediate A concentration (13%-8%) and a-alkylated product concentration (90%-88%) decrease during 200-700 minutes, respectively. This value indicates that, acetophenone almost got completely consumed and transfer to corresponding product (intermediate A). But as reaction progressed, after 700 minutes enone intermediates A get transfer to a-alkylated product. a-alkylated product concentration (88%-95%) increase during 700-900 minutes. This clearly indicates that reaction has other parallel pathways for formation.

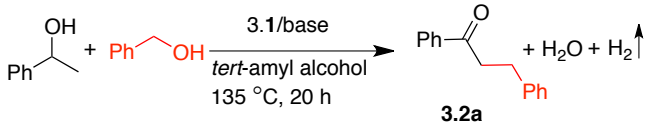
Figure 3.1 Monitoring the manganese-catalyzed *α*-alkylation using GC. Concentrations of acetophenone (black Line), product **3.2b** (blue line), intermediates *α,β*-unsaturated ketones (red line) and 4-methylbenzyl aldehyde (green line) in the catalytic *α*-alkylation of acetophenone.



In an attempt to further develop these benign catalytic alkylation reactions, cross-coupling of secondary alcohols with primary alcohols, which can result in selective *β*-alkylation of secondary alcohols leading to the exclusive formation of *a*-alkylated ketones was envisaged. Thus, using catalyst **3.1**, the cross-coupling reaction between 1-phenyl-1-ethanol and benzyl alcohol was subjected to optimization studies and the results are summarized in Table 3.5. Initial experiments with different load of catalyst **3.1** (3-1 mol %) and base (Cs_2CO_3, 10 mol %) provided moderate to complete conversions (entries 1-3). Spectral analyses of the isolated product clearly indicated the formation of *α*-alkylated ketone product, 1,3-diphenylpropan-1-one (**3.2a**). Upon performing the experiment using 2 mol % of catalyst **3.1** and 5 mol % of Cs_2CO_3, quantitative conversion of 1-phenyl-1-ethanol was observed and the alkylated product **3.2a** was isolated in 90% yield (entry 4). Further decrease of the catalyst and base loads turned out to be detrimental to the progress of the reaction as incomplete conversions were observed after 20 h (entries 5-6). Control experiments using only catalyst **3.1**, base (Cs_2CO_3) alone, and an experiment without catalyst and base (entries 7-9) proved that this alkylation requires a catalyst and a base. Further, under similar reaction conditions the effect of different bases was also explored. K_2CO_3 and KOH provided moderate yields of product (83% and 40%, respectively). However, use of bases such as NaH, NaOH, Na_2CO_3, and KO^{t}Bu resulted in poor conversion of secondary alcohols. Surprisingly, the in situ generation of ketones from the oxidation of secondary alcohols provided facile *a*-alkylation reactions by primary alcohols. Using only 5 mol % base the reaction was completed in 20 h compared to the requirement of higher load of base, higher temperature and longer reaction time required for the direct ketone alkylation by primary alcohols (Table 3.5). *tert*-Amyl alcohol is tertiary alcohol were oxidation of alcohol is not possible using manganese

pincer catalyst **3.1**, due to lack of α-hydrogen in the alcohol. Under the optimized reaction condition β-alkylated secondary alcohol has not formed. This is due to catalyst and carefully optimized reaction condition, which avoided reduction of β-alkylated ketones to corresponding β-alkylated secondary alcohols in presence of Cs_2CO_3. However, Kempe and co-worker have reported such reaction using stoichiometric amount strong base such as KO^{t}Bu with respective alcohols in the presences of same manganese catalyst.[12c]

Table 3.5 Optimization of the Reaction Conditions for the β-Alkylation of Secondary Alcohols[a]



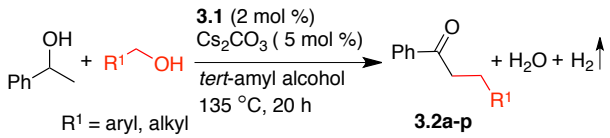
3.2a

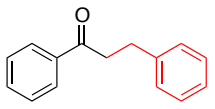
entry	**3.1** (mol %)	base (mol %)	conv. (%)[b]	yield. (%)[c]
1	3	Cs_2CO_3 (10)	>99	80
2	2	Cs_2CO_3 (10)	>99	88
3[d]	1	Cs_2CO_3 (10)	87	54
4	2	Cs_2CO_3 (5)	>99	90
5[d]	1	Cs_2CO_3 (5)	37	23
6[d]	2	Cs_2CO_3 (2.5)	51	42
7	2	-	5	0
8	-	Cs_2CO_3 (5)	15	0
9	-	-	0	0

[a]Reaction conditions: 1-phenyl-1-ethanol (0.5 mmol), benzyl alcohol (0.6 mmol), *tert*-amyl alcohol (2 mL), catalyst **3.1**, and base were heated at 135 °C with open condition under an argon flow. [b]Conversion of 1-phenyl-1-ethanol was determined by GC using toluene as an internal standard. [c]Isolated yields after column chromatography. [d]A minor amount of *E*-chalcone formation also observed.

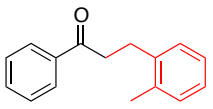
As shown in Table 3.6 a wide range of primary alcohols was subjected to manganese-catalyzed β-alkylation of 1-phenyl-1-ethanol, which provided α-alkylated ketones in moderate to excellent yields. Reaction of different benzyl alcohols with 2 mol % of catalyst **3.1** and 5 mol % of Cs_2CO_3, good conversion of 1-phenyl-1-ethanol was observed and the β -alkylated products (**3.2a-c, 3.2l, 3.2m,** and **3.2n**) were isolated in 73-90% yields. Further, a series of primary aliphatic alcohols (non benzylic) such as 4-phenyl-1-butanol, 3-(pyridin-2-yl)propan-1-ol, 1-hexanol, 1-octanol, 3,5,5-trimethylhexanol and 2-cyclohexylethanol were investigated as alkylating partners and in general excellent conversions as well as yields were obtained (**3.2o, 3.2p, 3.2g, 3.2i** and **3.2j**). Manganese catalyzed cross-coupling of 1-phenyl-1-ethanol with benzyl alcohols was reported using strong base KO^{t}Bu.[51b]

Table 3.6 Manganese-Catalyzed Cross-Coupling of 1-Phenyl-1-ethanol with Primary Alcohols[a]

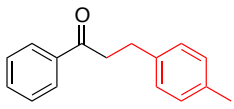




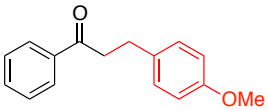
3.2a, 90% (>99%)



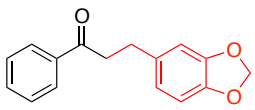
3.2l, 79% (>99%)



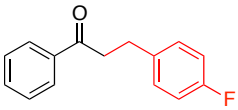
3.2b, 80% (97%)



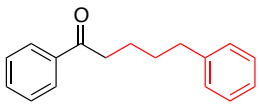
3.2m, 73% (91%)



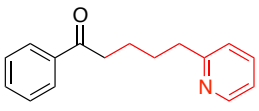
3.2n, 90% (99%)



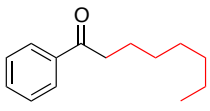
3.2c, 79% (97%)



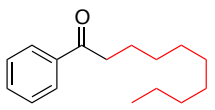
3.2o, 83% (99%)



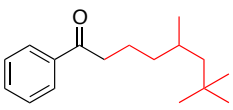
3.2p, 74% (99%)



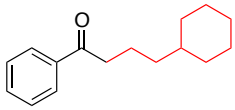
3.2k, 95% (99%)



3.2g, 90% (99%)



3.2i, 96% (99%)

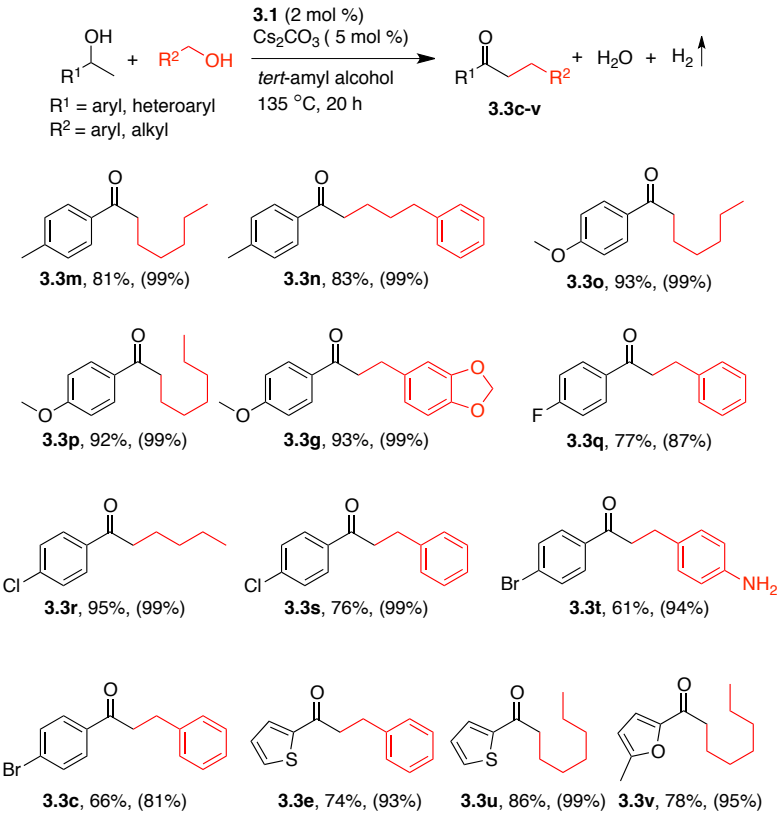


3.2j, 76% (92%)

[a]Reaction conditions: 1-phenyl-1-ethanol (0.5 mmol), primary alcohol (0.6 mmol), *tert*-amyl alcohol (2 mL), catalyst **3.1** (0.01 mmol), and Cs_2CO_3 (0.025 mmol) were heated at 135 °C in open condition under an argon flow. Yield of the products corresponds to isolated pure compounds after column chromatography. Conversion of 1-phenyl-1-ethanol was determined by GC using toluene as an internal standard and given within parentheses.

Next, substrate scope of structurally diverse secondary alcohols was investigated in the catalytic cross-coupling reactions with various primary alcohols. Initially, different secondary alcohol derivatives bearing electron donating and electron withdrawing substituents were subjected to coupling with benzylic and aliphatic alcohol (Table 3.7). In general, non-activated primary aliphatic alcohols provided the corresponding alkylated products **3.3m-3.3p** in higher yields than aryl alcohols. Notably, electron-withdrawing halogen containing secondary alcohols underwent facile *β*-alkylation reaction and provided the corresponding alkylated products **3.3q-3.3s,** and **3.3c** in 66-95% yields. Remarkably, as observed in ketone alkylation reactions, the amine functionality is tolerated in the catalytic alkylation reactions. When (4-bromophenyl)-1-ethanol was reacted with (4-aminophenyl)methanol the desired alkylated product **3.3t** was obtained in 61% yield. Notably, the N-alkylated product was not observed in this condition, which indicates the chemoselective C-alkylation over N-alkylation. Heteroaryl secondary alcohols were also successfully alkylated using this manganese catalysis and alkylated heteroaryl ketones **3.3u, 3.3v,** and **3.3e** were isolated in moderate to good yields (Table 3.7). Nickel catalyzed cross-coupling of secondary alcohols with primary alcohols is reported, which required the use of higher load of base (KOH, 50 mol %).[51c]

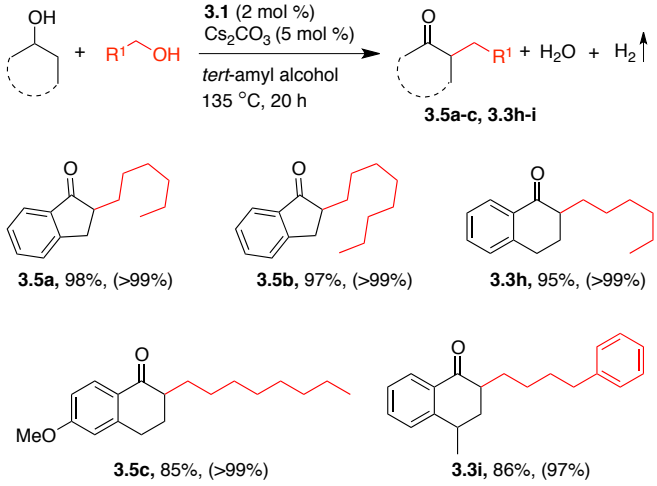
Table 3.7 Manganese-Catalyzed Dehydrogenative Cross-Coupling of Secondary Alcohols with Primary Alcohols[a]



[a]Reaction conditions: same as in footnote of Table 3.6, except that different secondary alcohols were used.

Further, the substrate scope was extended to cyclic secondary alcohols (Table 3.8). Thus, the reactions of 1-indanol with 1-hexanol and 1-octanol, the corresponding alkylated products **3.5a** and **3.5b** were obtained in 98% and 97% isolated yield, respectively. Gratifyingly, 1,2,3,4-tetrahydronaphthalen-1-ol and its derivatives efficiently reacted with 1-hexanol, and 4-phenyl-1-butanol and afforded the alkylated products **3.5c,** and **3.3h-i** in 85-95% isolated yields (Table 3.8).

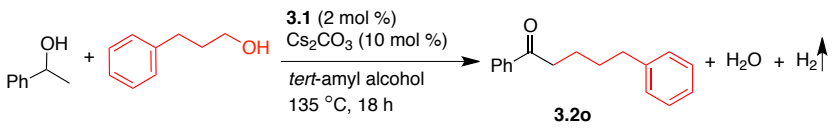
Table 3.8 Manganese-Catalyzed Cross-Coupling of Cyclic Secondary Alcohols with Primary Alcohols[a]

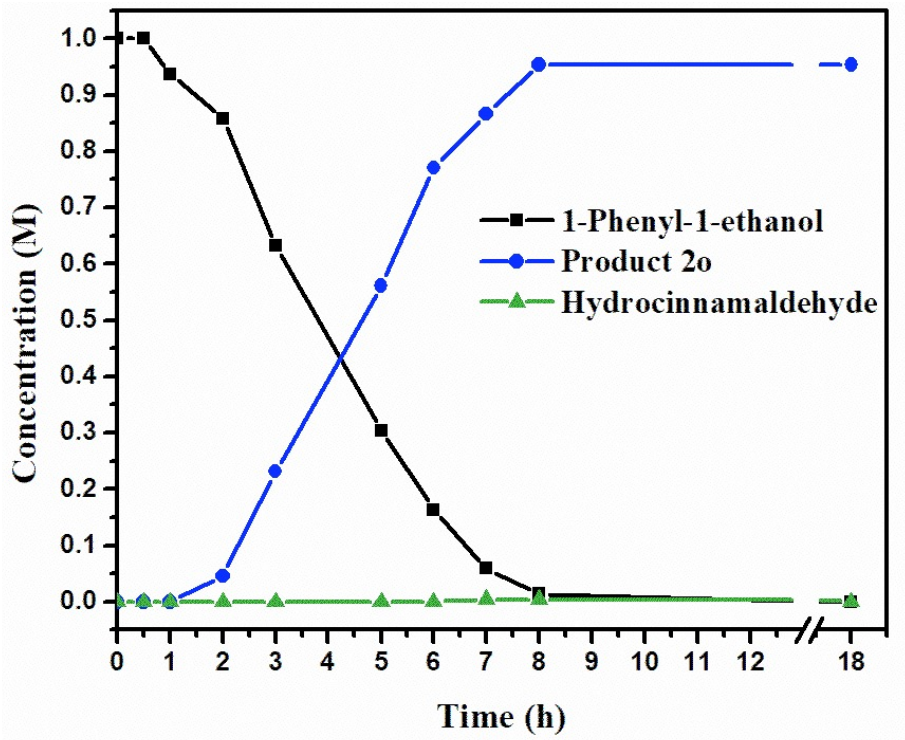


[a]Reaction conditions: same as in footnote of Table 3.6, except that different secondary alcohols were used.

The reaction progress on *β*-alkylation reaction of 1-phenyl-1-ethanol with 3-phenyl-1-propanol catalyzed by **3.1** was monitored using GC, which indicated zero order kinetics for the conversion of secondary alcohols as well for the formation of *β*-alkylated ketone product **3.2o** (Figure 3.2). Notably, upon oxidation of 3-phenyl-1-propanol, the in situ formed intermediate hydrocinnamaldehyde was observed in trace amount. Further, the rapid condensation of aldehyde with in situ generated acetophenone from 1-phenyl-1-ethanol provides *α,β*-unsaturated ketone intermediate. However, ketone and *α,β*-unsaturated ketone intermediates were not observed in the reaction; perhaps they undergo concomitant condensation and hydrogenation reactions, respectively.

Figure 3.2 Monitoring the manganese-catalyzed *β*-alkylation of secondary alcohols by a primary alcohols using GC. Concentrations of 1-phenyl-1-ethanol (black Line), product 3.2o (blue line) and hydrocinnamaldehyde (green line).



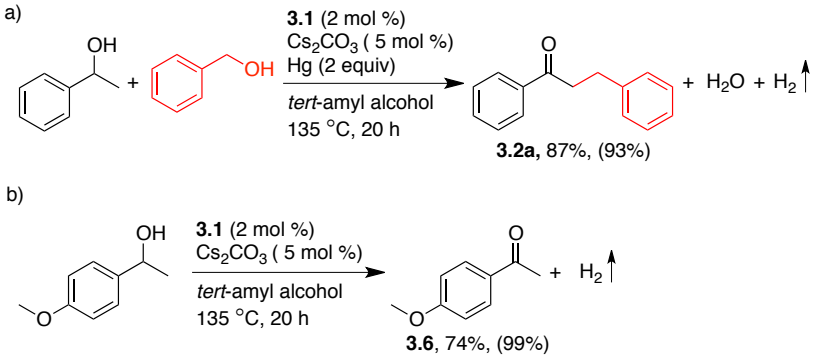


In a further attempt to identify the intermediates involved in this transformation, the catalytic reaction of 1-phenyl-1-ethanol with benzyl alcohol was intervened and the reaction mixture was subjected to ^{1}H NMR analysis, which resonated a characteristic singlet at δ 10.05 ppm and a distinct doublet at δ 7.85 ppm with a coupling constant J = 16 Hz that corresponds to aldehyde proton of benzaldehyde and olefin protons of E-chalcone, respectively.[64]

Moreover, a mercury-poisoning experiment was performed to examine the involvement of any metal nano-particles formed from complex **3.1**. When the dehydrogenative and dehydrative coupling of 1-phenyl-1-ethanol with benzylalcohol was carried out in the presence of mercury (2 equiv, relative to substrate), nearly 93% conversion of 1-phenyl-1-ethanol was observed and the alkylated ketone **3.2a** was obtained in 87% (see Scheme 3.3), indicating, the involvement of molecular intermediates. Further, when 1-(4-methoxyphenyl)ethanol independently reacted with catalyst **3.1** under optimized experimental conditions, exclusive formation of 1-(4-

methoxyphenyl)ethanone was observed in 74% yield, confirming the catalytic oxidation of secondary alcohols to ketones.

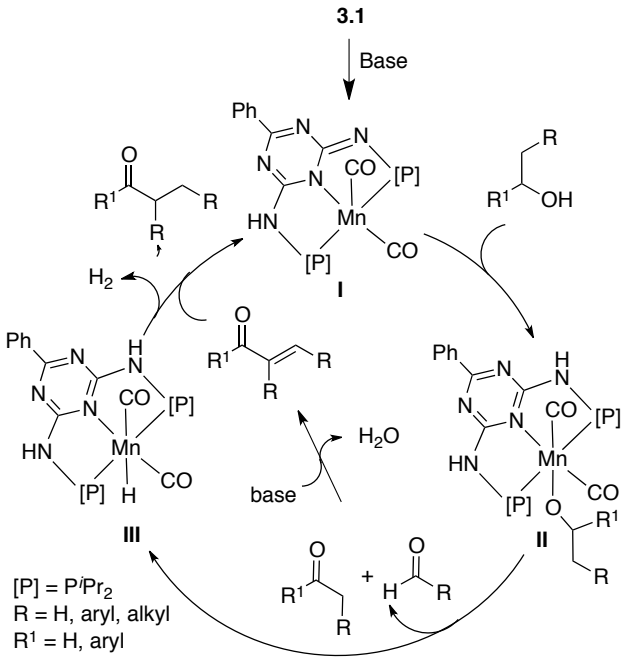
Scheme 3.3 Mercury Poisoning Test and Observation of Ketone Intermediate



On the basis of these observations and the experimental studies involving catalyst **3.1** in recent reports,[55b, 63d] the plausible catalytic cycle is proposed in Scheme 3.4. In the presence of catalytic amount of base, the dearomatized coordinatively unsaturated intermediate **I** is generated from catalyst **3.1** upon amine deprotonation and debromination from the metal center. O−H activation of the primary and secondary alcohol by intermediate **I** via proton transfer to the dearomatized imine nitrogen, results in the formation of alkoxo intermediate **II**, which undergoes *β*-hydride elimination to release the aldehyde, ketones and generates a saturated monohydrido manganese complex **III**. Notably, Liu[65a] and Milstein[65b] have previously reported in which stoichiometric reaction of similar metal pincer complexes and alcohols in the presence of base the resulted in manganese alkoxo monohydrido complexes. Deprotonation of the *α*-acidic protons of carbonyl compound by base possibly generates the carbon nucleophile. Nucleophilic attack by the deprotonated methyl or methylene group of the ketone on the in situ formed aldehyde intermediate leads to an aldol condensation, resulting in formation of *α,β*-unsaturated ketone intermediate (observed experimentally) and water. Interestingly, deprotonation of the methyl or

methylene groups requires only catalytic amount of a mild base. The manganese hydride complex **III** concomitantly hydrogenates *α,β*-unsaturated ketone intermediates to afford the redox neutral alkylated product along with the regeneration of catalytically active intermediate **I**. The dearomatization-aromatization metal-ligand cooperation operative in manganese intermediates maintain the same oxidation state (+1) at all intermediate complexes and plays important role in this selective catalytic coupling of ketones and secondary alcohols with primary alcohols. We didn't performed catalytic reaction using a ligand framework in which NH is replaced with NR.

Scheme 3.4 Proposed Reaction Mechanism for Cross-coupling of Secondary and Primary Alcohols



3.4. CONCLUSIONS

In summary, manganese pincer **3.1** catalyzed cross coupling of ketones and secondary alcohols with primary alcohols leading to the selective *α*-alkylation of ketones is demonstrated. Primary alcohols serve as alkylating reagents. Remarkably, using a

catalyst (2 mol %) and base (5 to 10 mol %), various ketones and secondary alcohols can be efficiently alkylated with an assortment of linear primary alcohols in excellent yields. Ethylation of ketones using ethanol is also demonstrated. Chemoselective *α*-alkylation of ketones is observed with primary alcohol in the presence of non-benzylic secondary alcohol. Moreover, chemoselective catalytic C-alkylations of ketone and secondary alcohols over N-alkylation of aryl amine are achieved. Mechanistic studies confirm the formation of aldehyde, ketone and *α,β*-unsaturated ketone intermediates. Accordingly, a catalytic cycle incorporating the formation of these intermediates eventually leading to the *α*-alkylated ketones is proposed. One equivalent of hydrogen liberated from oxidation of primary and secondary alcohols, is utilized by the catalyst for the hydrogenation of *α,β*-unsaturated ketones to deliver the *β*-alkylated ketones. Overall, the catalytic coupling of ketones with alcohol release one equivalent of water, while the cross-coupling of secondary and primary alcohols produce one equivalent of water and molecular hydrogen from the reactions as the only byproducts.

3.5. EXPERIMENTAL SECTION

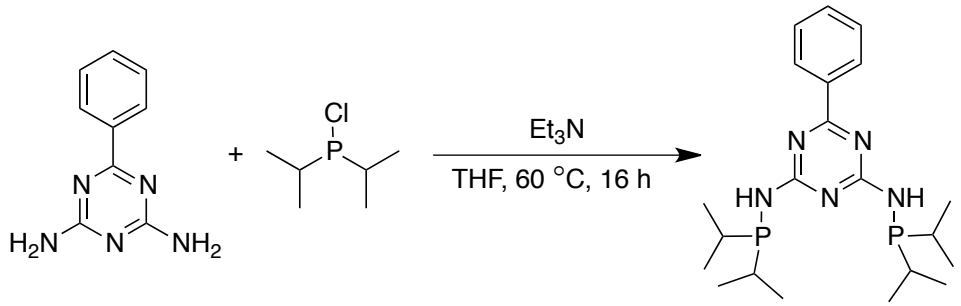
General Experimental: All stoichiometric reactions were performed in nitrogen atmosphere. All catalytic reactions were performed under nitrogen atmosphere using standard Schlenk techniques. Dry solvents were prepared according to standard procedures.[31b] ^{1}H, $^{13}C\{^{1}H\}$ NMR chemical shifts were reported in ppm downfield from tetramethyl silane. All NMR Spectra were recorded at 298K. Multiplicity is abbreviated as: s, singlet; d, doublet; dd, doublet of doublets; dt, doublet of triplets; t, triplet; q, quartet; dq, doublet of quartets; td, triplet of doublets; m, multiplet; br,

broad. IR spectra were recorded in an FT-IR spectrometer by using KBr pellets. Mass spectra were recorded on a micrOTOF-Q II Spectrometer.

Experimental Procedure:

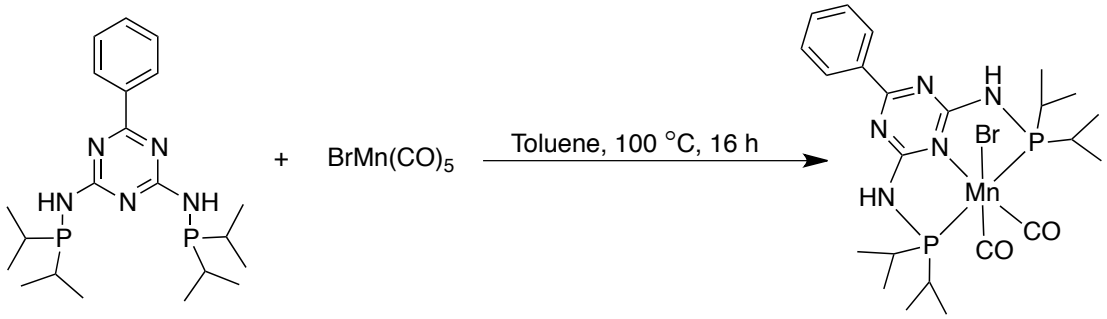
Scheme 3.5 Synthesis of Ligand (4-Ph)Tr(NHP(iPr)$_2$)$_2$ (L4):[55d]

Ligand and complexes were prepared by following reported literature procedure.[17d]



Inside glove box, a 15 mL sealed tube was charged with stir bar, 2,4-diamino-6-phenyl-1,3,5-triazine (2 mmol, 0.374 g), dry THF (8 mL) under nitrogen atmosphere. The solution was cooled to 0 °C and then chlorodiisopropylphosphine (4.2 mmol, 0.665 mL) was added drop wise into the reaction mixture. Triethylamine (8 mmol, 1.112 mL) was added to the reaction mixture. The reaction mixture was allowed to warm to room temperature and stirred vigorously for 16 h at 60 °C. The suspension was filtered over a glass filter frit with a pad of Celite (3 cm) and washed with 10 mL of THF. The combined organic phase was concentrated in *vacuo* yielding (4-Ph)Tr(NHP(*i*Pr)$_2$)$_2$ **(L4)** as a colorless solid (712 mg, 85 %). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.38 (m, 2H), 7.40-7.45 (m, 3H), 5.17 (s, 2H), 1.81-1.87 (m, 4H), 1.07-1.11 (m, 24H) ppm. $^{13}C\{^1H\}$ NMR (176 MHz, $CDCl_3$): δ 171.6, 169.8 (d, J = 9.0 Hz), 136.8, 131.5, 128.6, 128.3, 26.2 (d, J = 14.1 Hz), 18.8 (d, J = 19.4 Hz), 17.7 (br) ppm.

Scheme 3.6 Synthesis of [(4-Ph)Tr(NHP(*i*Pr)$_2$)$_2$Mn(CO)$_2$Br] (3.1):[55d]



To the orange -yellow suspension of [$MnBr(CO)_5$] (1 mmol, 275 mg) in toluene (15 mL), a solution of (4-Ph)Tr($NHP(iPr)_2)_2$ **(L4)** (1 mmol, 420 mg,) in toluene was added dropwise. The suspension turned into a clear yellow solution within 10 min. The reaction mixture was heated to 100 °C and further stirred for 16 h under nitrogen leading to formation of yellow precipitate. The reaction mixture was cooled to room temperature and the supernatant solution was filtered off and the precipitate was dried *in vacuo* at 100 °C to afford [(4-Ph)Tr($NHP(iPr_2))_2Mn(CO)_2Br$] (**3.1**) as a bright yellow powder (501 mg, 82%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.17-8.18 (m, 2H), 7.37-7.43 (m, 3H), 6.05 (s_br, 2H), 3.52 (s_br, 2H), 2.66 (s_br, 2H), 1.36 (s br, 24H) ppm. $^{31}P\{^1H\}$ NMR (162 MHz, $CDCl_3$): δ 135.5, 134.2. IR (KBr, pellet, cm^{-1}): 1937, 1867 ($\nu_{2CO\ symmetric} + \nu_{2CO\ antisymmetric}$).

General Procedure for α-Alkylation of Acetophenone Using Alcohols:

Inside a nitrogen atmosphere glove box, 25 mL Schlenk tube was charged with a stir bar, catalyst **3.1** (0.01 mmol), base (0.05 mmol), acetophenone (0.5 mmol), solvent (2 mL) and alcohol (0.6 mmol) in the same order. The reaction flask was taken out of the glove box, and then refluxed (oil bath temperature 140 °C) with stirring in an open system under argon flow for 24 h. The reaction mixture was then cooled down to room temperature. The solvent was evaporated under reduced pressure and 0.5 mmol of internal standard (toluene) was added into the reaction mixture and then diluted

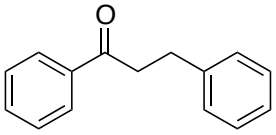
with 0.8 mL acetone. An aliquot of the solution was passed through a small Celite plug and analyzed by GC. The solvent was evaporated under reduced pressure and crude reaction mixture was purified by column chromatography over silica-gel (60-120 mesh) using ethyl acetate /pet ether mixture as an eluent. The conversion of acetophenone was calculated using GC analysis and yields of pure products were determined after column chromatography.

General Procedure for Dehydrogenative Cross-Coupling of Alcohols:

Inside a nitrogen atmosphere glove box, 25 mL Schlenk tube was charged with a stir bar, catalyst **3.1** (0.01 mmol), Cs_2CO_3 (0.025 mmol), secondary alcohol (0.5 mmol), *tert*-amyl alcohol (2 mL) and primary alcohol (0.6 mmol), in the same order. The reaction flask was taken out of the glove box, and then refluxed (oil bath temperature 135 °C) with stirring in an open system under argon flow for 24 h. The reaction mixture was then cooled down to room temperature. The solvent was evaporated under reduced pressure and 0.5 mmol of internal standard (toluene) was added into the reaction mixture and then diluted with 0.8 mL of acetone. An aliquot of the solution was passed through a small Celite plug and analyzed by GC. The solvent was evaporated under reduced pressure and crude reaction mixture was purified by column chromatography over silica-gel (60-120 mesh) using ethyl acetate /pet ether mixture as an eluent. The conversion of secondary alcohol was calculated using GC analysis and yields of pure products were determined after column chromatography.

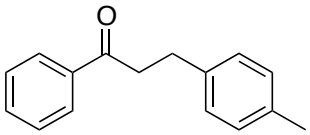
Spectral Data of *a*-Alkylated Ketone Products:

1,3-Diphenylpropan-1-one[49c] **(3.2a)**: White solid. Yield for Table 3.1 (90 mg, 86%), Yield for Table 3.6 (95 mg, 90%). IR (DCM): 3061, 3025, 2950, 2922, 2864, 1682, 1602, 1595, 1580, 1495, 1448, 1410, 1364, 1209, 1075, 744, 701, 689 cm^{-1}. ^1H NMR

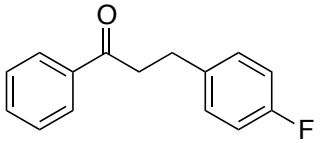


(400 MHz, $CDCl_3$): δ 7.88 (d, J = 7.2 Hz, 2H), 7.48 (t, J = 7.2 Hz, 1H), 7.38 (t, J = 7.6 Hz, 2H), 7.11-7.25 (m, 5H), 3.23 (t, J = 8.0 Hz, 2H), 3.00 (t, J = 7.6 Hz, 2H). $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$): δ 199.3, 141.4, 137.0, 133.2, 128.7, 128.6, 128.5, 128.1, 126.2, 40.5, 30.2.

1-Phenyl-3-(*p*-tolyl)propan-1-one[49c] **(3.2b)**: White solid. Yield for Table 3.2 (102 mg, 91%), Yield for Table 3.6 (90 mg, 80%). IR (DCM): 3053, 3022, 2921, 2861, 1686, 1597, 1580, 1514, 1203, 973, 811, 742 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.96 (d, J = 8.0 Hz, 2H), 7.56 (t, J = 7.6 Hz, 1H), 7.46 (t, J = 7.6 Hz, 2H), 7.11-7.17 (m, 4H), 3.29 (t, J = 7.6 Hz, 2H), 3.04 (t, J = 7.6 Hz, 2H), 2.33 (s, 3H). $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$): δ 199.5, 138.3, 137.0, 135.8, 133.2, 129.3, 128.7, 128.4, 128.2, 40.8, 29.9, 21.1.



3-(4-Fluorophenyl)-1-phenylpropan-1-one[66] **(3.2c)**: White solid. Yield for table 3.2 (95 mg, 83%), Yield for table 3.6 (91 mg, 79%). IR (DCM): 3062, 2930, 1685, 1598, 1509, 1448, 1221, 1206, 828, 743, 689 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.96 (d, J = 7.2 Hz, 2H), 7.56 (t, J = 7.6 Hz, 1H), 7.46 (t, J = 7.2 Hz, 2H), 7.19-7.23 (m, 2H), 6.98 (t, J = 8.4 Hz, 2H), 3.28 (t, J = 7.6 Hz, 2H), 3.05 (t, J = 7.2 Hz, 2H). $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$): δ 199.2, 161.5 (d, $^1J_{C\text{-}F}$ = 243.5 Hz), 137.0 (d, $^4J_{C\text{-}F}$ = 3.1 Hz), 136.9, 133.3, 130.0 (d, $^3J_{C\text{-}F}$ = 8.0 Hz), 128.8, 128.1, 115.4 (d, $^2J_{C\text{-}F}$ = 20.0 Hz), 40.5, 29.4.



1-Phenyl-3-(4-(trifluoromethyl)phenyl)propan-1-one[51a] **(3.2d):** White solid. Yield (77 mg, 56%). IR (DCM): 3061, 2930, 1686, 1618, 1597, 1449, 1325, 1163, 1121, 1067, 1018, 828, 743 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.96 (d, J = 7.2 Hz, 2H), 7.54-7.59 (m, 3H), 7.37 (d, J = 8.0 Hz, 2H), 3.33 (t, J = 7.6 Hz, 2H), 3.14 (t, J = 7.2 Hz, 2H). $^{13}C\{^{1}H\}$ NMR (100.6 MHz, $CDCl_3$): δ 198.7, 145.6, 136.8, 133.4, 128.9, 128.8, 128.1, 124.21 (q, $^{1}J_{C\text{-}F}$ = 271.0 Hz), 40.0, 29.9. ^{19}F (376 MHz, $CDCl_3$): δ -62.33.

3-(Furan-2-yl)-1-phenylpropan-1-one[49c] **(3.2e):** Brown solid. Yield (84 mg, 84%). IR (DCM): 3060, 2920, 2359, 2341, 1716, 1683, 1597, 1448, 1211, 1018, 1001, 745 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.9 (d, J = 7.2 Hz, 2H), 7.49 (tt, ^{1}J = 7.6 Hz, ^{2}J = 1.2 Hz, 1H), 7.38 (t, J = 7.2 Hz, 2H), 7.23 (d, J = 1.2 Hz, 1H), 6.20-6.21 (m, 1H), 5.97-5.98 (m, 1H), 3.26 (t, J = 7.6 Hz, 2H), 3.01 (t, J = 7.6 Hz, 2H). $^{13}C\{^{1}H\}$ NMR (100.6 MHz, $CDCl_3$): δ 198.8, 154.9, 141.2, 136.8, 133.3, 128.7, 128.1, 110.4, 105.4, 37.0, 22.6.

1-Phenylhexan-1-one[51a] **(3.2f):** Colorless oil. Yield (85 mg, 97%). IR (DCM): 3057, 2929, 2861, 1681, 1597, 1465, 1448, 1405, 1370, 745, 725 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.95-7.97 (m, 2H), 7.55 (t, J = 7.2 Hz, 1H), 7.46 (t, J = 7.2 Hz, 2H), 2.96 (t, J = 7.6 Hz, 2H), 1.73 (q, J = 4 Hz, 2H), 1.34-1.39 (m, 4H), 0.89-0.93 (m, 3H). $^{13}C\{^{1}H\}$ NMR (100.6 MHz, $CDCl_3$): δ 200.8, 137.2, 133.0, 128.7, 128.2, 38.7, 31.7, 24.2, 22.7, 14.1.

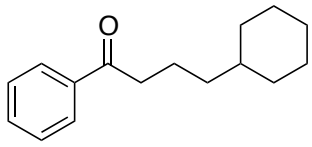
1-Phenyldecan-1-one[49c] **(3.2g):** Colorless oil. Yield for Table 3.2 (108 mg, 93%), Yield for Table 3.6 (104 mg, 90%). IR (DCM): 3084, 3056, 3026, 2948, 2916, 2849, 1686, 1474, 1462, 1447, 1406, 1376, 1072, 750, 734 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.87-7.89 (m, 2H), 7.47 (t, J = 7.6 Hz, 1H), 7.38 (t, J = 9.2 Hz, 2H), 2.88 (t, J = 7.6 Hz, 2H), 1.66 (pentet, J = 7.6 Hz, 2H), 1.19-1.28 (m, 12H), 0.80 (t, J = 7.2 Hz, 3H). $^{13}C\{^{1}H\}$ NMR (100.6 MHz, $CDCl_3$): δ 200.7, 137.2, 133.0, 128.7, 128.2, 38.8, 32.0, 29.6, 29.5, 29.4, 24.5, 22.8, 14.2.

4-Ethyl-1-phenylhexan-1-one (3.2h): Colorless oil. Yield (74 mg, 75%). IR (DCM): 2961, 2930, 2873, 1686, 1620, 1597, 1459, 1448, 1379, 1205, 735 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.95-7.97 (m, 2H), 7.53-7.58 (m, 1H), 7.46 (t, J = 7.6 Hz, 2H), 2.94 (t, J = 7.6 Hz, 2H), 1.67-1.72 (m, 2H), 1.25-1.38 (m, 5H) 0.87 (t, J = 7.6 Hz, 6H). $^{13}C\{^{1}H\}$ NMR (100.6 MHz, $CDCl_3$): δ 201.1, 137.2, 133.0, 128.7, 128.2, 40.3, 36.2, 27.3, 25.4, 11.0. HRMS (ESI) m/z calcd for $C_{14}H_{21}O$ $(M+H)^{+}$: 205.1587, found: 205.1567.

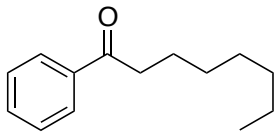
5,7,7-Trimethyl-1-phenyloctan-1-one (3.2i): Pale-yellow oil. Yield for Table 3.2 (112 mg, 91%), Yield for Table 3.6 (119 mg, 96%). IR (DCM): 2953, 2902, 2866, 1688, 1597, 1580, 1448, 1363, 1232, 1206, 1001, 752, 730 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.88 (d, J = 7.2 Hz, 2H), 7.48 (t, J = 7.6 Hz, 1H), 7.38 (t, J = 7.2 Hz, 2H), 2.87 (t, J = 7.2 Hz, 2H), 1.61-1.71 (m, 2H), 1.40-1.45 (m, 1H), 1.23-1.32 (m, 1H), 1.14-1.19 (m, 2H), 0.97 (dd, ^{1}J = 14.0 Hz, ^{2}J = 6.4 Hz, 1H), 0.86 (d, J = 6.4 Hz, 3H), 0.81 (s, 9H). $^{13}C\{^{1}H\}$ NMR (100.6 MHz, $CDCl_3$): δ 200.7, 137.3, 133.0, 128.7,

128.2, 51.3, 39.3, 39.0, 31.2, 30.2, 29.4, 22.7, 22.2. HRMS (ESI) m/z calcd for $C_{17}H_{27}O$ $(M+H)^+$: 247.2056, found: 247.2051.

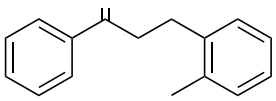
4-Cyclohexyl-1-phenylbutan-1-one[67] **(3.2j)**: Colorless liquid. Yield for Table 3.2 (112 mg, 97%), Yield for Table 3.6 (87 mg, 76%). IR (DCM): 2953, 2902, 2866, 1687, 1597, 1465, 1448, 1363, 1232, 1206, 731 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.95 (d, J = 7.3 Hz, 2H), 7.52-7.56 (m, 1H), 7.45 (t, J = 7.2 Hz, 2H), 2.93 (t, J = 7.2 Hz, 2H), 1.65-1.74 (m, 7H), 1.15-1.27 (m, 6H), 0.87-0.92 (m, 2H). $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$): δ 200.8, 137.3, 133.0, 128.7, 128.2, 39.1, 37.7, 37.3, 33.4, 26.8, 26.5, 21.9.



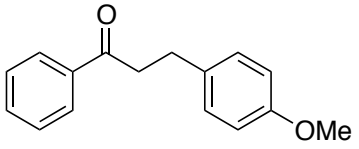
1-Phenyloctan-1-one[69] **(3.2k):** Colorless oil. Yield (97 mg, 95%). IR (DCM): 2954, 2927, 2855, 1687, 1597, 1448, 1220, 750, 690 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.96 (d, J = 7.2 Hz, 2H), 7.53-7.59 (m, 1H), 7.44-7.47 (m, 2H), 2.96 (t, J = 7.2 Hz, 2H), 1.73 (quintet, J = 7.2 Hz, 2H), 1.29-1.35 (m, 12H, 6XCH_2), 0.88 (t, J = 7.2 Hz, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 200.8, 137.3, 133.0, 128.7, 128.2, 38.8, 31.9, 29.5, 29.3, 24.5, 22.8, 14.2.



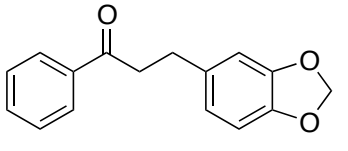
1-Phenyl-3-(o-tolyl)propan-1-one[49a] **(3.2l):** White solid. Yield (87 mg, 79%). IR (DCM): 3061, 3023, 2927, 1686, 1597, 1580, 1492, 1448, 1315, 1203, 1026, 974, 746, 690 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.97-7.99 (m, 2H), 7.55-7.59 (m, 1H), 7.45-7.49 (m, 2H), 7.14-7.19 (m, 4H), 3.26 (t, J = 7.0 Hz, 2H), 3.07 (t, J = 8.0 Hz, 2H), 2.36 (s, 3H). $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$): δ 199.5, 139.5, 137.0, 136.1, 133.2, 130.5, 128.9, 128.8, 128.2, 126.5, 126.3, 39.2, 27.6, 19.5.



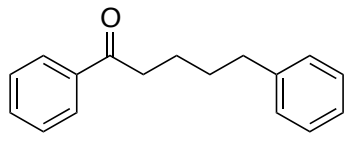
3-(4-Methoxyphenyl)-1-phenylpropan-1-one[51a] **(3.2m)**: White solid. Yield (88 mg, 73%). IR (DCM): 2957, 2933, 2835, 1681, 1609, 1512, 1205, 1033, 825, 743, 689 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.96 (d, J = 7.6 Hz, 2H), 7.56 (t, J = 7.6 Hz, 1H), 7.46 (t, J = 7.6 Hz, 2H), 7.18 (d, J = 8.0 Hz, 2H), 6.85 (d, J = 8.0 Hz, 2H), 3.79 (s, 3H), 3.28 (t, J = 7.2 Hz, 2H), 3.02 (t, J = 8.0 Hz, 2H). $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$): δ 199.5, 158.1, 137.0, 133.4, 133.1, 129.5, 128.7, 128.1, 114.0, 55.4, 40.8, 29.4.



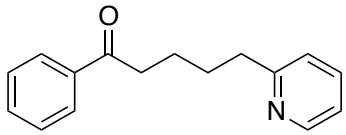
3-(Benzo[d][1,3]dioxol-5-yl)-1-phenylpropan-1-one[52b] **(3.2n)**: White solid. Yield (114 mg, 90%). IR (DCM): 2894, 1681, 1502, 1444, 1244, 1203, 1037, 927, 742 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.96 (d, J = 7.2 Hz, 2H), 7.56 (t, J = 7.6 Hz, 1H), 7.46 (t, J = 7.6 Hz, 2H), 6.69-6.75 (m, 3H), 5.91 (s, 2H), 3.26 (t, J = 7.6 Hz, 2H), 2.99 (t, J = 7.6 Hz, 2H). $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$): δ 199.3, 147.7, 145.9, 136.9, 135.2, 133.2, 128.7, 128.1, 121.3, 109.0, 108.4, 100.9, 40.8, 29.9.



1,5-Diphenylpentan-1-one[68] **(3.2o)**: Colorless liquid. Yield (99 mg, 83%). IR (DCM): 3060, 3025, 2933, 1685, 1597, 1448, 1220, 749, 698 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.91 (d, J = 7.2 Hz, 2H), 7.51 (t, J = 7.2 Hz, 1H), 7.42 (t, J = 7.6 Hz, 2H), 7.22-7.24 (m, 2H), 7.14-7.16 (m, 3H), 2.95 (t, J = 7.2 Hz, 2H), 2.64 (t, J = 7.6 Hz, 2H), 1.65-1.79 (m, 4H). $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$): δ 200.4, 142.4, 137.2, 133.0, 128.7, 128.5, 128.4, 125.9, 38.5, 35.9, 31.2, 24.1.

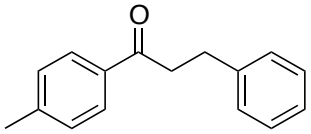


1-Phenyl-5-(pyridin-2-yl)pentan-1-one (3.2p): Colorless oil. Yield (88 mg, 74%).



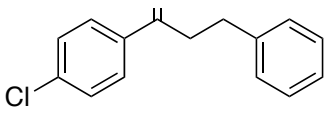
IR (DCM): 3061, 2935, 2860, 1684, 1595, 1474, 1448, 1434, 1219, 751, 691 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.50 (d, J = 4.8 Hz, 1H), 7.92-7.94 (m, 2H), 7.51-7.59 (m, 2H), 7.43 (t, J = 8.0 Hz, 2H), 7.15 (d, J = 8.0 Hz, 1H), 7.07-7.10 (m, 1H), 3.00 (t, J = 7.2 Hz, 2H), 2.84 (t, J = 7.2 Hz, 2H), 1.80-1.83 (m, 4H). $^{13}C\{^{1}H\}$ NMR (100.6 MHz, $CDCl_3$): δ 200.3, 161.9, 149.3, 137.1, 136.5, 133.0, 128.7, 128.1, 122.9, 121.1, 38.5, 38.2, 29.5, 24.0. HRMS (ESI) m/z calcd for $C_{16}H_{19}NO$ $(M+2H)^{+}$: 241.1461, found: 241.1468.

3-Phenyl-1-(p-tolyl)propan-1-one[49c] **(3.3a):** White solid. Yield (105 mg, 94%). IR

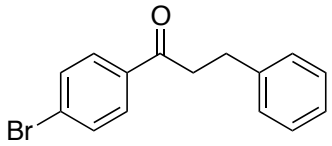


(DCM): 3061, 3026, 2920, 1679, 1606, 1494, 1451, 1408, 1179, 825, 774, 743, 699 cm^{-1}. ^{1}H NMR (700 MHz, $CDCl_3$): δ 7.78 (d, J = 7.7 Hz, 2H), 7.21-7.23 (m, 2H), 7.16-7.18 (m, 4H), 7.11-7.13 (m, 1H), 3.19 (t, J = 7.7 Hz, 2H), 2.98 (t, J = 7.7 Hz, 2H), 2.32 (s, 3H). $^{13}C\{^{1}H\}$ NMR (176 MHz, $CDCl_3$): δ 199.0, 144.0, 141.5, 134.5, 129.4, 128.64, 128.55, 128.4, 126.2, 40.5, 30.3, 21.8.

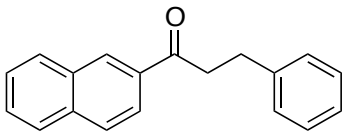
1-(4-Chlorophenyl)-3-phenylpropan-1-one[50a] **(3.3b):** White solid. Yield (107 mg, 88%). IR (DCM): 3085, 3059, 3026, 2950, 2925, 2861, 1681, 1587, 1491, 1405, 1281, 1095, 1075, 850, 832, 779, 745 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.79 (d, J = 8.4 Hz, 2H), 7.31 (d, J = 8.4 Hz, 2H), 7.19-7.23 (m, 2H), 7.10-7.16 (m, 3H), 3.17 (t, J = 8.0 Hz, 2H), 2.96 (t, J = 8.0 Hz, 2H). $^{13}C\{^{1}H\}$ NMR (100.6 MHz, $CDCl_3$): δ 198.0, 141.1, 139.6, 135.2, 129.5, 129.0, 128.7, 128.5, 126.3, 40.5, 30.1.



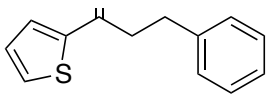
1-(4-Bromophenyl)-3-phenylpropan-1-one[50a] **(3.3c):** White solid. Yield for Table 3.3 (120 mg, 84%), Yield for Table 3.7 (95 mg, 66%). IR (DCM): 3083, 3057, 3024, 2929, 1682, 1583, 1493, 1451, 843, 829, 778 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.84 (d, J = 8.8 Hz, 2H), 7.62 (d, J = 8.8 Hz, 2H), 7.31-7.35 (m, 2H), 7.22-7.26 (m, 3H), 3.29 (t, J = 7.2 Hz, 2H), 3.06 (t, J = 7.2 Hz, 2H). $^{13}C\{^{1}H\}$ NMR (100.6 MHz, $CDCl_3$): δ 198.3, 141.1, 135.6, 132.0, 129.7, 128.7, 128.5, 128.36, 126.35, 40.5, 30.1.



1-(Naphthalen-2-yl)-3-phenylpropan-1-one[50a] **(3.3d):** White solid. Yield (97 mg, 75%). IR (DCM): 3059, 3025, 2948, 2928, 1681, 1494, 1365, 1289, 1173 1123, 865, 819, 749 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.37 (s, 1H), 7.95 (dd, J_1 = 8.8 Hz, J_2 = 1.6 Hz, 1H), 7.77-7.85 (m, 3H), 7.43-7.53 (m, 2H), 7.20-7.26 (m, 4H), 7.14-7.16 (m, 1H), 3.35 (t, J = 7.6 Hz, 2H), 3.04 (t, J = 7.2 Hz, 2H). $^{13}C\{^{1}H\}$ NMR (100.6 MHz, $CDCl_3$): δ 199.3, 141.5, 135.7, 134.2, 132.6, 129.8, 129.7, 128.7, 128.59, 128.58, 128.57, 127.9, 126.9, 126.3, 123.9, 40.7, 30.4.

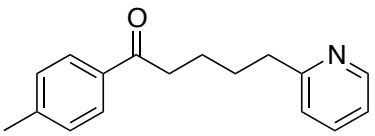


3-Phenyl-1-(thiophen-2-yl)propan-1-one[50a] **(3.3e):** Pale-yellow oil. Yield (70 mg, 65%). IR (DCM): 3085, 3061, 3026, 2925, 1660, 1517, 1495, 1415, 1238, 1209, 1079, 1062, 852, 723, 699 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.60 (dd, J_1 = 4.0 Hz, J_2 = 1.2 Hz, 1H), 7.52 (dd, J_1 = 4.8 Hz, J_2 = 1.2 Hz, 1H), 7.20-7.23 (m, 2H), 7.10-7.17 (m, 3H), 7.02 (dd, J_1 = 5.2 Hz, J_2 = 4.0 Hz, 1H), 3.15 (t, J = 7.6 Hz, 2H), 2.98 (t,



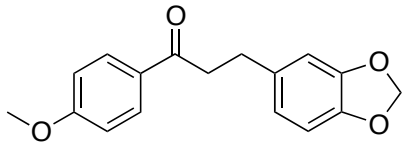
J = 7.6 Hz, 2H). $^{13}C\{^{1}H\}$ NMR (100.6 MHz, $CDCl_3$): δ 192.3, 144.2, 141.1, 133.7, 131.9, 128.6, 128.5, 128.2, 126.3, 41.2, 30.4.

5-(Pyridin-2-yl)-1-(*p*-tolyl)pentan-1-one (3.3f): Yellow oil. Yield (57 mg, 45%). IR



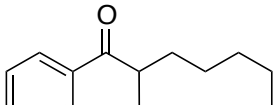
(DCM): 2927, 2860, 1680, 1606, 1569, 1474, 1434, 1180, 819, 767 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.50 (d, J = 4.4 Hz, 1H), 7.83 (d, J = 8.0 Hz, 2H), 7.57 (td, J_1 = 7.6 Hz, J_2 = 1.2 Hz, 1H), 7.23 (d, J = 8.0 Hz, 2H), 7.14 (d, J = 7.6 Hz, 1H), 7.08 (m, 1H), 2.97 (t, J = 7.2 Hz, 2H), 2.83 (t, J = 7.2 Hz, 2H), 2.38 (s, 3H), 1.81-1.83(m, 4H). $^{13}C\{^{1}H\}$ NMR (100.6 MHz, $CDCl_3$): δ 200.0, 162.0, 149.3, 143.7, 136.4, 134.6, 129.3, 128.3, 122.9, 121.1, 38.4, 38.2, 29.5, 24.2, 21.7. HRMS (ESI) m/z calcd for $C_{17}H_{20}NO$ $(M+H)^{+}$: 254.1545, found: 254.1572.

3-(Benzo[d][1,3]dioxol-5-yl)-1-(4-methoxyphenyl)propan-1-one[70] (3.3g): Colorless oil. Yield for Table 3.3 (88 mg, 62%), Yield for Table 3.7 (132 mg, 93%). IR (DCM):



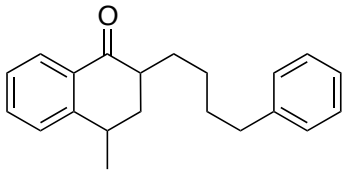
2925, 2840, 1474, 1600, 1575, 1503, 1488, 1443, 1245, 1209, 1170, 1037, 979, 837, 809 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.93 (d, J = 8.8 Hz, 2H), 6.91 (d, J = 8.8 Hz, 2H), 6.68-6.74 (m, 3H), 5.91 (s, 2H), 3.86 (s, 3H), 3.19 (t, J = 7.6 Hz, 2H), 2.97 (d, J = 7.6 Hz, 2H). $^{13}C\{^{1}H\}$ NMR (100.6 MHz, $CDCl_3$): δ 197.9, 163.6, 147.7, 145.9, 135.3, 130.4, 130.1, 121.2, 113.8, 109.0, 108.3, 100.9, 55.5, 40.4, 30.2.

2-Hexyl-3,4-dihydronaphthalen-1(2*H*)-one (3.3h): Yellow oil. Yield for Table 3.3

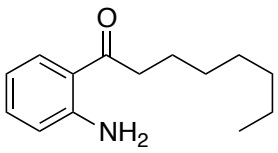


(90 mg, 78%), Yield for Table 3.8 (109 mg, 95%). IR (DCM): 2925, 2856, 1683, 1601, 1445, 1289, 1223, 915, 774, 741 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.95 (d, J = 7.6 Hz, 1H), 7.37 (t, J = 7.2 Hz, 1H), 7.21 (t, J = 7.6 Hz, 1H), 7.15 (d, J = 7.6 Hz, 1H), 2.88-2.93 (m, 2H), 2.35-2.42 (m, 1H), 2.12-2.18 (dq, J_1 = 13.2 Hz, J_2 = 4.8 Hz, 1H), 1.81-1.87 (m, 2H), 1.22-1.43 (m, 9H), 0.81 (t, J = 6.8 Hz, 3H). $^{13}C\{^{1}H\}$ NMR (100.6 MHz, $CDCl_3$): δ 200.6, 144.1, 133.2, 132.7, 128.6, 127.6, 126.6, 47.6, 31.9, 29.6, 29.5, 28.4, 28.3, 27.1, 22.8, 14.2. HRMS (ESI) m/z calcd for $C_{16}H_{23}NO$ $(M+H)^+$: 231.1743, found: 231.1753.

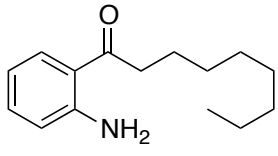
4-Methyl-2-(4-phenylbutyl)-3,4-dihydronaphthalen-1(2H)-one (3.3i): Mixture of two diastereoisomers, ca. 1:1. Colorless oil. Yield (129 mg, 88%). IR (DCM): 3061, 3025, 2929, 2856, 1682, 1600, 1495, 1479, 1454, 1228, 752, 772, 699 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.92-7.97 (m, 2H), 7.38-7.45 (m, 2H), 7.30-7.32 (m, 1H), 7.16-7.24 (m, 7H), 7.07-7.12 (m, 6H), 3.06-3.10 (m, 1H), 2.54-2.62 (m, 5H), 2.37-2.42 (m, 1H), 1.95-2.09 (m, 5H), 1.55-1.63 (m, 5H), 1.38-1.46 (m, 6H), 1.33 (d, 3H). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.92-7.97 (m, 2H), 7.38-7.45 (m, 2H), 7.30-7.32 (m, 1H), 7.16-7.24 (m, 7H), 7.07-7.12 (m, 6H), 3.06-3.10 (m, 1H), 2.54-2.62 (m, 5H), 2.37-2.42 (m, 1H), 1.95-2.09 (m, 5H), 1.55-1.63 (m, 5H), 1.38-1.46 (m, 6H), 1.30 (d, 3H). $^{13}C\{^{1}H\}$ NMR (100.6 MHz, $CDCl_3$): δ 200.6, 200.5, 148.7, 148.1, 142.8, 142.82, 142.75, 133.5, 133.4, 132.7, 131.7, 128.53, 128.52, 128.4, 128.1, 127.6, 127.5, 126.6, 126.5, 126.4, 125.7, 48.0, 43.0, 38.1, 36.0, 35.9, 35.2, 33.2, 31.8, 31.6, 31.2, 29.7, 29.5, 26.8, 26.7, 21.6, 20.4. HRMS (ESI) m/z calcd for $C_{21}H_{25}O$ $(M+H)^+$: 293.1905, found: 293.1933.



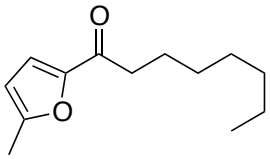
1-(2-Aminophenyl)octan-1-one (3.3j): Yellow oil. Yield (58 mg, 53%). IR (DCM): 3465, 3342, 2920, 2926, 2854, 1646, 1614, 1581, 1549, 1451, 1218, 1160, 747, 668 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.76 (d, J = 7.7 Hz, 1H), 7.27 (m, 1H), 6.66 (d, J = 7.0 Hz, 2H), 6.29 (s, 2H), 2.95 (t, J = 7.7 Hz, 2H), 1.74 (quintate, J = 7.7 Hz, 2H), 1.30-1.40 (m, 8H), 0.91 (t, J = 7.7 Hz, 3H). $^{13}C\{^{1}H\}$ NMR (176.0 MHz, $CDCl_3$): δ 203.4, 150.5, 134.2, 131.4, 118.2, 117.5, 115.9, 39.5, 31.9, 29.6, 29.6, 29.3, 25.1, 22.8, 14.2. HRMS (ESI) m/z calcd for $C_{14}H_{22}NO$ $(M+H)^+$: 220.1696, found: 220.1689.



1-(2-Aminophenyl)nonan-1-one (3.3k): Yellow oil. Yield (53 mg, 46%). IR (DCM): 3467, 3343, 2925, 2854, 1650, 1614, 1581, 1484, 1451, 1214, 1160, 747 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.67 (d, J = 8.4 Hz, 1H), 7.16-7.19 (m, 1H), 6.55-6.58 (m, 2H), 6.19 (s, 2H), 2.85 (t, J = 8.4 Hz, 2H), 1.64 (quintet, J = 7.6 Hz, 2H), 1.20-1.27 (m, 10H), 0.81 (t, J = 6.8 Hz, 3H). $^{13}C\{^{1}H\}$ NMR (100.6 MHz, $CDCl_3$): δ 203.4, 150.5, 134.2, 134.4, 118.2, 117.5, 115.8, 39.5, 32.0, 29.6, 29.3, 25.1, 22.8, 14.2. HRMS (ESI) m/z calcd for $C_{15}H_{24}NO$ $(M+H)^+$: 234.1852, found: 234.1834.

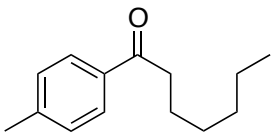


1-(5-Methylfuran-2-yl)octan-1-one (3.3l): Brown oil. Yield for Table 3.3 (88 mg, 85%), Yield for Table 3.7 (90 mg, 86%). IR (DCM): 2927, 2856, 1714, 1515, 1466, 1209, 1168, 930 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.06 (d, J = 3.2 Hz, 1H), 6.12 (d, J = 2.4 Hz, 1H), 2.73 (t, J = 7.6 Hz, 2H), 2.37 (s, 3H), 1.66-1.73 (m, 2H), 1.27-1.32 (m, 8H), 0.87 (t, J = 4.8 Hz, 3H). $^{13}C\{^{1}H\}$ NMR (100.6 MHz, $CDCl_3$): δ 189.3, 157.7, 151.7,



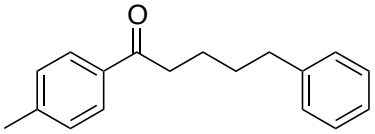
119.0, 108.9, 38.3, 31.6, 29.4, 29.2, 24.9, 22.7, 14.2, 14.1. HRMS (ESI) m/z calcd for $C_{13}H_{21}O_2$ $(M+H)^+$: 209.1542, found: 209.1555.

1-(*p*-Tolyl)heptan-1-one[71] **(3.3m)**: White solid. Yield (82 mg, 81%). IR (DCM):

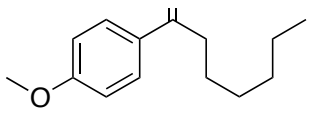


2924, 2857, 1677, 1607, 1466, 1406, 1181, 827, 791, 728 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.78 (d, J = 8.0 Hz, 2H), 7.17 (d, J = 8.0 Hz, 2H), 2.85 (t, J = 7.6 Hz, 2H), 2.32 (s, 3H), 1.60-1.68 (m, 2H), 1.21-1.29 (m, 6H), 0.81 (t, J = 7.2 Hz, 3H). $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$): δ 200.4, 143.7, 134.7, 129.3, 128.3, 38.6, 31.8, 29.2, 24.6, 22.7, 21.7, 14.2.

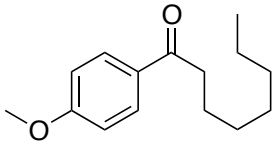
5-Phenyl-1-(p-tolyl)pentan-1-one[68] **(3.3n)**: Colorless oil. Yield (105 mg, 83%). IR (DCM): 3023, 2931, 2858, 1681, 1460, 1450, 1407, 827, 781, 741, 700 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.76 (d, J = 8.4 Hz, 2H), 7.15-7.21 (m, 4H), 7.07-7.11 (m, 3H), 2.87 (t, J = 7.2 Hz, 2H), 2.58 (t, J = 7.6 Hz, 2H), 2.32 (s, 3H), 1.61-1.73 (m, 4H). $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$): δ 200.1, 143.8, 142.4, 134.7, 129.4, 128.5, 128.4, 128.3, 125.8, 38.4, 35.9, 31.3, 24.2, 21.7.



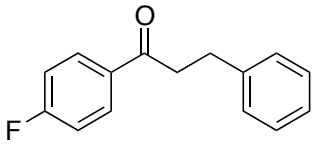
1-(4-Methoxyphenyl)heptan-1-one[72] **(3.3o):** White solid. Yield (102 mg, 93%). IR (DCM): 2931, 2858, 1672, 1603, 1509, 1468, 1449, 1258, 1176, 1034, 837, 821, 798, 731 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.93 (d, J = 8.8 Hz, 2H), 6.92 (d, J = 8.8 Hz, 2H), 3.85 (s, 3H), 2.89 (t, J = 7.6 Hz, 2H), 1.71 (quintate, J = 7.2 Hz, 2H), 1.30-1.35 (m, 6H), 0.88 (t, J = 6.8 Hz, 3H). $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$): δ 199.3, 163.4, 130.4, 130.3, 113.8, 55.5, 38.4, 31.8, 29.2, 24.7, 22.7, 14.2.



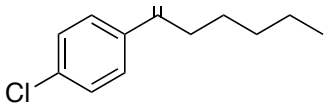
1-(4-Methoxyphenyl)octan-1-one[73] **(3.3p):** White solid. Yield (107 mg, 92%). IR (DCM): 2953, 2932, 2852, 1670, 1603, 1509, 1468, 1255, 1199, 1177, 1034, 847, 828, 738 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.93 (d, J = 8.8 Hz, 2H), 6.92 (d, J = 8.8 Hz, 2H), 3.85 (s, 3H), 2.89 (t, J = 7.6 Hz, 2H), 1.71 (quintate, J = 7.6 Hz, 2H), 1.28-1.34 (m, 8H), 0.87 (t, J = 7.2 Hz, 3H). $^{13}C\{^{1}H\}$ NMR (100.6 MHz, $CDCl_3$): δ 199.4, 163.4, 130.4, 130.3, 113.8, 55.5, 38.4, 31.8, 29.5, 29.3, 24.8, 22.7, 14.2.



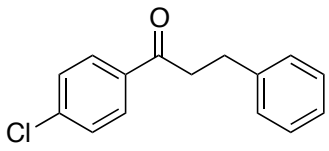
1-(4-Fluorophenyl)-3-phenylpropan-1-one[49c] **(3.3q)**: colorless oil. Yield (88 mg, 77%). IR (DCM): 3062, 3027, 2927, 1635, 1598, 1505, 1452, 1408, 1231, 1270, 1156, 1098, 840, 699, 603 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.90-7.94 (m, 2H), 7.13-7.24 (m, 5H), 7.03-7.07 (m, 2H), 3.21 (t, J = 8.0 Hz, 2H), 3.00 (t, J = 8.0 Hz, 2H). $^{13}C\{^{1}H\}$ NMR (100.6 MHz, $CDCl_3$): δ 197.7, 165.8 (d, $^{1}J_{C\text{-}F}$ = 253.0 Hz), 141.3, 133.4, 130.7 (d, $^{3}J_{C\text{-}F}$ = 9.2 Hz), 128.7, 128.5, 126.3, 115.8 (d, $^{2}J_{C\text{-}F}$ = 21.7 Hz), 40.5, 30.2.



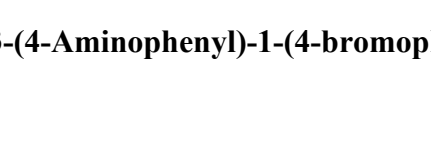
1-(4-Chlorophenyl)hexan-1-one[73] **(3.3r):** White solid. Yield (100 mg, 95%). IR (DCM): 2954, 2932, 2861, 1682, 1589, 1487, 1402, 1265, 1091, 1029, 776, 698 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.88 (d, J = 8.4 Hz, 2H), 7.41 (d, J = 8.8 Hz, 2H), 2.91 (t, J = 7.2 Hz, 2H), 1.68-1.73 (m, 2H), 1.33-1.36 (m, 4H), 0.90 (t, J = 7.2 Hz, 3H). $^{13}C\{^{1}H\}$ NMR (100.6 MHz, $CDCl_3$): δ 199.4, 139.4, 135.5, 129.6, 129.0, 38.7, 31.6, 24.1, 22.6, 14.1.



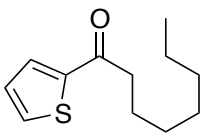
1-(4-Chlorophenyl)-3-phenylpropan-1-one[50a] **(3.3s)**: White solid. Yield (93 mg, 76%). IR (DCM): 3061, 3085, 3027, 2927, 1687, 1588, 1452, 1203, 1091, 1029, 776, 698 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.83 (d, J = 8.8 Hz, 2H), 7.36 (d, J = 8.8 Hz, 2H), 7.13-7.24 (m, 5H), 3.21 (t, J = 8.4 Hz, 2H), 3.00 (t, J = 8.0 Hz, 2H). $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$): δ 198.1, 141.2, 139.6, 135.3, 129.6, 129.0, 128.7, 128.5, 126.3, 40.5, 30.2.



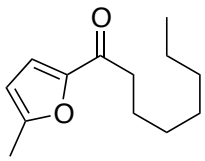
3-(4-Aminophenyl)-1-(4-bromophenyl)propan-1-one (3.3t): Orange solid. Yield (90 mg, 61%). IR (DCM): 3446, 3365, 3029, 2923, 1682, 1624, 1584, 1516, 1396, 1201, 1070, 978, 815 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.80 (d, J = 8.8 Hz, 2H), 7.58 (d, J = 8.4 Hz, 2H), 7.02 (d, J = 8.4 Hz, 2H), 6.63 (d, J = 8.0 Hz, 2H), 3.52 (*br*s, 2H), 3.20 (t, J = 8.0 Hz, 2H), 2.94 (t, J = 7.6 Hz, 2H). $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$): δ 198.7, 144.7, 135.8, 132.0, 131.1, 129.7, 129.3, 128.2, 115.5, 40.9, 29.4. HRMS (ESI) m/z calcd for $C_{15}H_{15}BrNO$ $(M+H)^+$: 304.0332, found: 304.0339.



1-(Thiophen-2-yl)octan-1-one[74] **(3.3u):** Yellowish oil. Yield (90 mg, 86%). IR (DCM): 2954, 2926, 2855, 1663, 1416, 1234, 720, 857 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.69-7.70 (m, 1H), 7.59-7.61 (m, 1H), 7.10-7.12 (m, 1H), 2.85-2.90 (m, 2H), 1.69-1.75 (m, 2H), 1.23-1.33 (m, 8H), 0.85-0.89 (m, 3H). $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$): δ 193.7, 144.7, 133.4, 131.8, 128.1, 39.6, 31.8, 29.4, 29.2, 24.9, 22.7, 14.2.



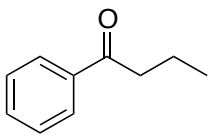
1-(5-Methylfuran-2-yl)octan-1-one (3.3v): Yellow oil. Yield (81 mg, 78%). IR (DCM): 2955, 2926, 2855, 1672, 1516, 1206, 1026, 795 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.08 (d, J = 3.2 Hz, 1H), 6.13 (d, J = 3.2 Hz, 1H), 2.72-2.75 (m, 2H), 2.38 (s, 3H), 1.63-1.71 (m, 2H), 1.27-1.32 (m, 8H), 0.87 (t, J = 7.2 Hz, 3H). $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$): δ 189.4, 157.7, 151.7, 119.0, 108.9, 38.4, 31.8, 29.5, 29.2, 24.9, 22.7, 14.20, 14.19. HRMS (ESI) m/z calcd for $C_{13}H_{21}O_2$ $(M+H)^+$: 209.1542, found: 209.1555.

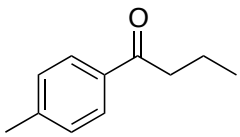


General Procedure for α -Ethylation of Ketones Using Ethanol

Inside a nitrogen atmosphere glove box, a 38 mL sealed tube was charged with a stir bar, catalyst **3.1** (0.01 mmol, 2 mol %), Cs_2CO_3 (0.05 mmol, 10 mol %), ketone (0.5 mmol), *tert*-amyl alcohol (1 mL) ethanol (1 mL) in the same order. The reaction mixture was refluxed (oil bath temperature 140 °C) with stirring for 24 h under closed condition. After cooling, solvent was evaporated under reduced pressure and the crude mixture was purified by column chromatography over silica-gel (60-120 mesh) using ethyl acetate/pet-ether mixture as an eluent.

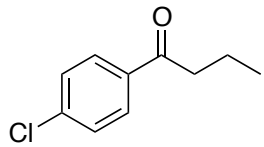
1-Phenylbutan-1-one[51a] **(3.4a):** Colorless oil. Yield (43 mg, 58%). IR (DCM): 2962, 2932, 2873, 1686, 1597, 1448, 1273, 1213, 1002, 753, 735, 690 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.96 (d, J = 8.4 Hz, 2H), 7.53-7.57 (m, 1H), 7.44-7.47 (m, 2H), 2.94 (t, J = 7.6 Hz, 2H), 1.73-1.82 (m, 2H), 1.01 (t, J = 7.6 Hz, 3H). $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$): δ 200.6, 137.3, 133.0, 128.7, 128.2, 40.7, 17.9, 14.0.



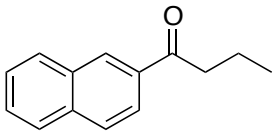
1-(p-Tolyl)butan-1-one[75] **(3.4b):** Colorless oil. Yield (53 mg, 65%). IR (DCM): 

2961, 2931, 2873, 1683, 1607, 1456, 1408, 1222, 1207, 1180, 809 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.89 (d, J = 8.0 Hz, 2H), 7.28 (d, J = 8.0 Hz, 2H), 2.94 (t, J = 7.6 Hz, 2H), 2.43 (s, 3H), 1.74-1.84 (m, 2H), 1.03 (t, J = 7.6 Hz, 3H). $^{13}C\{^{1}H\}$ NMR (100.6 MHz, $CDCl_3$): δ 200.2, 143.7, 134.8, 129.3, 128.3, 40.5, 21.7, 18.0, 14.0.

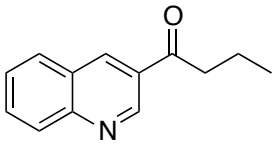
1-(4-Chlorophenyl)butan-1-one[76] **(3.4c):** Colorless oil. Yield (57 mg, 63%). IR (DCM): 2963, 2933, 2874, 1686, 1588, 1487, 1401, 1366, 1210, 1092, 1013, 998, 988, 817 cm^{-1}. ^{1}H NMR (700 MHz, $CDCl_3$): δ 7.89 (d, J = 8.4 Hz, 2H), 7.42 (d, J = 8.4 Hz, 2H), 2.91 (t, J = 7.7 Hz, 2H), 1.77 (m, 2H), 1.00 (t, J = 7.7 Hz, 3H). $^{13}C\{^{1}H\}$ NMR (100.6 MHz, $CDCl_3$): δ 199.3, 139.4, 135.5, 129.6, 129.0, 40.6, 17.8, 14.0.



1-(Naphthalen-2-yl)butan-1-one (3.4d): Colorless oil. Yield (65 mg, 66%). IR (DCM): 3058, 2961, 2931, 2873, 1681, 1627, 1467, 1371, 1304, 1277, 1210, 1185, 1125, 855, 822, 753 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.4 (s, 1H), 8.04 (dd, J_1 = 8.8 Hz, J_1 = 1.6 Hz, 1H), 7.96 (d, J = 8.0 Hz, 1H), 7.86 -7.90 (m, 2H), 7.53-7.61 (m, 2H), 3.08 (t, J = 7.2 Hz, 2H), 1.79-1.89 (m, 2H), 1.05 (t, J = 7.6 Hz, 3H). $^{13}C\{^{1}H\}$ NMR (100.6 MHz, $CDCl_3$): δ 200.5, 135.6, 134.6, 132.7, 129.7, 129.6, 129.5, 128.4, 127.9, 126.8, 124.1, 40.7, 18.1, 14.1. HRMS (ESI) m/z calcd for $C_{14}H_{15}O$ $(M+H)^+$: 199.1123, found: 199.1132.



1-(Quinolin-3-yl)butan-1-one (3.4e): Yellow solid. Yield (23 mg, 23%). IR (DCM): 2959, 2929, 2871, 1683, 1618, 1595, 1463, 1402, 1381, 1178, 963, 787, 751 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 9.42 (d, J = 2.0 Hz, 1H), 8.70 (d, J = 2.0 Hz, 1H), 8.15 (d, J = 8.4 Hz, 1H), 7.93 (d, J = 8.0 Hz, 1H), 7.80-7.84 (m, 1H), 7.62 (t, J = 7.2 Hz, 1H), 3.07 (t, J = 7.2 Hz, 2H), 1.79-1.88 (m, 2H), 1.05 (t, J = 7.2 Hz, 3H). $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$): δ 199.2, 149.8, 149.3, 137.1, 132.0, 129.5, 129.45, 129.4, 127.6, 127.0, 41.0, 17.7, 14.0. HRMS (ESI) m/z calcd for $C_{13}H_{14}O$ $(M+H)^+$: 200.1075, found: 200.1083.



Chemoselective α-C Alkylation of Acetophenone by Primary Alcohols over Secondary Alcohols:

Inside glove box, 25 mL Schlenk tube was charged with a magnetic stir bar, catalyst **3.1** (0.01 mmol), Cs_2CO_3 (0.05 mmol), acetophenone (0.5 mmol), *tert*-amyl alcohol (2 mL), 1-hexanol (0.6 mmol) and cyclohexanol (0.6 mmol) sequentially under nitrogen atmosphere. The reaction flask was taken out of the glove box, and then refluxed (oil bath temperature 140 °C) with stirring in an open system under argon flow for 24 h. The reaction mixture was then cooled to room temperature. The solvent was evaporated under reduced pressure and 0.5 mmol of internal standard (toluene) was added into the reaction mixture and then diluted with 0.8 mL acetone. Afterwards, an aliquot of this reaction mixture was quickly filtered through a small plug of Celite and analyzed by GC. The solvent was evaporated under reduced pressure and crude reaction mixture was purified by column chromatography over silica-gel (60-120 mesh) using ethyl acetate/pet ether mixture as an eluent. The

conversion of product was calculated using GC analysis and yield of pure product was determined after column chromatography.

Chemoselective α-C Alkylation of Acetophenone by Primary Alcohols over Secondary Alcohols:

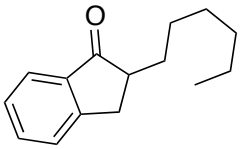
Inside glove box, 25 mL Schlenk tube was charged with a magnetic stir bar, catalyst **3.1** (0.01 mmol), Cs_2CO_3 (0.05 mmol), acetophenone (0.5 mmol), *tert*-amyl alcohol (2 mL), 1-hexanol (0.6 mmol) and 3-pentanol (0.6 mmol) sequentially under nitrogen atmosphere. The reaction flask was taken out of the glove box, and then refluxed (oil bath temperature 140 °C) with stirring in an open system under argon flow for 24 h. The reaction mixture was then cooled to room temperature. The solvent was evaporated under reduced pressure and 0.5 mmol of internal standard (toluene) was added into the reaction mixture and then diluted with 0.8 mL acetone. Afterwards, an aliquot of this reaction mixture was quickly filtered through a small plug of Celite and analyzed by GC. The solvent was evaporated under reduced pressure and crude reaction mixture was purified by column chromatography over silica-gel (60-120 mesh) using ethyl acetate/pet ether mixture as an eluent. The conversion of product was calculated using GC analysis and yield of pure product was determined after column chromatography.

Chemoselective α-C Alkylation of Acetophenone by Primary Alcohols over N-Alkylation of Aniline:

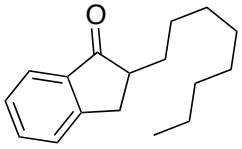
Inside a nitrogen atmosphere glove box, 25 mL Schlenk tube was charged with a stir bar, catalyst **3.1** (0.01 mmol), Cs_2CO_3 (0.05 mmol), acetophenone (0.5 mmol), *tert*-amyl alcohol (2 mL), 1-hexanol (0.6 mmol) and aniline (0.5 mmol) in the same order.

The reaction flask was taken out of the glove box, equipped with a condenser and the reaction mixture was refluxed (oil bath temperature 140 °C) with stirring in an open system under the flow of argon for 24 h. The reaction mixture was then cooled down to room temperature. The solvent was evaporated under reduced pressure and 0.5 mmol of internal standard (toluene) was added into the reaction mixture and the solution was quickly filtered through a small plug of Celite. Afterwards, an aliquot of this reaction mixture was dissolved in 0.8 mL acetone and analyzed by GC analysis. The solvent was evaporated under reduced pressure and crude reaction mixture was purified by column chromatography over silica-gel (60-120 mesh) using ethyl acetate /pet ether mixture as an eluent. The conversion of product was calculated using GC analysis and yield of pure product was determined after column chromatography.

2-Hexyl-2,3-dihydro-1H-inden-1-one[77] **(3.5a):** Yellow oil. Yield (106 mg, 98%). IR (DCM): 2924, 2853, 1713, 1609, 1464, 1294, 1276, 750, 721 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.74 (d, J = 8.0 Hz, 1H), 7.57 (t, J = 7.2 Hz, 1H), 7.45 (t, J = 7.6 Hz, 1H), 7.35 (t, J = 7.2 Hz, 1H), 3.32 (dd, J_1 = 17.2 Hz, J_2 = 8.0 Hz, 1H), 2.81 (dd, J_1 = 17.2 Hz, J_2 = 3.6 Hz, 1H), 2.62-2.68 (m, 1H), 1.92-1.98 (m, 1H), 1.28-1.46 (m, 9H), 0.87 (t, J = 6.4 Hz, 3H). $^{13}C\{^{1}H\}$ NMR (100.6 MHz, $CDCl_3$): δ 209.4, 154.0, 137.0, 134.7, 127.4, 126.7, 124.0, 47.6, 33.0, 31.8, 31.6, 29.4, 27.5, 22.7, 14.2.

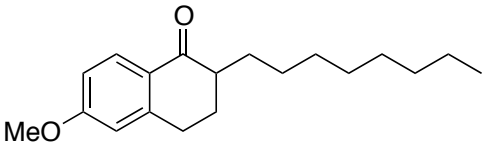


2-Octyl-2,3-dihydro-1H-inden-1-one[78] **(3.5b):** Yellow oil. Yield (120 mg, 97%). IR (DCM): 2924, 2853, 1713, 1609, 1464, 1294, 1276, 750, 721 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.75 (d, J = 7.6 Hz, 1H),

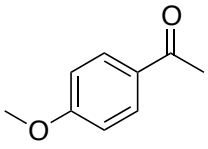


7.55-7.59 (m, 1H), 7.45 (d, J = 7.6 Hz, 1H), 7.35 (t, J = 7.6 Hz, 1H), 3.32 (dd, J_1 = 17.2 Hz, J_2 = 7.6 Hz, 1H), 2.81 (dd, J_1 = 16.8 Hz, J_2 = 4 Hz, 1H), 2.62-2.68 (m, 1H), 1.92-1.95 (m, 1H), 1.26-1.43 (m, 13H), 0.87 (t, J = 7.2 Hz, 3H). $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$): δ 209.3, 153.9, 137.0, 134.7, 127.4, 126.7, 124.0, 47.6, 33.0, 32.0, 31.6, 29.8, 29.6, 29.4, 27.6, 22.8, 14.2.

6-Methoxy-2-octyl-3,4-dihydronaphthalen-1(2H)-one (3.5c): Colorless oil. Yield (120 mg, 85%). IR (DCM): 2924, 2854, 1675, 1600, 1572, 1464, 1354, 1251, 1227, 1133, 1028, 846, 830 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.99 (d, J = 8.8 Hz, 1H), 6.80 (dd, J_1 = 8.8 Hz, J_2 = 2 Hz, 1H), 6.67 (d, J = 2 Hz, 1H), 3.84 (s, 3H), 2.91-2.95 (m, 2H), 2.39-2.43 (m, 1H), 2.18-2.22 (m, 1H), 1.87-1.92 (m, 2H), 1.26-1.47 (m, 13H), 0.87 (t, J = 7.2 Hz, 3H). $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$): δ 199.5, 163.4, 146.5, 130.0, 126.3, 113.1, 112.5, 55.5, 47.3, 32.0, 29.9, 29.7, 29.6, 29.4, 28.7, 28.3, 27.2, 22.8, 14.2. HRMS (ESI) m/z calcd for $C_{19}H_{29}O_2$ $(M+H)^+$: 289.2162, found: 289.2148.



1-(4-Methoxyphenyl)ethanone[81] **(3.6):** Pale yellow solid. Yield (56 mg, 74%). ^1H NMR (400 MHz, $CDCl_3$): δ 7.93 (dd, J_1 = 8.8 Hz, J_2 = 1.6 Hz, 2H), 6.92 (dd, J_1 = 8.8 Hz, J_2 = 1.6 Hz, 2H), 3.86 (d, J_1 = 2.0 Hz, 3H), 2.55 (d, J_1 = 2.0 Hz, 3H). $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$): δ 197.0, 163.6, 130.7, 130.4, 113.8, 55.6, 26.5.



GC Monitoring of the Reaction Mixture 3.2o:

Inside a nitrogen atmosphere glove box, 25 mL Schlenk tube equipped with stir bar was added catalyst **3.1** (0.02 mmol), Cs_2CO_3 (0.05 mmol), 1-phenyl-1-ethanol (1 mmol), 3-phenyl-1-propanol (1.2 mmol), mesitylene (1 mmol, as an internal standard) and *tert*-amyl alcohol (4 mL) sequentially. The reaction flask was taken out of the glove box, and equipped with a condenser and solution was refluxed (oil bath temperature 135 °C) with stirring in open system under the flow of argon. Aliquots were collected from reaction mixture periodically, further diluted with acetone (0.5 mL) and analyzed by GC. The conversion of 1-phenyl-1-ethanol and yield of **3.2h** was calculated using GC analysis.

Mercury Poisoning Test

Inside a nitrogen atmosphere glove box, 25 mL Schlenk tube was charged with a stir bar, catalyst **3.1** (0.01 mmol), Cs_2CO_3 (0.025 mmol), 1-phenyl-1-ethanol (0.5 mmol), solvent (2 mL), benzyl alcohol (0.6 mmol) and mercury (2 equiv 200 mg) in the same order. The reaction flask was taken out of the glove box, and then refluxed (oil bath temperature 135 °C) with stirring in an open system under argon flow for 24 h. The reaction mixture was then cooled down to room temperature. The solvent was evaporated under reduced pressure and 0.5 mmol of an internal standard (toluene) was added into the reaction mixture and then diluted with 0.8 mL acetone. An aliquot of the solution was passed through a small Celite plug and analyzed by GC. The solvent was evaporated under reduced pressure and crude reaction mixture was purified by column chromatography over silica-gel (60-120 mesh) using ethyl acetate /pet ether mixture as an eluent. The conversion of 1-phenyl-1-ethanol was calculated using GC analysis and yield of pure product was determined after column chromatography.

Observation of Ketone Intermediate

In a glove box, 25 mL Schlenk tube was charged with a stir bar, catalyst **3.1** (0.01 mmol), Cs_2CO_3 (0.025 mmol), 1-(4-methoxyphenyl)ethanol (0.5 mmol) and solvent (2 mL) under nitrogen atmosphere. The flask was taken out of the glove box, equipped with a condenser and solution was refluxed (oil bath temperature 135 °C) with stirring in an open system under a flow of argon for 20 h. After cooling to room temperature, 0.5 mmol of an internal standard (dodecane) was added and the reaction mixture was subjected GC analysis. The solvent was evaporated and crude reaction mixture was purified by column chromatography over silica-gel (100-200 mesh) using ethyl acetate/ pet ether as an eluent. The conversion of 1-(4-methoxyphenyl)ethanol was calculated using GC analysis and yield for pure products after column chromatography.

NMR Spectra of *α*-Alkylated Ketone Products

Figure 3.3 ^{1}H NMR spectrum of 1,3-diphenylpropan-1-one **(3.2a)**:

Figure 3.4 ^{13}C NMR spectrum of 1,3-diphenylpropan-1-one **(3.2a)**:

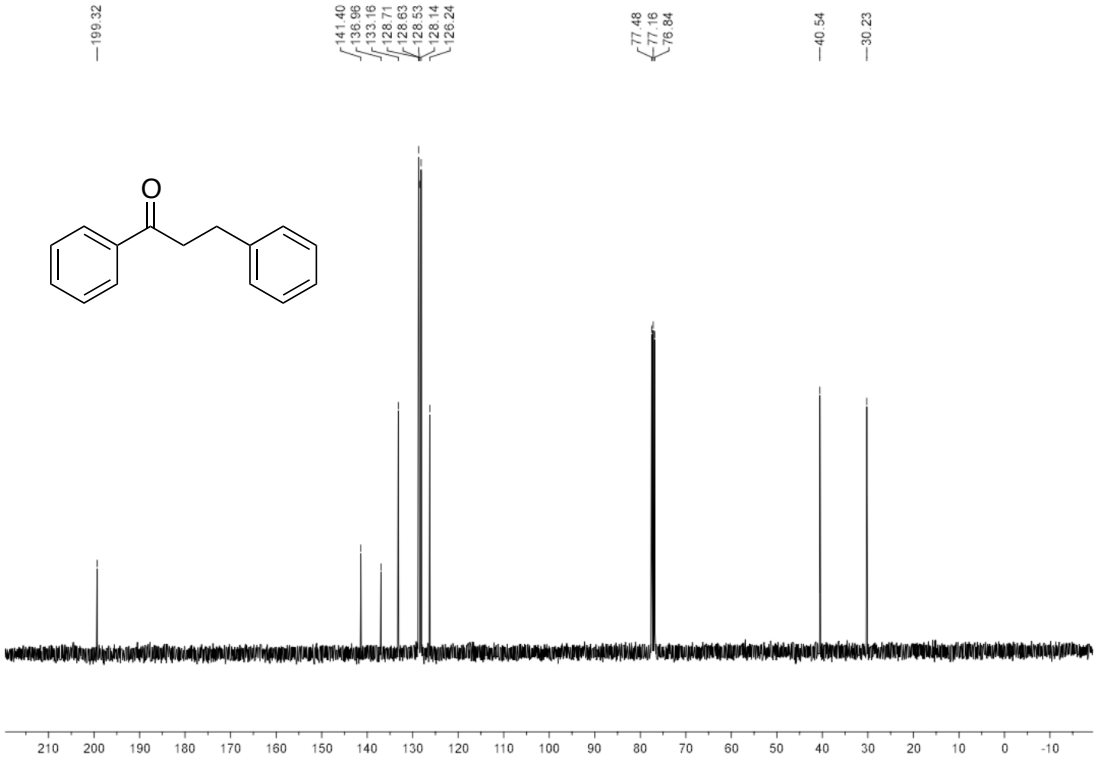


Figure 3.5 ^{1}H NMR spectrum of 4-cyclohexyl-1-phenylbutan-1-one **(3.2j)**:

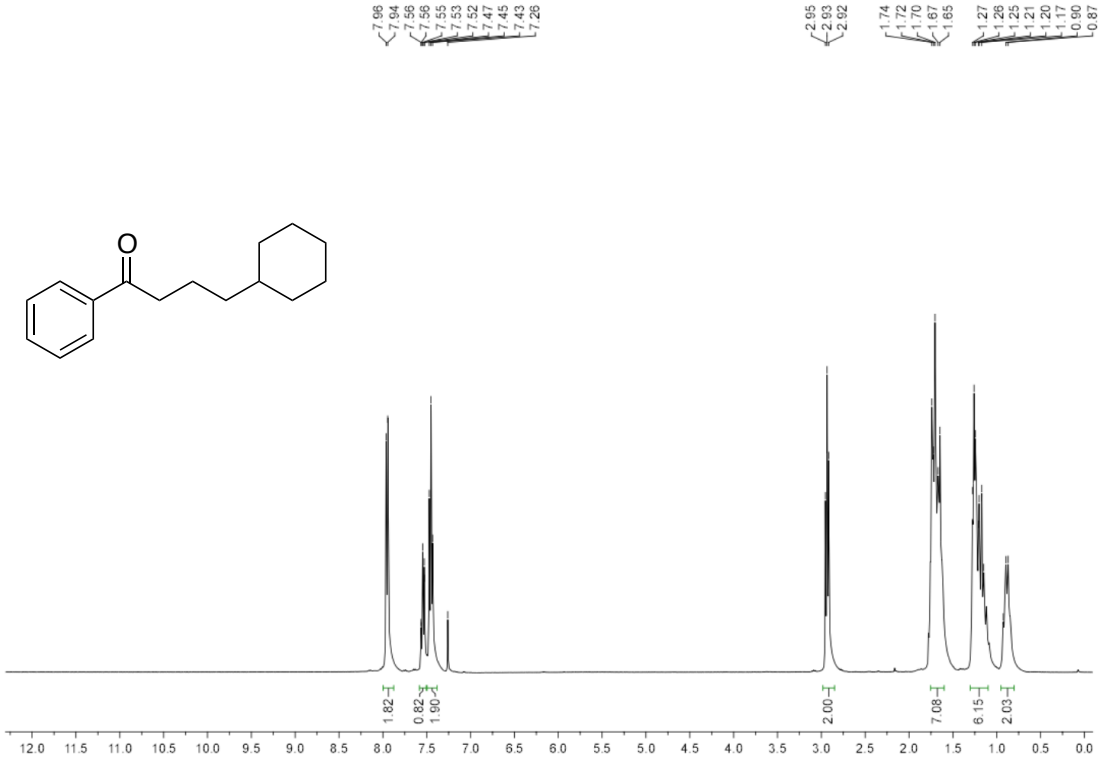


Figure 3.6 ^{13}C NMR spectrum of 4-cyclohexyl-1-phenylbutan-1-one **(3.2j)**:

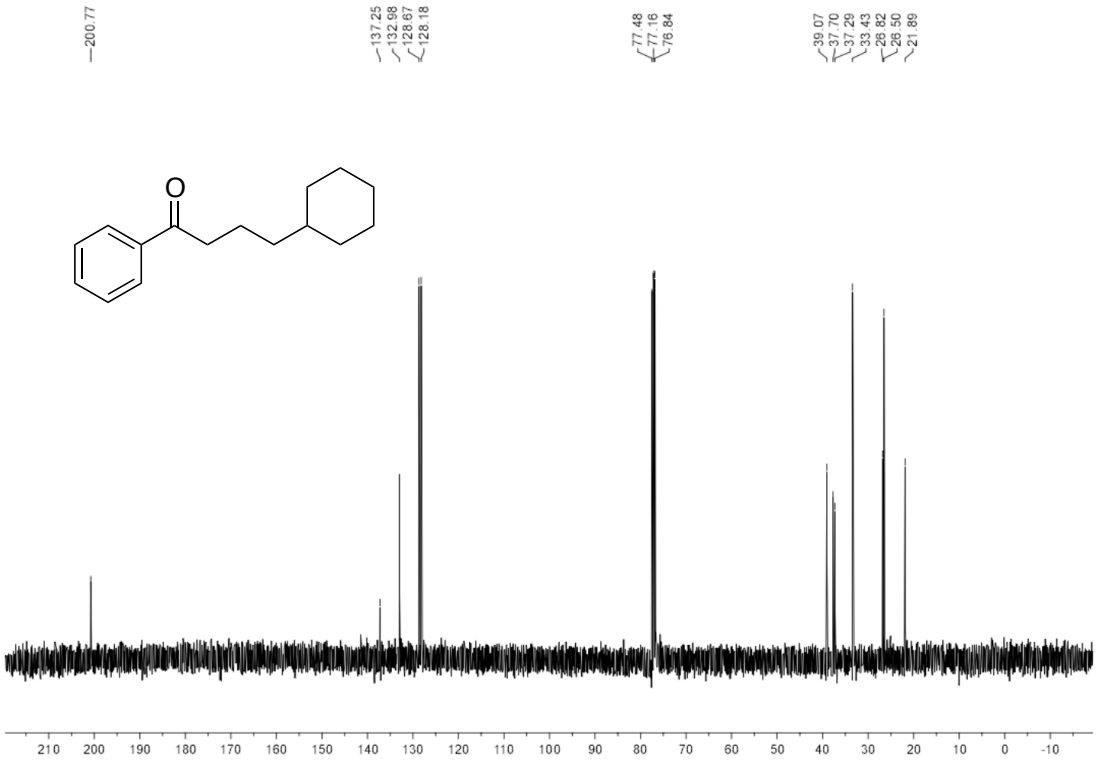


Figure 3.7 ^{1}H NMR spectrum of 1,5-diphenylpentan-1-one **(3.2o)**:

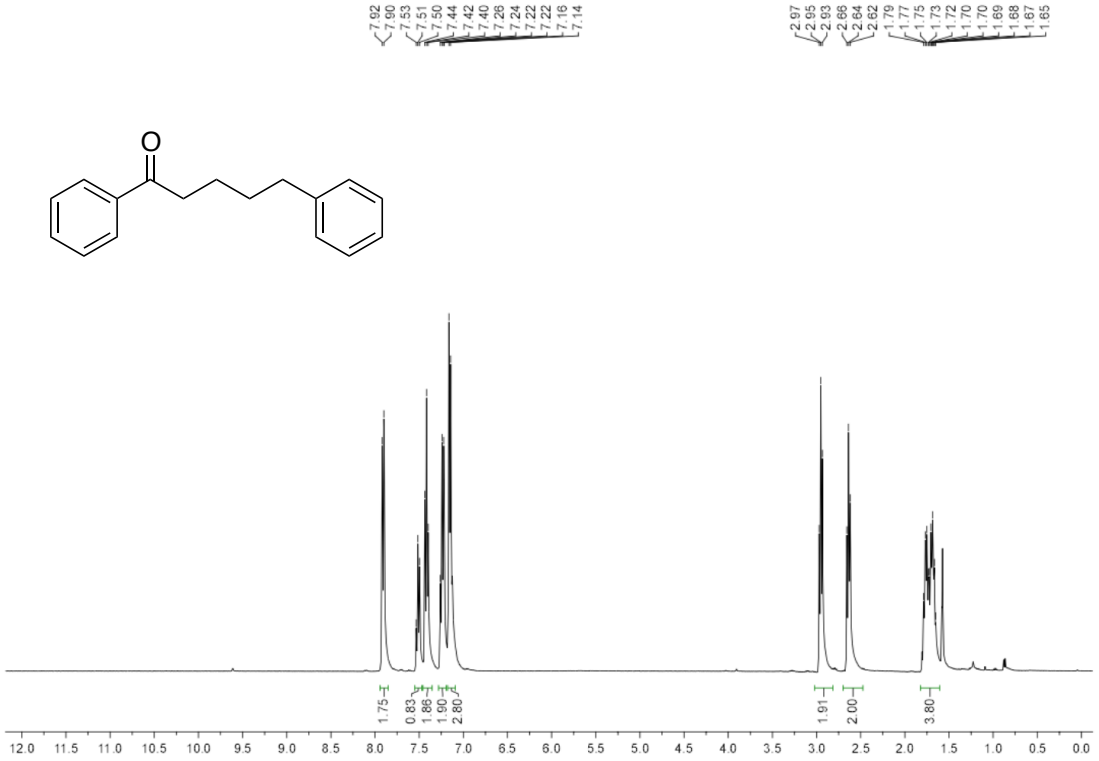


Figure 3.8 ^{13}C NMR spectrum of 1,5-diphenylpentan-1-one **(3.2o)**:

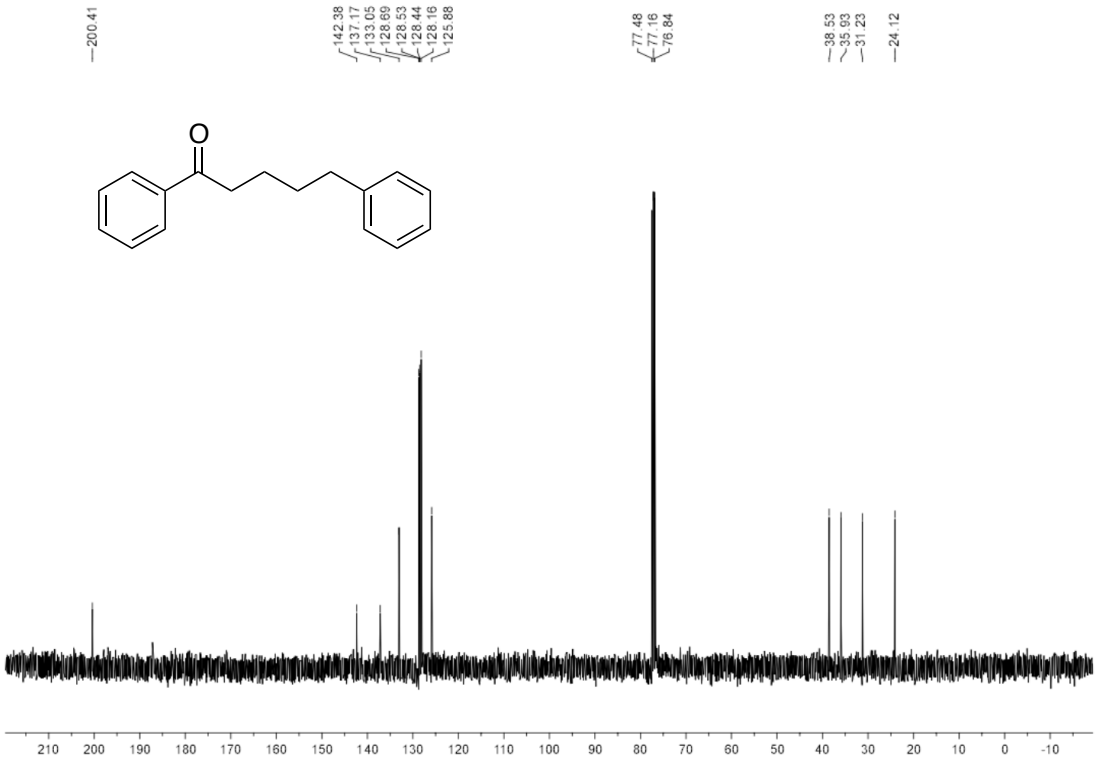


Figure 3.9 ^{1}H NMR spectrum of 3-phenyl-1-(thiophen-2-yl)propan-1-one **(3.3e)**:

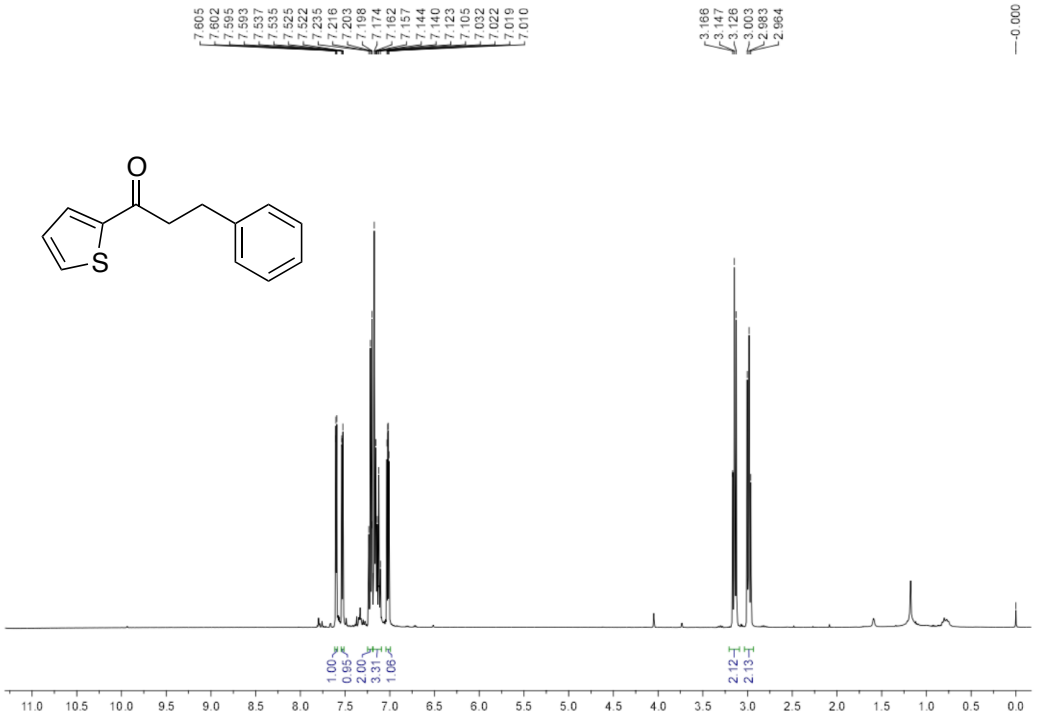


Figure 3.10 ^{13}C NMR spectrum of 3-phenyl-1-(thiophen-2-yl)propan-1-one **(3.3e)**:

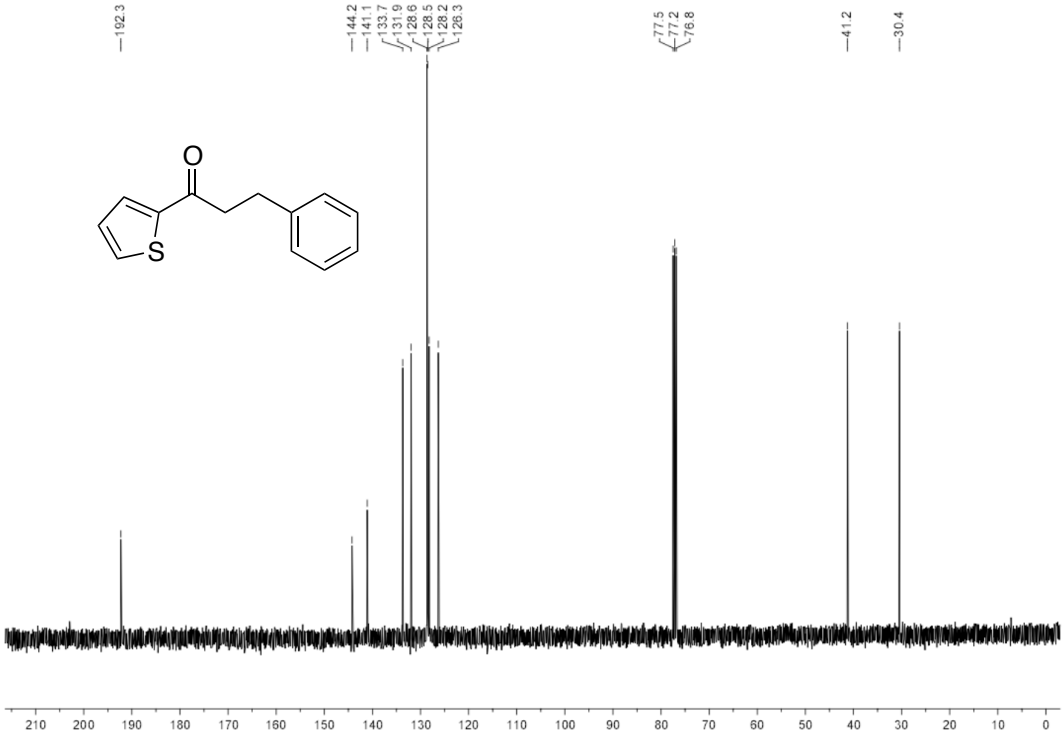


Figure 3.11 ^{1}H NMR spectrum of 1-(2-aminophenyl)nonan-1-one **(3.3k)**:

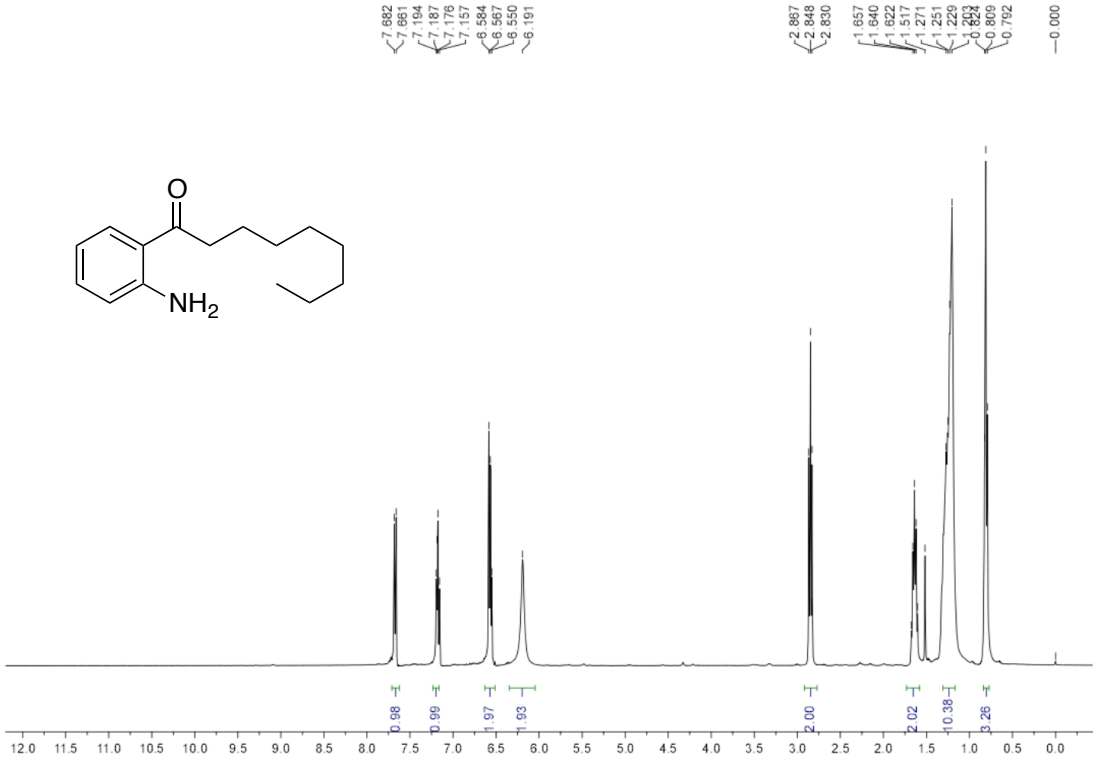


Figure 3.12 ^{13}C NMR spectrum of 1-(2-aminophenyl)nonan-1-one **(3.3k)**:

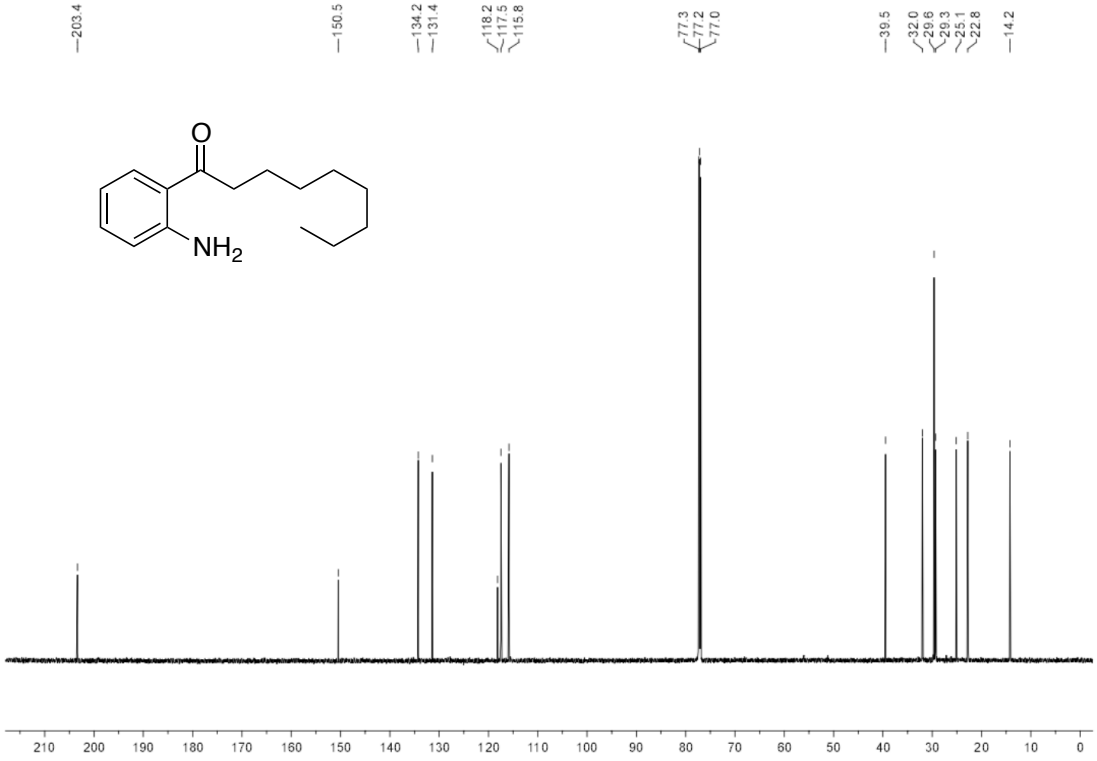


Figure 3.13 ^{1}H NMR spectrum of 1-(4-chlorophenyl)butan-1-one **(3.4c)**:

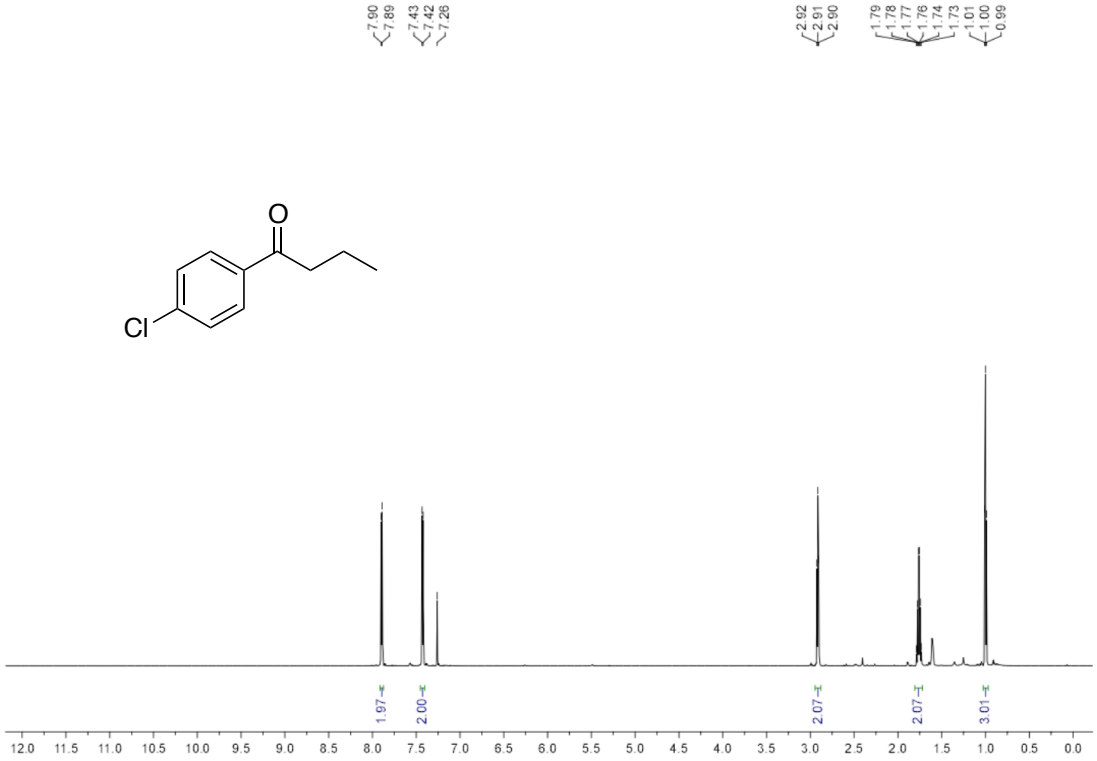


Figure 3.14 ^{13}C NMR spectrum of 1-(4-chlorophenyl)butan-1-one **(3.4c)**:

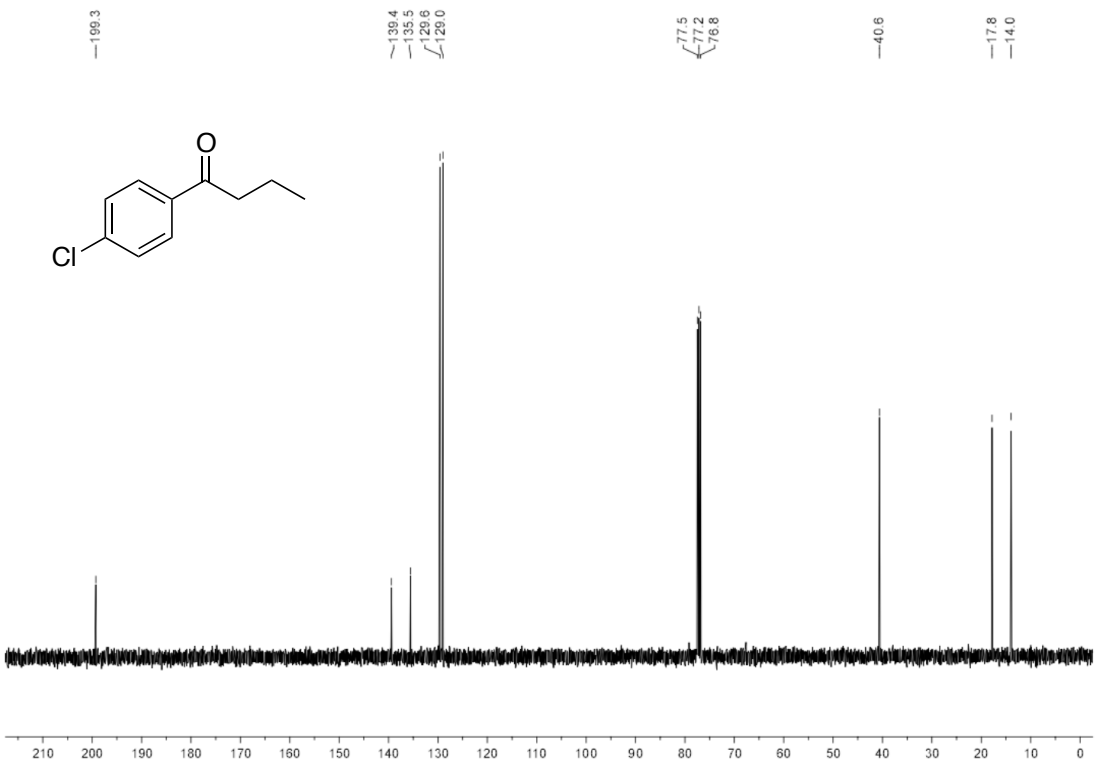


Figure 3.15 ^{1}H NMR spectrum of 6-methoxy-2-octyl-3,4-dihydronaphthalen-1(2*H*)-one **(3.5c)**:

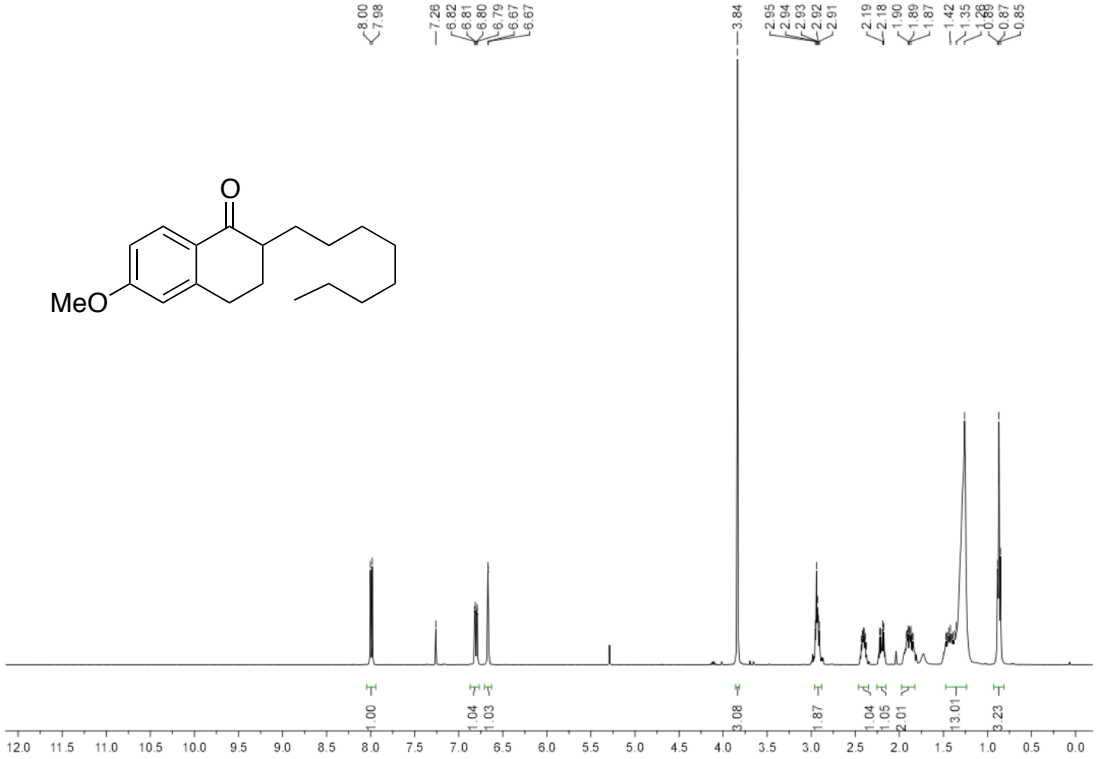


Figure 3.16 ^{13}C NMR spectrum of 6-methoxy-2-octyl-3,4-dihydronaphthalen-1(2*H*)-one **(3.5c)**:

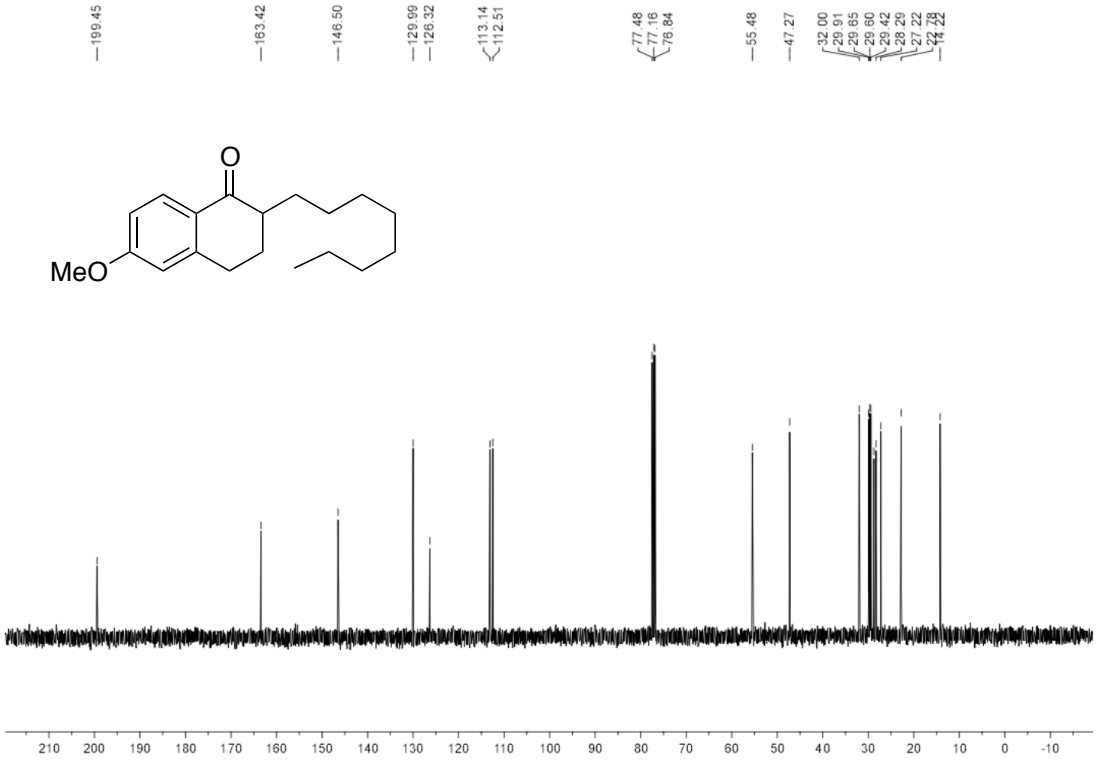


Figure 3.17 ^{1}H NMR spectrum of 1-(4-Methoxyphenyl)ethanone **(3.6):**

Figure 3.18 ^{13}C NMR spectrum of 1-(4-Methoxyphenyl)ethanone **(3.6):**

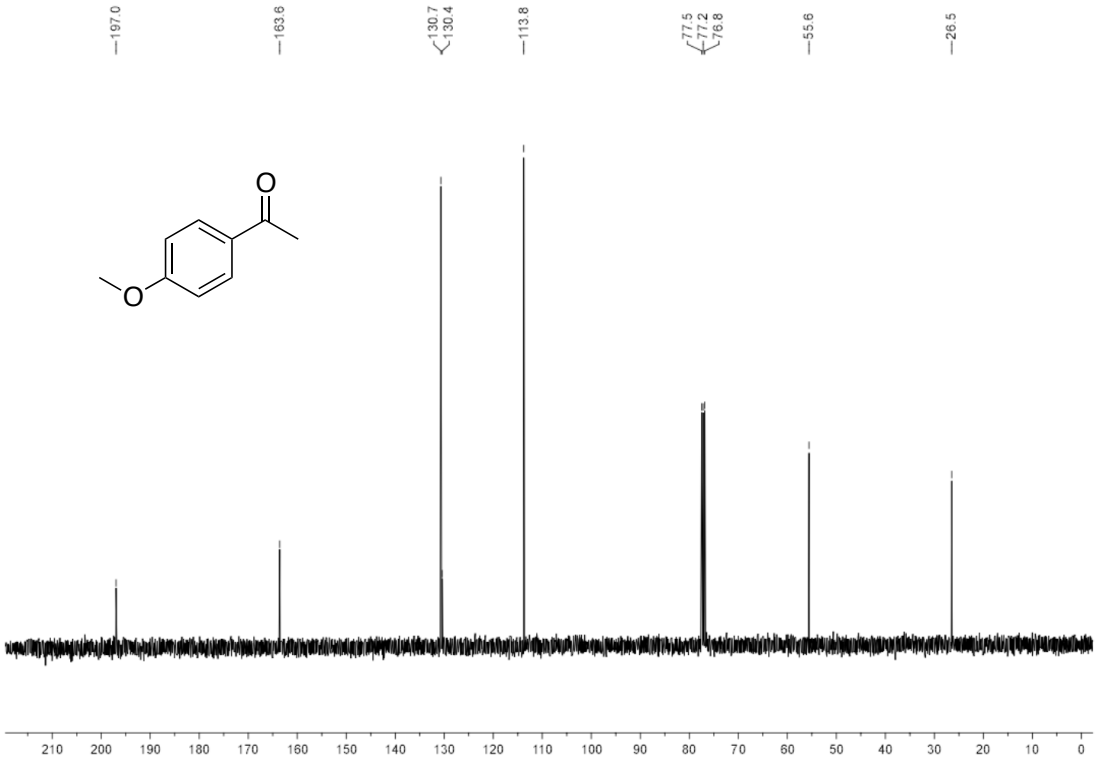
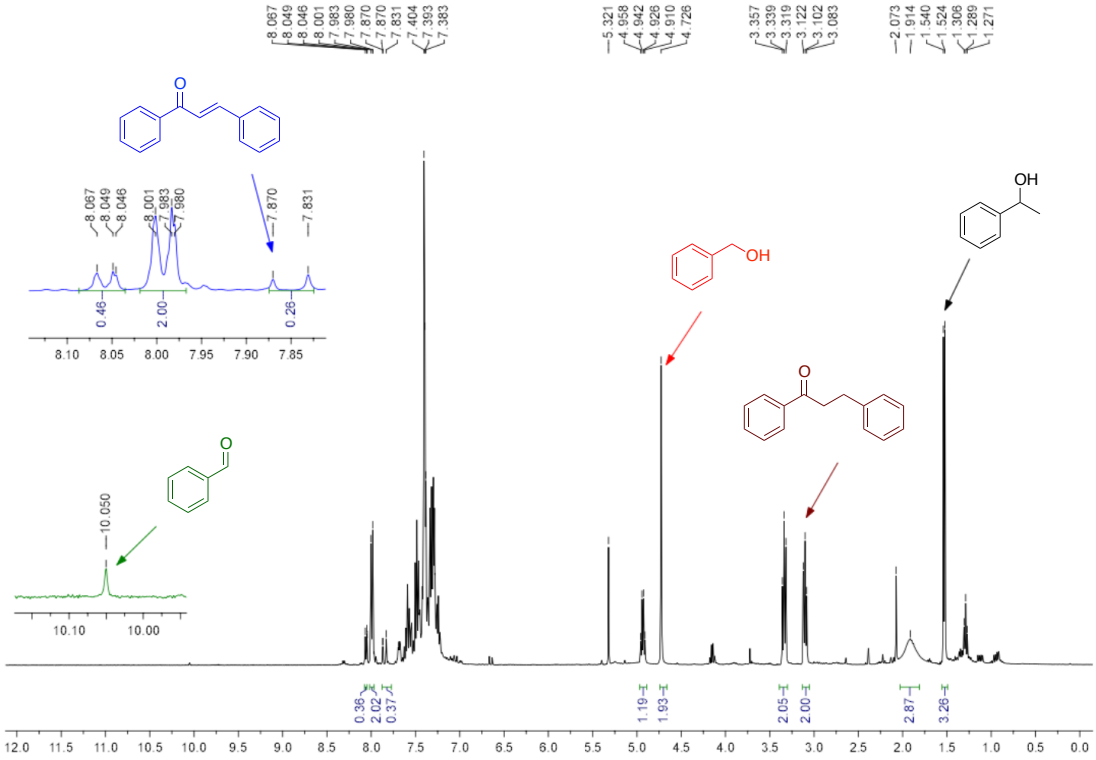


Figure 3.19 ^{1}H NMR Spectrum of Reaction Mixture **3.2a:** Observation of Aldehyde and α,β–Unsaturated Ketone Intermediates



CHAPTER 4

Manganese(I)-Catalyzed *α*-Alkenylation of Ketones Using Primary Alcohols

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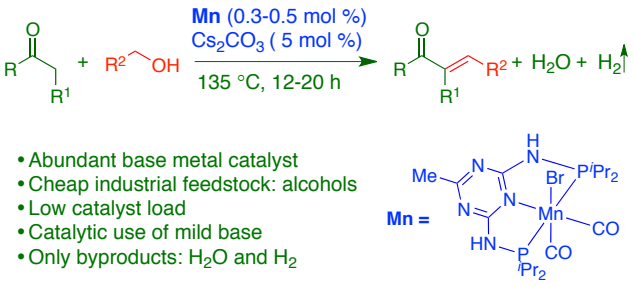
4.1 ABSTRACT



A simple protocol of manganese catalyzed selective α-alkenylation of ketones using primary alcohols is reported. The reactions proceeded well with a low loading of catalyst (0.3 mol %). The overall transformation operates through O−H bond activation of primary alcohols via dearomatization-aromatization metal ligand cooperation in the catalyst to provide the corresponding aldehydes, which further undergo condensation with methylene ketones to deliver α,β-unsaturated ketones. This selective α-alkenylation proceeds with the release of water and liberation of molecular hydrogen.

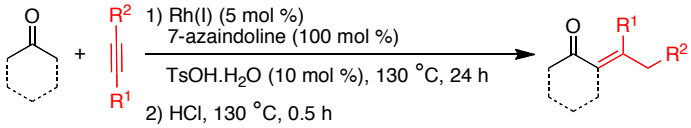
4.2 INTRODUCTION

Synthesis of *α,β*-unsaturated ketones is one of the important reactions in organic synthesis due to the extensive applications of such unsaturated ketones in the synthesis of pharmaceuticals, biologically active compounds, pesticides, food additives, solar creams, and other functional materials.[79] In conventional synthesis, aldol condensation between ketones and aldehydes is employed for the preparation of *α,β*-unsaturated ketones using a stoichiometric amount of strong base. In addition to the high cost, aldehydes are prone to air oxidation resulting in contamination with

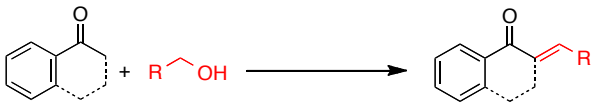
carboxylic acids, which creates a problem in storing these reactive compounds and requires purification before use.[80] These drawbacks urged the development of alternative methods for the synthesis of *α,β*-unsaturated ketones. Rhodium-catalyzed direct *α*-alkenylation of ketones using internal alkynes was reported recently; however, this method suffers from the requirement of high catalyst loading and use of bifunctional ligands in stoichiometric amounts (Scheme 1a).[81] Synthesis of *α,β*-unsaturated ketones directly from the alcohols and ketones can result in synthetic brevity and circumvent the isolation and purification of intermediates. Thus, tandem synthetic methods are developed combining the oxidation of alcohols to aldehydes and condensation of aldehydes with ketones. Precious transition metals on alkaline solid supports, such as Pd/AlO(OH),[82a] Pd/MgO-Al_2O_3,[82b] Au/AlO(OH),[82c] and Pt/ CeO_2,[82d] containing active sites for oxidation of alcohols and condensation reactions were developed, which also required excess alkali additives.[83] Moreover, heterogeneous base metal catalysts such as TiN, NbN, and NbCN were also developed for the synthesis of *α,β*-unsaturated ketones, but the preparation of these catalysts requires tedious and harsh nitridation of the parent metal oxides.[84a, b] Recently, CrO_3 and CeO_2 catalysts have been reported, while the chromium is toxic, catalysis by cerium oxide is limited to chalcone synthesis (Scheme 1b).[84c,d]

Scheme 4.1 Methods for the *α*- Alkenylation of Ketones

a) Synthesis of α,β-unsaturated ketones using ketones & alkynes



b) Transition metal catalyzed coupling of alcohols with ketones

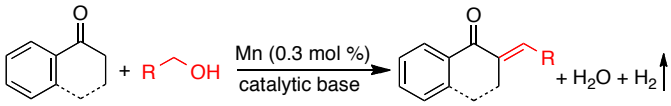


i) $Pd/AlO(OH)$, $Pd/MgO\text{-}Al_2O_3$, Pt/CeO_2, $Au/AlO(OH)$ — use of precious metals together with alkaline support

ii) TiN, NbN and NbCN — preparation of catalyst required harsh condition

iii) CeO_2 & CrO_3 — limited substrate scope, poor yields and toxic

This work



- abundant base metal catalysis
- catalytic use of mild base
- requires only low catalyst load
- only byproducts: H_2O and H_2

Alternatively, acceptorless dehydrogenative coupling of alcohols[85] and ketones is one of the most prominent synthetic method for the preparation of *α,β*-unsaturated ketones, which produce water and H_2 as the only byproducts. Over the decades, homogeneous organometallic complexes have been developed as catalysts for the acceptorless dehydrogenation of alcohols followed by condensation of in situ generated aldehydes, with C-H acidic compounds to afford atom economical and sustainable chemical transformations.[12b,13a,58c] Often hydrogen obtained from dehydrogenation of alcohols is utilized for the hydrogenation of condensation products, thus, resulting in the term "borrowing hydrogen methods",[42a,45,44] which attracted increasing attention for the C-C and C-N bond formation reactions. The direct use of alcohols in dehydrogenative coupling reactions for the synthesis of *α,β*-unsaturated ketones compound is challenging, because C-C double bonds undergo facile hydrogenation to deliver the α- alkylated ketones or alcohols.[51,52b,63a,66] In this

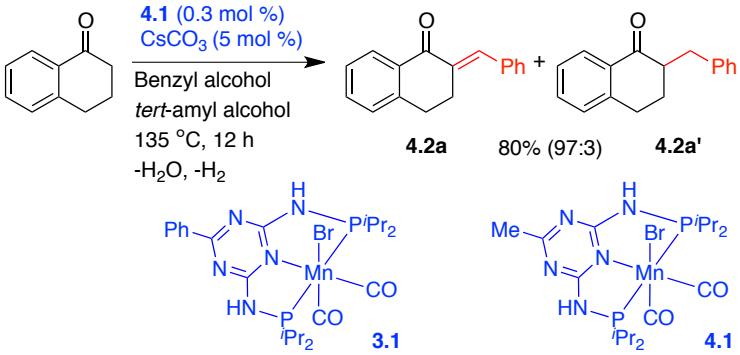
direction, Yus and co-workers reported the ruthenium-catalyzed α-olefination of ketones by acceptorless dehydrogenative coupling alcohols. However, poor yields, limited substrate scope, and requirement of a stoichiometric base necessitate the need for an alternative protocol.[86]

In recent years, in order to attain sustainability in catalysis, replacement of precious noble-metal catalysts with economical and environmentally benign earth-abundant base-metal catalysts is in high demand. Thus, atom-economical dehydrogenative coupling of alcohols and ketones to *α,β*-unsaturated ketones by base-metal catalysis is a desirable transformation. In this direction, Mn is one of the most earth-abundant transition metals, third only to Fe and Ti, and chemists have already developed excellent catalytic transformations using manganes complexes. [11b,53d,87] Encouraged by our recent results in developing atom economical and sustainable catalytic methods,[63a,b] herein, we report a dehydrogenative coupling of alcohols and ketones catalyzed by Kempe' s Mn PNP pincer complexes,[12a-c,17] which selectively produce the α -alkenyl ketones, H_2O and H_2. To our knowledge, there is no literature report on *α*-olefination of ketones catalyzed by Mn complexes.

4.3 RESULTS AND DISCUSSIONS

Using 1-tetralone and benzyl alcohol as model substrates, extensive optimization studies were carried out to determine suitable experimental conditions for catalytic *α* -alkenylation of ketones catalyzed by complexes **3.1** and **4.1** (Scheme 4.2 and Table 4.1).

Scheme 4.2 *a*-Alkenylation of 1-Tetralone

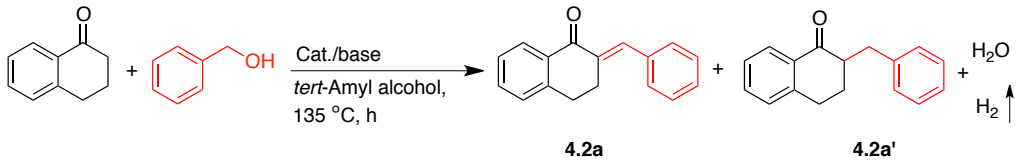


Observations revealed that 4-methyl substituted catalyst **4.1** is better than catalyst **3.1** containing a phenyl group in the backbone. Refluxing a *tert*-amyl alcohol solution of 1-tetralone (0.5 mmol) and benzyl alcohol (0.6 mmol) in the presence of catalyst **3.1** (0.5 mol%) and Cs_2CO_3 (5 mol%) at 135 °C for 20 h resulted in 97% conversion, and 64% isolated products with 92:8 (**4.2a:4.2a'**) selectivity for α-alkenylation and α-alkylation of ketone, respectively (entry 1). When similar experiment was carried out using 0.5 mol% of catalyst **4.1**, both conversion of 1-tetralone (98%) and yield of the product (80%) increased with higher selectivity 97:3 (**4.2a:4.2a'**) for α-alkenylation of ketone (entry 2), indicating that methyl substituent on PNP ligand of **4.1** provided better selectivity than phenyl group in **3.1**. A similar outcome was obtained when catalyst load was lowered to (0.3 mol%), α-alkenylation of ketones provided quantitative conversion and 80% yield of the product after 20 h (entry 3). Further, decreasing the amount of Cs_2CO_3 (3 mol%) resulted in diminished conversion of 1-tetralone (92%) and 68% yield of the product **4.2a** without altering selectivity (entry 4). However, under similar reaction condition increasing the amount of Cs_2CO_3 (8 mol%) provided poor selectivity 94:6 (**4.2a:4.2a'**) for α-alkenylation of ketone (entry 5). Lowering the catalyst load to 0.1 mol% turned out to be adverse for product (**4.2a**, 69%) formation (entry 6). Further, different inorganic bases such as KO^{t}Bu, NaO^{t}Bu, K_2CO_3, Na_2CO_3, KOH, and NaOH were screened for direct α-alkenylation of ketone

and they are found to be comparatively inefficient for this transformation (entries 7-12). The reaction without a metal catalyst in the presence of a catalytic amount of base showed only 12% conversion, whereas no conversion was observed in the absence of base, confirming the requirement of catalyst and base for the *α*-alkenylation reaction (entries 13-14).

Control experiments with base alone (without catalyst) and without both base and catalyst proved that the combination of catalyst and base is essential for this transformation. In above alkenylation reaction, we have used the catalyst **4.1** with 4-methyl substituted triazine based manganese catalyst instead of **3.1** with 4-phenyl substitution used for the alkylation reaction in Chapter 3. In addition to 4-methyl substituted triazine based manganese catalyst gives preference to the unsaturated alkenylation product, further optimization resulted in selective isolation of alkenylation products. If we increased catalyst load in above optimized reaction condition, considerable amount of alkylated product formation can occur. But that has been avoided by choosing stericaly hindred substrate such as 1-tetralone and benzyl alcohols (as compare to 1-tetralone and 1-hexanol (3.3h, table 3.8) in chapter 3), 4-methyl substituted triazine based manganese catalyst and optimization study.

Table 4.1 Optimization of the Reaction Conditions for the *α*- Alkenylation of 1-Tetralone[a]



entry	cat.	cat. (mol %)	base	base (mol %)	conv. (%)[b]	yield (%)[c]	ratio (**4.2a/4.2a'**)
1[d]	**3.1**	0.5	Cs_2CO_3	5	97	64	92/8

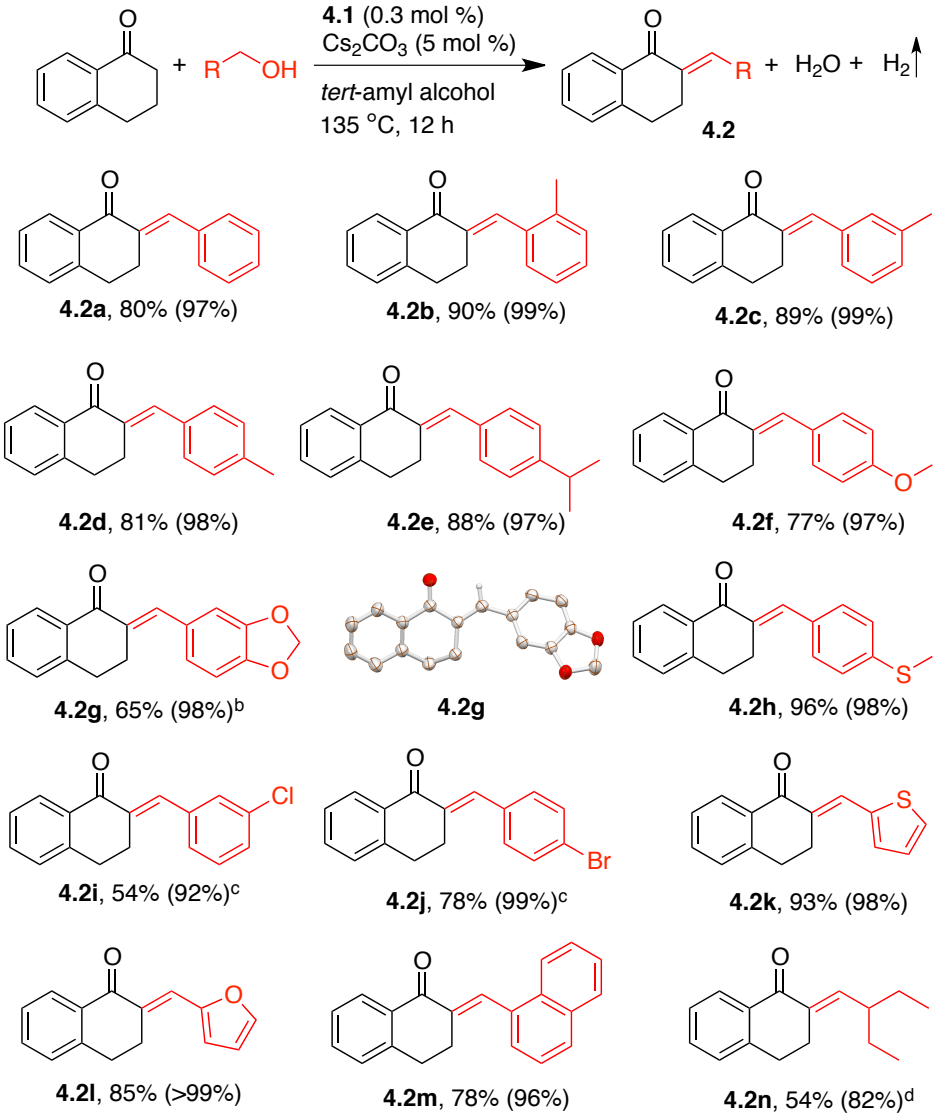
2	**4.1**	0.5	Cs_2CO_3	5	98	80	97/3
3	**4.1**	0.3	Cs_2CO_3	5	97	80	97/3
4	**4.1**	0.3	Cs_2CO_3	3	92	68	99/1
5	**4.1**	0.3	Cs_2CO_3	8	98	79	94/6
6	**4.1**	0.1	Cs_2CO_3	5	94	69	96/4
7[d]	**4.1**	0.5	KO^tBu	5	60	43	99/1
8	**4.1**	0.5	NaO^tBu	5	51	27	92/8
9	**4.1**	0.5	Na_2CO_3	5	34	0	0
10	**4.1**	0.5	K_2CO_3	5	29	14	100/0
11	**4.1**	0.5	NaOH	5	15	3	100/0
12	**4.1**	0.5	KOH	5	44	35	100/0
13	-	-	Cs_2CO_3	5	12	trace	-
14	-	-	-		-	-	-

[a]Reaction conditions: 1-tetralone (0.5 mmol), benzyl alcohol (0.6 mmol), *tert*-amyl alcohol (1.5 mL), catalyst, and base were heated at 135 °C for 20 h in an open system under an argon flow. [b]Conversion of 1-tetralone was determined by GC using toluene as an internal standard. [c]Isolated yields after column chromatography. [d]Reaction carried out for 12 h.

Using the optimized reaction conditions, a wide range of primary alcohols were subjected to manganese-catalyzed α-olefination of 1-tetralone (Scheme 4.3). In general, benzyl alcohols bearing electron-donating substituents such as methyl, methoxy afforded the corresponding α-alkenyl ketones in good yields with excellent conversion. Electron-rich benzyl alcohols substituted with an ortho and a meta methyl group were converted into **4.2b** and **4.2c** in excellent (90% and 89%, respectively) yields, whereas, para -methylbenzyl alcohol provided **4.2d** in 81% yield. The α-

alkenylation of 1-tetralone with 4-methoxy, 4-isopropyl, and piperonyl benzyl alcohols afforded the corresponding products **4.2e**−**4.2g** in 88%, 77%, and 65% yields, respectively. Notably, 4-methylthiolate substituted benzyl alcohol provided complete conversion under standard experimental conditions, and the corresponding product **4.2h** was obtained in 96% yield. The presence of an electronwithdrawing substituent such as 3-chloro and 4-bromo on the aryl ring of benzyl alcohol required a longer reaction time (20 h) to provide good selectivity, and the *α*-alkenyl ketones **4.2i** and **4.2j** were obtained in 54% and 78% yields, respectively. Importantly, heteroaryl methanols were tolerated in this catalytic direct *α*-alkenylation of ketones. 2-Thiophenemethanol and furfuryl alcohol provided *α*-alkenylated products **4.2k** and **4.2l** in good yields with excellent conversion. Similarly, 1-naphthalenemethanol performed well in this transformation and delivered **4.2m** in 78% isolated yield. When *α*-branched aliphatic alcohol such as 2-ethyl-1-butanol was subjected to catalysis under standard experimental conditions, *α*-alkenylated product **4.2n** was isolated in poor yields (37%). Thus, the catalyst load was increased to 0.5 mol %, which provided the product **4.2n** in 54% yield. In all these reactions, *α*-alkylated ketone products were formed in less than 5% yield.

Scheme 4.3 Manganese-Catalyzed Direct *α*-Alkenylation of 1-Tetralone Using Primary Alcohols[a]



[a]Reaction conditions: 1-tetralone (0.5 mmol), alcohol (0.6 mmol), *tert*-amyl alcohol (1.5 mL) catalyst **4.1** (0.3 mol%), and Cs_2CO_3 (5 mol%) were heated at 135 °C under open conditions with an argon flow. Reported yields correspond to isolated pure compounds. Conversion of 1-tetralone is given within parenthesis and determined by GC analysis using toluene as an internal standard. α-Alkylated ketone products were observed less than 5%, in all reactions. [b]α-alkylated ketone products were observed in 10%. [c]Reaction time of 20 h. [d]Using 0.5 mol% catalyst **4.1** and 5 mol% base

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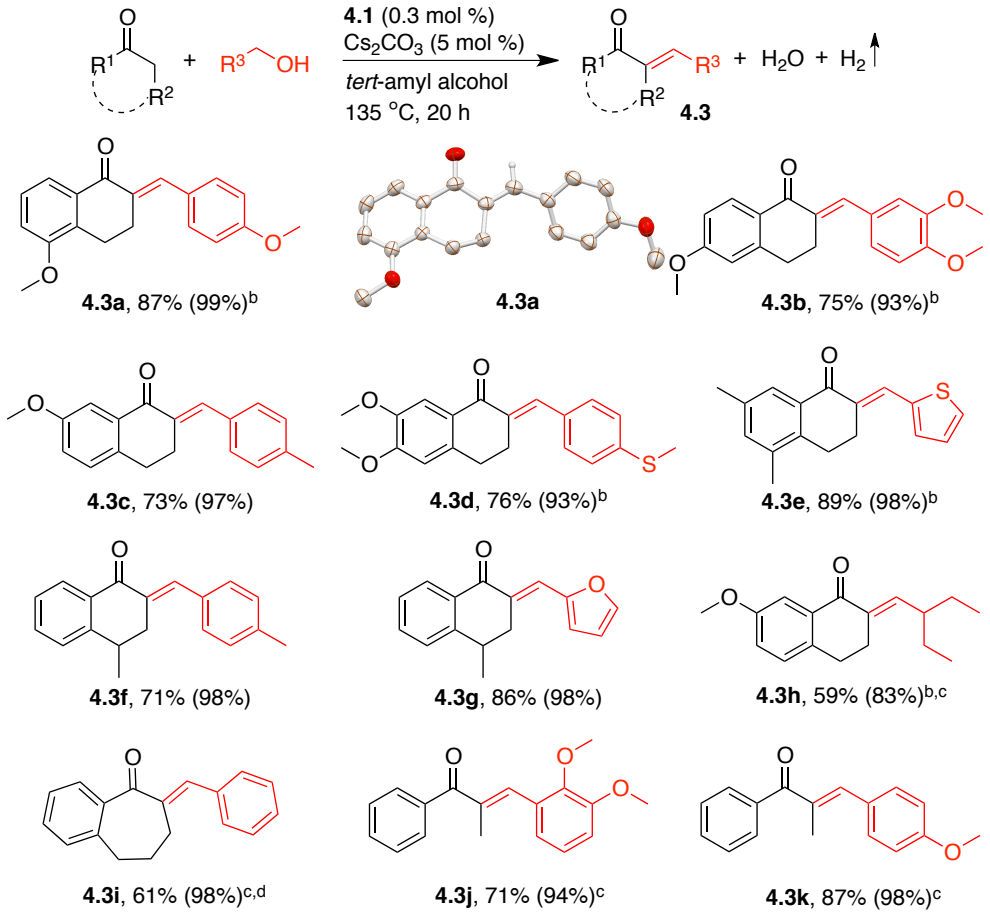
The scope of various aryl ketones with respect to the catalytic α-alkenylation reaction using different alcohols was further investigated (Scheme 4.4). In general, a variety of which provided α-alkenylated product **4.3h** in 59% yield. To expand the substrate scope beyond tetralones, 6,7,8,9- tetrahydro-5H-benzo[7]annulen-5-one was reacted

with benzyl alcohol, which delivered **4.3i** in 61% isolated yield. Remarkably, acyclic methylene ketone such as propiophenone was reacted with 2,3-dimethoxybenzyl alcohol and 4-methoxybenzyl alcohol and the corresponding *α*-alkenylated products **4.3j** and **4.3k** were obtained in 71% and 87% yields, respectively.

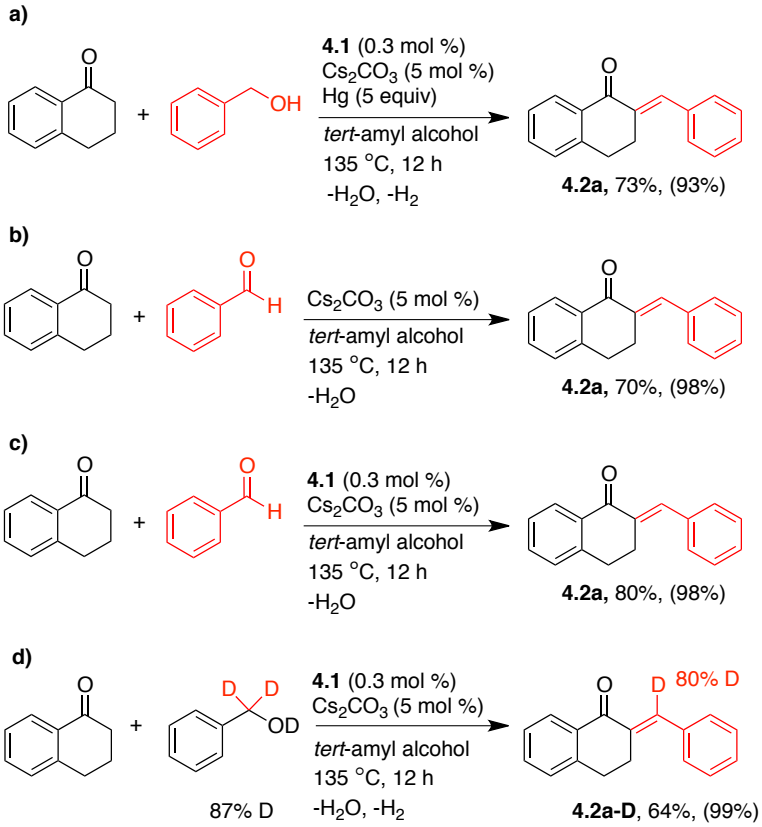
Scheme 4.4 Manganese-Catalyzed Dehydrogenative *α*-Alkenylation of Ketones Using Primary Alcohols[a]



[a]Reaction conditions: ketone (0.5 mmol), alcohol (0.6 mmol), tert-amyl alcohol (1.5 mL) catalyst **4.1** (0.3 mol%), and Cs_2CO_3 (5 mol%) were heated at 135 °C under open conditions with an argon flow. Reported yields correspond to isolated pure compounds. Conversion of ketone is given within parenthesis and determined by GC analysis using toluene as an internal standard. [b]Conversion determined from 1H NMR analysis of reaction mixture using 1,2 dibromoethane as an internal standard. [c]Catalyst **4.1** (0.6 mol%) and base (10 mol%) were used. [d]*α*-Alkylated ketone product was observed in 35%

A mercury-poisoning experiment was performed to examine the involvement of any metal nanoparticles formed from complex **4.1**. The catalytic reaction of 1-tetralone with benzyl alcohol was carried out in the presence of mercury (5 equiv, relative to 1-tetralone), which provided the corresponding alkenylated ketone **4.2a** in 73% isolated yield (against the 80% yield in the absence of mercury), indicating that the reaction proceeds with involvement of molecular intermediates (Scheme 4.5a). To probe whether the PN_5P- Mn complex **4.1** is also involved in the C−C bond formation in the aldol reaction, reaction of benzaldehyde with 1-tetralone in the presence and absence of the catalyst were performed, which resulted in formation of 80% and 70% of **4.2a**, respectively (Scheme 4.5b and 4.5c). This enhanced formation of **4.2a** is an indication that the catalyst might have moderate involvement in the key C−C bond formation process. Upon reaction of α-deuterated benzyl alcohol-d3, product **4.2a-D** was obtained in which incorporation of 80% deuterium was observed at the vinyl position (Scheme 4.5d).

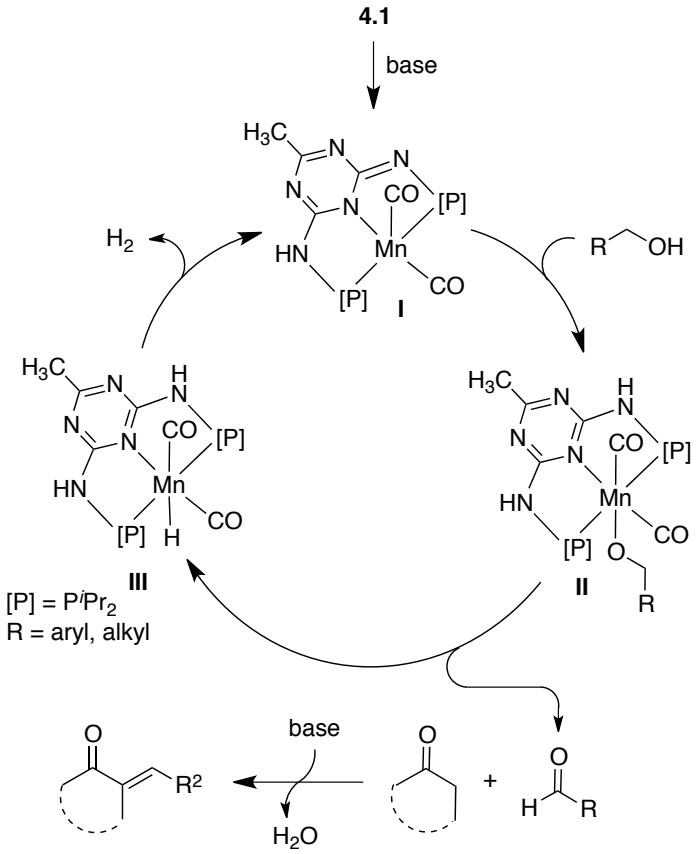
Scheme 4.5 Mechanistic Studies for the α-Alkenylation of Primary Alcohols



On the basis of these experimental observations and the previous studies involving the PN_5P manganese pincer catalyst,[12a,c,17] the plausible reaction mechanism for acceptorless dehydrogenative coupling of alcohols and ketones is proposed in Scheme 4.5 . Complex **4.1** reacts with a catalytic amount of base to generate the dearomatized coordinatively unsaturated intermediate **I**. Further this intermediate **I** reacts with alcohol to provide alkoxy-ligated manganese complex **II**, through O−H activation of alcohols. Similar manganese alkoxy complexes have been isolated previously by Milstein,[65b] Yu,[62] and Liu.[13c] β-Hydride elimination of manganese-ligated alkoxy ligand with saturated intermediate **II** provides the corresponding aldehyde and Mn-hydride complex **III**. The liberated aldehyde then undergoes aldol condensation with ketone to provide the α-alkenylated ketone and water as the byproduct. Intermediate **III** liberates H_2 to attain dearomatized intermediate **I**, completing one loop in a catalytic cycle. The aromatization and dearomatization metal−ligand cooperation in

manganese intermediates **I**–**III** maintains the same oxidation state (+1) in all intermediate complexes and plays an important role in this transformation.

Scheme 4.6 Proposed Reaction Mechanism for Dehydrogenative α-Alkenylation of Ketones Catalyzed by Manganese Pincer Complex 4.1



4.4 CONCLUSIONS

A manganese pincer complex catalyzed selective synthesis of α- alkenyl ketones by acceptorless dehydrogenative coupling of primary alcohol with ketones is demonstrated. Notably, using a minimal base metal-manganese catalyst (0.3 mol %) and a mild base Cs_2CO_3 (5 mol %), an assortment of cyclic and acyclic aryl ketones can be efficiently and selectively α-alkenylated with primary alcohols in moderate to excellent yields. Notably, under these catalytic conditions, heteroaryl, aliphatic, and

benzylic primary alcohols containing methoxy, thiomethyl, chloro, and bromo functionalities are well tolerated. Mechanistic studies confirm the involvement of an aldehyde intermediate. The acceptorless dehydrogenative coupling of alcohols and ketones proceeds via dearomatization-aromatization metal ligand cooperation. Overall, 1 equiv of water and molecular hydrogen are liberated from the reaction as the only byproducts in this environmentally benign transformation.

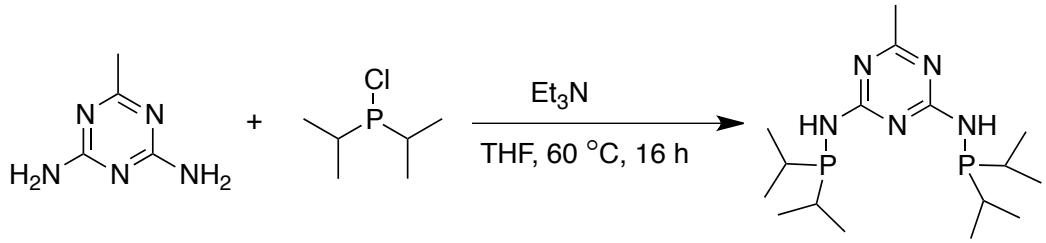
4.5 EXPERIMENTAL SECTION

General Experimental: All stoichiometric reactions were performed in nitrogen atmosphere MBRAUN glove box. All catalytic reactions were performed under nitrogen atmosphere using standard Schlenk techniques. Chemicals were purchased from Acros, Sigma-Aldrich, Alfa-aesar, Himedia chemicals and used without further purification. Dry solvents were prepared according to standard procedures.[31b] ^{1}H, ^{13}C spectra were recorded at Bruker AV-400 (^{1}H: 400 MHz, ^{13}C: 100.6 MHz) and Ascend - 700 (^{1}H: 700 MHz, ^{13}C: 176 MHz). ^{1}H and $^{13}C\{1H\}$ NMR chemical shifts were reported in ppm downfield from tetramethyl silane. All NMR Spectra were recorded at 298K. Multiplicity is abbreviated as: s, singlet; d, doublet; dd, doublet of doublets; dt, doublet of triplets; t, triplet; q, quartet; dq, doublet of quartets; td, triplet of doublets; m, multiplet; br, broad. Assignment of spectra was done based on one-dimensional (DEPT-135) NMR techniques. Mass spectra were recorded on Bruker micrOTOF-Q II Spectrometer.

Synthesis of Ligand (4-Ph)Tr(NHP(*i*Pr)$_2$)$_2$ (L4) and Synthesis of [(4-Ph)Tr(NHP(*i*Pr)$_2$)$_2$Mn(CO)$_2$Br] (Catalyst 3.1)

Ligand and complexes (**3.1)** procedure were given in chapter 3, scheme 3.5 and 3.6.[17d]

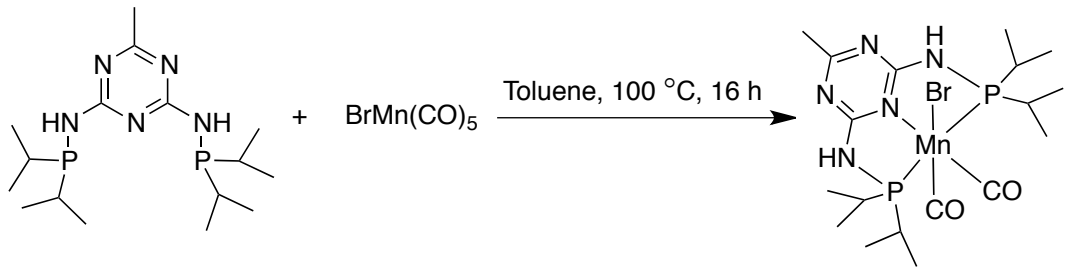
Scheme 4.7 Synthesis of Ligand (4-Me)Tr(NHP(*i*Pr)$_2$)$_2$ (L5)



Inside glove box, a 35 mL sealed tube was charged with stir bar, 2,4-diamino-6-methyl-1,3,5-triazine **(L5)** (4.0 mmol, 0.500 g) and dry THF (25 mL) under nitrogen atmosphere. The solution was cooled to 0 °C and then chlorodiisopropylphosphine (8.8 mmol, 1.394 mL) was added drop wise into the reaction mixture. Triethylamine (16.0 mmol, 2.225 mL) was added to the reaction mixture. The reaction mixture was allowed to warm to room temperature and stirred vigorously for 16 h at 60 °C. The suspension was filtered over a glass filter frit with a pad of Celite (3 cm) and washed with 10 mL of THF. The combined organic phase was concentrated in *vacuo* yielding (4-Me)Tr(NHP(*i*Pr)$_2$)$_2$ **(L5)** as a colorless solid (999 mg, 70%).

^{1}H NMR (400 MHz, $CDCl_3$): δ 5.04 (s, 2H), 2.32 (s_br, 3H), 1.81 (s_br, 4H), 1.05-1.10 (m, 24H), ppm.

Scheme 4.8 Synthesis of [(4-Me)Tr(NHP(*i*Pr)$_2$)$_2$Mn(CO)$_2$Br] (Catalyst 4.1):



In a Schlenk tube, to the orange-yellow suspension of [$MnBr(CO)_5$] (1 mmol, 275 mg) in toluene, a solution of (4-Me)Tr(NHP(*i*Pr)$_2$)$_2$ (1 mmol, 357 mg) in toluene (15 mL) was added dropwise. The suspension turned into a yellow solution within 10 min. The reaction mixture was heated to 100 °C and further stirred for 16 h under

nitrogen leading to formation of yellow precipitate. The reaction mixture was cooled to room temperature and the supernatant solution was filtered off and the precipitate was dried *in vacuo* at 100 °C to afford [(4-Me)Tr(NHP(iPr$_2$))$_2$Mn(CO)$_2$Br] (**4.1**) as a bright yellow powder (400 mg, 73%).

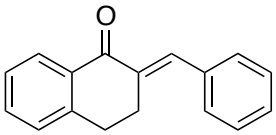
^{1}H NMR (400 MHz, C_6D_6): δ = 3.62 (s_br, 2H), 2.24 (s_br, 4H), 2.11 (s_br, 3H), 0.83-1.36 (m, br, 24H) ppm. ^{31}P{^{1}H} NMR (162 MHz, $CDCl_3$): δ 136.27. IR (KBr, pellet, cm^{-1}): 1937, 1868 ($\nu_{2CO\ symmetric} + \nu_{2CO\ antisymmetric}$).

General Procedure for α-Alkenylation of Ketones Using Alcohols:

A Schlenk flask (25 mL) was equipped with a stir bar, catalyst **4.1** (0.0015 mmol), Cs_2CO_3 (0.025 mmol), ketone (0.5 mmol), *tert*-amyl alcohol (1.5 mL) and primary alcohol (0.6 mmol) under nitrogen atmosphere in a glove box. The reaction flask was taken out of the glove box, equipped with a condenser and solution was heated at 135 °C (oil bath temperature) with stirring in an open system under argon flow for 24 h. The completion of the reaction mixture was monitored using GC analysis. After cooling to room temperature, the solvent was evaporated under reduced pressure and 0.5 mmol of internal standard (toluene) was added into the reaction mixture and then diluted with 1.0 mL of acetone. An aliquot of the solution was passed through a small Celite plug and analyzed by GC. The solvent was evaporated under reduced pressure and crude reaction mixture was purified by column chromatography over silica-gel (60-120 mesh) using ethyl acetate /pet ether mixture as an eluent. The conversion of ketone was calculated using GC analysis and yields of pure products were determined after column chromatography.

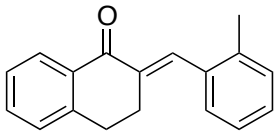
Spectral Data of α-Alkenylated of Ketone Products:

(*E*)-2-benzylidene-3,4-dihydronaphthalen-1(2*H*)-one[20] **(4.2a)**: White solid.



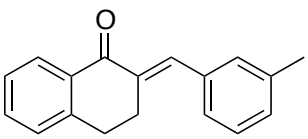
(Olefination:alkylation ratio = 97:3). Yield (94 mg, 80%). IR (DCM): 3057, 3024, 2932, 2844, 1667, 1603, 1490, 1456, 1446, 1314, 1297, 1247, 1222, 1156, 1136, 1023, 950, 755, 739, 706 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.04 (d, J = 7.6 Hz, 1H), 7.78 (s, 1H), 7.31-7.40 (m, 4H), 7.23-7.29 (m, 3H), 7.14 (d, J = 7.2 Hz, 1H), 3.02 (t, J = 7.0 Hz, 2H), 2.83 (t, J = 7.0 Hz, 2H). $^{13}C\{^{1}H\}$ NMR (100.6 MHz, $CDCl_3$): δ 187.9, 143.3, 136.7, 135.9, 135.5, 133.5, 133.3, 129.9, 128.6, 128.5, 128.3, 127.1, 28.9, 27.2. HRMS (ESI) m/z calcd for $C_{17}H_{15}O$ $(M+H)^+$: 235.1117, found: 235.1126.

(*E*)-2-(2-methylbenzylidene)-3,4-dihydronaphthalen-1(2*H*)-one (4.2b): Yellow



oil. (Olefination:alkylation ratio = 97:3). Yield (112 mg, 90%). IR (DCM): 3063, 3021, 2944, 2844, 1668, 1603, 1482, 1313, 1298, 1247, 1224, 1156, 1137, 1023, 951, 782, 748, 723, 705 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.08 (d, J = 7.2 Hz, 1H), 7.83 (s, 1H), 7.39-7.43 (m, 1H), 7.27-7.31 (m, 1H), 7.15-7.17 (m, 5H), 2.85-2.89 (m, 4H), 2.26 (s, 3H). $^{13}C\{^{1}H\}$ NMR (100.6 MHz, $CDCl_3$): δ 188.1, 143.6, 137.9, 136.1, 135.8, 135.2, 133.6, 133.5, 130.4, 129.0, 128.6, 128.43, 128.39, 127.1, 125.6, 29.4, 27.4, 20.2. HRMS (ESI) m/z calcd for $C_{18}H_{17}O$ $(M+H)^+$: 249.1274, found: 249.1284.

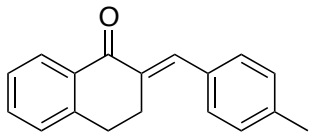
(*E*)-2-(3-methylbenzylidene)-3,4-dihydronaphthalen-1(2*H*)-one (4.2c): Yellow



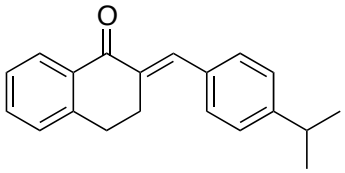
solid. (Olefination:alkylation ratio = 97:3). Yield (110 mg, 89%). IR (DCM): 3026, 2921, 2844, 1667, 1602, 1456, 1317, 1297, 1235, 1156, 1136, 960, 780, 758, 705 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.05 (d, J = 7.6 Hz, 1H), 7.76 (s, 1H), 7.37-7.41 (m, 1H), 7.20-7.29 (m,

2H), 7.15-7.17 (m, 3H), 7.08 (d, J = 7.2 Hz, 1H), 3.02-3.06 (m, 2H), 2.85 (t, J = 6.4 Hz, 2H), 2.31 (s, 3H). $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$): δ 188.0, 143.4, 138.2, 137.0, 135.9, 135.4, 133.6, 133.3, 130.7, 129.5, 128.4, 128.32, 128.28, 127.1, 127.0, 29.0, 27.3, 21.6. HRMS (ESI) m/z calcd for $C_{18}H_{17}O$ $(M+H)^+$: 249.1274, found: 249.1266.

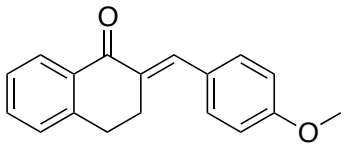
(*E*)-2-(4-methylbenzylidene)-3,4-dihydronaphthalen-1(2*H*)-one[21] **(4.2d)**: White solid. (Olefination:alkylation ratio = 96:4). Yield (101 mg, 81%). IR (DCM): 3051, 2959, 1662, 1601, 1586, 1509, 1456, 1310, 1298, 1227, 1137, 955, 949, 816, 740 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 8.06 (d, J = 7.6 Hz, 1H), 7.79 (s, 1H), 7.40-7.43 (m, 1H), 7.28-7.31 (m, 3H), 7.15-7.19 (m, 3H), 3.05-3.09 (m, 2H), 2.87 (t, J = 6.4 Hz, 2H), 2.32 (s, 3H). $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$): δ 188.1, 143.3, 138.9, 136.9, 134.8, 133.7, 133.3, 133.1, 130.1, 129.3, 128.34, 128.27, 127.1, 29.0, 27.4, 21.5. HRMS (ESI) m/z calcd for $C_{18}H_{16}ONa$ $(M+Na)^+$: 271.1093, found: 271.1096.



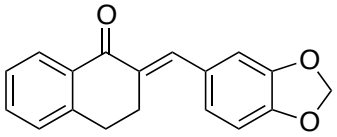
(*E*)-2-(4-isopropylbenzylidene)-3,4-dihydronaphthalen-1(2*H*)-one[22] **(4.2e)**: Yellow oil. (Olefination:alkylation ratio = 93:7). Yield (121 mg, 88%). IR (DCM): 2959, 2930, 2869, 1667, 1604, 1506, 1456, 1295, 1314, 1248, 1223, 1156, 1136, 950, 739 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 8.05 (d, J = 7.6 Hz, 1H), 7.78 (s, 1H), 7.37-7.41 (m, 1H), 7.27-7.32 (m, 3H), 7.15-7.21 (m, 3H), 3.07 (t, J = 6.0 Hz, 2H), 2.84-2.87 (m, 3H), 1.19 (d, J = 6.8 Hz, 6H). $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$): δ 188.0, 149.8, 143.3, 136.9, 134.8, 133.7, 133.5, 133.3, 130.2, 128.3, 128.2, 127.1, 126.7, 34.1, 29.0, 27.4, 24.0. HRMS (ESI) m/z calcd for $C_{20}H_{21}O$ $(M+H)^+$: 277.1587, found: 277.1590.



(*E*)-2-(4-methoxybenzylidene)-3,4-dihydronaphthalen-1(2*H*)-one[21] **(4.2f)**: Yellow solid. (Olefination:alkylation ratio = 93:7). Yield (102 mg, 77%). IR (DCM): 2946, 2908, 2835, 1665, 1602, 1570, 1509, 1454, 1439, 1301, 1253, 1177, 1032, 951, 840, 795 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.04 (d, J = 6.4 Hz, 1H), 7.77 (s, 1H), 7.34-7.41 (m, 3H), 7.26-7.29 (m, 1H), 7.15-7.17 (m, 1H), 6.87 (d, J = 8.4 Hz, 2H), 3.77 (s, 3H), 3.06 (d, J = 6.4 Hz, 2H), 2.86 (t, J = 6.4 Hz, 2H). $^{13}C\{^{1}H\}$ NMR (100.6 MHz, $CDCl_3$): δ 188.0, 160.1, 143.2, 136.8, 133.8, 133.7, 133.2, 131.9, 128.5, 128.3, 128.2, 127.1, 114.1, 55.5, 28.9, 27.3. HRMS (ESI) m/z calcd for $C_{18}H_{17}O_2$ $(M+H)^+$: 265.1223, found: 265.1199.

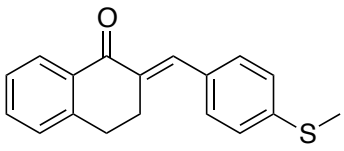


(*E*)-2-(benzo[*d*][1,3]dioxol-5-ylmethylene)-3,4-dihydronaphthalen-1(2*H*)-one[21] **(4.2g)**: Yellow solid. (Olefination:alkylation ratio = 95:5). Yield (90 mg, 65%). IR (DCM): 2905, 2843, 1664, 1600, 1586, 1502, 1489, 1444, 1331, 1261, 1240, 1136, 1038, 916, 775 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.02 (d, J = 7.6 Hz, 1H), 7.70 (s, 1H), 7.39 (t, J = 7.6 Hz, 1H), 7.26 (t, J = 7.6 Hz, 1H), 7.14-7.17 (m, 1H), 6.86-6.90 (m, 2H), 6.77 (d, J = 8.0 Hz, 1H), 5.91 (s, 2H), 3.03 (t, J = 6.4 Hz, 2H), 2.85 (t, J = 6.4 Hz, 2H). $^{13}C\{^{1}H\}$ NMR (100.6 MHz, $CDCl_3$): δ 187.8, 148.1, 147.8, 143.1, 136.8, 134.1, 133.7, 133.3, 130.0, 128.3, 128.2, 127.1, 125.2, 109.9, 108.6, 101.5, 28.8, 27.4. HRMS (ESI) m/z calcd for $C_{18}H_{15}O_3$ $(M+H)^+$: 279.1016, found: 279.1012.

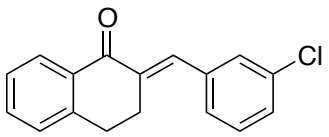


(*E*)-2-(4-(methylthio)benzylidene)-3,4-dihydronaphthalen-1(2*H*)-one (4.2h): Yellow solid. (Olefination:alkylation ratio = 98:2). Yield (134 mg, 96%). IR (DCM):

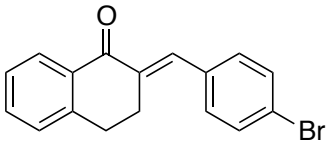
2944, 2925, 2848, 1666, 1591, 1454, 1439, 1320, 1299, 1123, 958, 837, 782, 740 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 8.04 (d, J = 7.6 Hz, 1H), 7.74 (s, 1H), 7.39 (t, J = 1.0 Hz, 1H), 7.27-7.30 (m, 3H), 7.15-7.20 (m, 3H), 3.04 (t, J = 6.0 Hz, 2H), 2.85 (t, J = 6.4 Hz, 2H), 2.42 (s, 3H). $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$): δ 187.8, 143.2, 140.0, 136.3, 134.9, 133.6, 133.3, 132.4, 130.5, 128.3, 128.2, 127.1, 125.9, 28.9, 27.4, 15.4. HRMS (ESI) m/z calcd for $C_{18}H_{17}OS$ $(M+H)^+$: 281.0995, found: 281.1008.



(*E*)-2-(3-chlorobenzylidene)-3,4-dihydronaphthalen-1(2*H*)-one[23] **(4.2i)**: Yellow solid. (Olefination:alkylation ratio = 96:4). Yield (72 mg, 54%). IR (DCM): 3063, 2938, 2842, 1670, 1593, 1474, 1455, 1315, 1296, 1248, 1222, 1156, 1136, 997, 958, 797, 739 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 8.05 (d, J = 7.6 Hz, 1H), 7.70 (s, 1H), 7.42 (t, J = 7.2 Hz, 1H), 7.21-7.32 (m, 5H), 7.17-7.18 (m, 1H), 3.01 (t, J = 6.4 Hz, 2H), 2.88 (t, J = 6.8 Hz, 2H). $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$): δ 187.7, 143.3, 137.8, 136.8, 135.0, 134.5, 133.6, 133.4, 129.8, 129.6, 128.6, 128.40, 128.37, 128.1, 127.2, 28.9, 27.3. HRMS (ESI) m/z calcd for $C_{17}H_{13}OClNa$ $(M+Na)^+$: 291.0547, found: 291.0539.

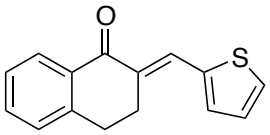


(*E*)-2-(4-bromobenzylidene)-3,4-dihydronaphthalen-1(2*H*)-one[23] **(4.2j)**: White solid. (Olefination:alkylation ratio =). Yield (122 mg, 78%). IR (DCM): 2945, 2916, 2848, 1667, 1603, 1592, 1455, 1439, 1422, 1399, 960, 839, 742 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 8.05 (d, J = 8.0 Hz, 1H), 7.70 (s, 1H), 7.29-7.48 (m, 4H), 7.22 (d, J = 8.0 Hz, 2H), 7.17 (d, J = 6.8 Hz, 1H), 3.01 (t, J = 6.0 Hz, 2H), 2.87 (t, J = 6.0 Hz, 2H). $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$): δ 187.7, 143.3, 136.2, 135.4, 134.8, 133.54,



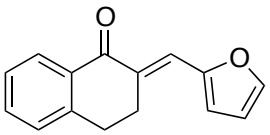
133.46, 131.8, 131.5, 128.4, 128.3, 127.2, 122.8, 28.9, 27.3. HRMS (ESI) m/z calcd for $C_{17}H_{14}OBr$ $(M+H)^+$: 313.0223, found: 313.0231.

(*E*)-2-(thiophen-2-ylmethylene)-3,4-dihydronaphthalen-1(2*H*)-one[81] **(4.2k)**: Yellow solid. (Olefination:alkylation ratio = 99:1). Yield (111 mg, 93%). IR (DCM):



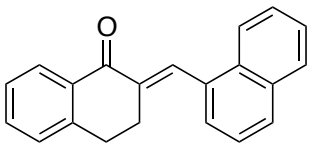
3107, 3066, 2931, 2900, 2843, 1660, 1577, 1455, 1437, 1311, 1246, 1222, 1132, 956, 735, 712 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 8.02 (d, J = 7.6 Hz, 1H), 7.97 (s, 1H), 7.39-7.44 (m, 2H), 7.26-7.32 (m, 2H), 7.19 (d, 1H), 7.05-7.07 (m, 1H), 3.13 (t, J = 6.8 Hz, 2H), 2.95 (t, J = 6.4 Hz, 2H). $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$): δ 187.3, 143.1, 139.2, 133.8, 133.4, 133.2, 132.0, 129.54, 129.49, 128.25, 128.20, 127.7, 127.1, 28.2, 27.2. HRMS (ESI) m/z calcd for $C_{15}H_{13}OS$ $(M+H)^+$: 241.0682, found: 241.0679.

(*E*)-2-(furan-2-ylmethylene)-3,4-dihydronaphthalen-1(2*H*)-one[22] **(4.2l)**: Yellow solid. (Olefination:alkylation ratio = 93:7). Yield (95 mg, 85%). IR (DCM): 3134,



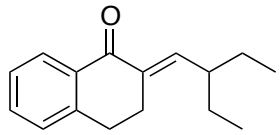
2940, 2844, 1662, 1603, 1473, 1317, 1297, 1246, 1172, 947, 919, 739 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 8.02 (d, J = 7.6 Hz, 1H), 7.51 (s, 1H), 7.48 (s, 1H), 7.37-7.42 (m, 1H), 7.26 (t, J = 7.6 Hz, 1H), 7.17-7.19 (m, 1H), 6.61 (d, J = 7.6 Hz, 1H), 6.43-6.44 (m, 1H), 3.24 (t, J = 6.0 Hz, 2H), 2.92 (t, J = 6.0 Hz, 2H). $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$): δ 187.5, 152.6, 144.5, 143.6, 133.7, 133.2, 132.0, 128.24, 128.22, 127.0, 122.9, 116.7, 112.3, 28.5, 26.8. HRMS (ESI) m/z calcd for $C_{15}H_{13}O_2$ $(M+H)^+$: 225.0910, found: 225.0905.

(*E*)-2-(naphthalen-1-ylmethylene)-3,4-dihydronaphthalen-1(2*H*)-one (4.2m):



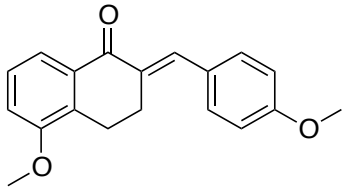
Yellow solid. (Olefination:alkylation ratio = 98:2). Yield (111 mg, 78%). IR (DCM): 3052, 3042, 2956, 2906, 2848, 1660, 1601, 1589, 1554, 1328, 1262, 1134, 1025, 804, 795, 779 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 8.29 (s, 1H), 8.12 (d, J = 7.6 Hz, 1H), 7.91-7.93 (m, 1H), 7.76-7.81 (m, 2H), 7.39-7.44 (m, 4H), 7.28-7.34 (m, 2H), 7.15 (d, J = 7.6 Hz, 1H), 2.87-2.90 (m, 2H), 2.80-2.83 (m, 2H). $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$): δ 187.9, 143.7, 137.6, 134.9, 133.65, 133.58, 133.5, 133.2, 132.1, 129.0, 128.7, 128.5, 128.4, 127.2, 126.9, 126.6, 126.3, 125.2, 125.0, 29.3, 27.8. HRMS (ESI) m/z calcd for $C_{21}H_{17}O$ $(M+H)^+$: 285.1274, found: 285.1291.

(*E*)-2-(2-ethylbutylidene)-3,4-dihydronaphthalen-1(2*H*)-one (4.2n): Colorless oil.



(Olefination:alkylation ratio = 95:5). Yield (61 mg, 54%). IR (DCM): 2960, 2928, 2872, 2854, 1676, 1621, 1598, 1455, 1311, 1295, 1235, 1119, 918, 739, 708 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 8.04 (d, J = 7.6 Hz, 1H), 7.39 (t, J = 7.2 Hz, 1H), 7.26 (t, J = 7.2 Hz, 1H), 7.16-7.19 (m, 1H), 6.60 (d, J = 10.8 Hz, 1H), 2.88 (t, J = 6.8 Hz, 2H), 2.73 (t, J = 6.4 Hz, 2H), 2.18-2.24 (m, 1H), 1.46-1.54 (m, 2H), 1.25-1.33 (m, 2H), 0.79 (t, J = 7.2 Hz, 6H). $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$): δ 187.6, 144.7, 143.8, 135.5, 133.8, 133.1, 128.4, 128.3, 127.0, 42.0, 29.5, 28.0, 26.4, 12.1. HRMS (ESI) m/z calcd for $C_{16}H_{21}O$ $(M+H)^+$: 229.1587, found: 229.1574.

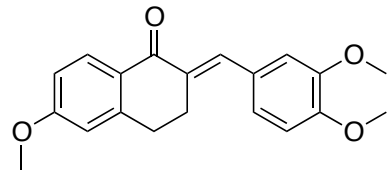
(*E*)-5-methoxy-2-(4-methoxybenzylidene)-3,4-dihydronaphthalen-1(2*H*)-one



(4.3a): Yellow solid. (Olefination:alkylation ratio = 95:5). Yield (128 mg, 87%). IR (DCM): 2932, 2836,

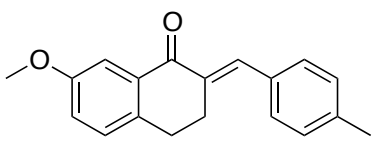
1664, 1600, 1583, 1510, 1472, 1322, 1300, 1260, 1224, 1150, 1026, 971, 855, 833, 744 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.81 (s, 1H), 7.76 (d, J = 8.0 Hz, 1H), 7.43 (d, J = 8.8 Hz, 2H), 7.31 (t, J = 8.0 Hz, 1H), 7.03 (d, J = 8.0 Hz, 1H), 6.95 (d, J = 8.8 Hz, 2H), 3.87 (s, 3H), 3.85 (s, 3H), 3.10 (t, J = 5.6 Hz, 2H), 2.92 (t, J = 6.4 Hz, 2H). $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$): δ 188.2, 160.0, 156.4, 136.4, 134.7, 133.7, 132.2, 131.8, 128.6, 127.2, 120.0, 114.3, 114.1, 55.8, 55.4, 26.6, 21.5. HRMS (ESI) m/z calcd for $C_{19}H_{19}O_3$ $(M+H)^+$: 295.1329, found: 295.1326.

(*E*)-2-(3,4-dimethoxybenzylidene)-6-methoxy-3,4-dihydronaphthalen-1(2*H*)-one



(4.3b): Yellow solid. (Olefination:alkylation ratio = 95:5). Yield (121 mg, 75%). IR (DCM): 3000, 2936, 2836, 1658, 1605, 1514, 1463, 1326, 1296, 1257, 1023, 971, 852, 766 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 8.10 (d, J = 8.8 Hz, 1H), 7.79 (s, 1H), 7.05 (d, J = 8.0 Hz, 1H), 6.97 (s, 1H), 6.85-6.91 (m, 2H), 6.70 (s, 1H), 3.91 (s, 3H), 3.90 (s, 3H), 3.86 (s, 3H), 3.13 (t, J = 6.0 Hz, 2H), 2.91 (t, J = 6.4 Hz, 2H). $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$): δ 186.8, 163.6, 149.5, 148.8, 145.6, 136.2, 134.1, 130.8, 128.9, 127.3, 123.2, 113.3, 112.3, 111.0, 56.0, 55.5, 29.3, 27.4. HRMS (ESI) m/z calcd for $C_{20}H_{21}O_4$ $(M+H)^+$: 325.1434, found: 325.1416.

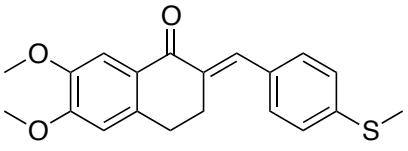
(*E*)-7-methoxy-2-(4-methylbenzylidene)-3,4-dihydronaphthalen-1(2*H*)-one



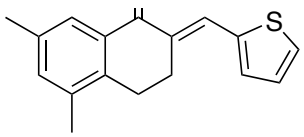
(4.3c): Yellow solid. (Olefination:alkylation ratio = 95:5). Yield (101 mg, 73%). IR (DCM): 2962, 1664, 1590, 1493, 1325, 1199, 1032, 828, 763 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.77 (s, 1H), 7.54 (d, J = 2.4 Hz, 1H), 7.28 (d, J = 8.0 Hz,

2H), 7.14-7.18 (m, 2H), 7.08 (d, J = 8.0 Hz, 1H), 6.97-7.00 (m, 1H), 3.79 (s, 3H), 3.03 (t, J = 5.6 Hz, 2H), 2.80 (t, J = 6.0 Hz, 2H), 2.31 (s, 3H). $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$): δ 188.0, 158.8, 138.9, 137.0, 136.0, 134.8, 134.5, 133.1, 130.1, 129.5, 129.3, 121.5, 110.4, 55.7, 28.2, 27.6, 21.5. HRMS (ESI) m/z calcd for $C_{19}H_{19}O_2$ $(M+H)^+$: 279.1380, found: 279.1372.

(*E*)-6,7-dimethoxy-2-(4-(methylthio)benzylidene)-3,4-dihydronaphthalen-1(2*H*)-one (4.3d): Yellow solid. (Olefination:alkylation ratio = 95:5). Yield (129 mg, 76%). IR (DCM): 2933, 2837, 1652, 1602, 1581, 1508, 1363, 1267, 1237, 1204, 1155, 1031, 885, 778, 577 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.76 (s, 1H), 7.62 (s, 1H), 7.36 (d, J = 8.4 Hz, 2H), 7.25-7.27 (m, 2H), 6.67 (s, 1H), 3.94 (s, 6H), 3.11 (t, J = 6.0 Hz, 2H), 2.88 (t, J = 6.8 Hz, 2H), 2.50 (d, J = 1.0 Hz, 3H). $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$): δ 186.7, 153.6, 148.4, 139.6, 138.2, 135.6, 135.0, 132.7, 130.4, 126.7, 126.0, 110.0, 109.8, 56.2, 28.7, 27.7, 15.5. HRMS (ESI) m/z calcd for $C_{20}H_{21}O_3S$ $(M+H)^+$: 341.1206, found: 341.1222.

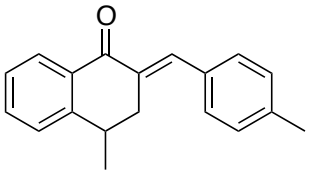


(*E*)-5,7-dimethyl-2-(thiophen-2-ylmethylene)-3,4-dihydronaphthalen-1(2*H*)-one (4.3e): Orange solid. (Olefination:alkylation ratio = 98:2). Yield (119 mg, 89%). IR (DCM): 2938, 1655, 1610, 1583, 1474, 1264, 1182, 1168, 888, 726, 670 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 8.00 (s, 1H), 7.81 (s, 1H), 7.50 (d, J = 5.2 Hz, 1H), 7.38 (d, J = 3.2 Hz, 1H), 7.20 (s, 1H), 7.12-7.14 (m, 1H), 3.19 (t, J = 6.4 Hz, 2H), 2.92 (t, J = 6.4 Hz, 2H), 2.36 (s, 3H), 2.32 (s, 3H). $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$): δ 187.9, 139.4, 138.7, 136.2, 135.8, 135.5, 133.8, 133.2, 132.1, 129.2, 128.9, 127.7,



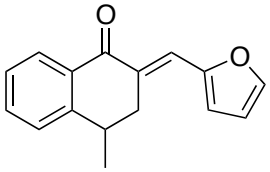
126.4, 26.9, 24.3, 21.0, 19.4. HRMS (ESI) m/z calcd for $C_{17}H_{17}OS$ $(M+H)^+$: 269.0995, found: 269.0980.

(*E*)-4-methyl-2-(4-methylbenzylidene)-3,4-dihydronaphthalen-1(2*H*)-one (4.3f):

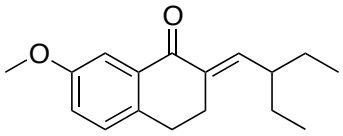


Yellow solid. (Olefination:alkylation ratio = (93 mg, 71%). IR (DCM): 2957, 2919, 2848, 1667, 1605, 1510, 1458, 1315, 1302, 1266, 1219, 1183, 1142, 961, 786, 759 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 8.04 (d, J = 7.6 Hz, 1H), 7.85 (s, 1H), 7.43 (t, J = 7.2 Hz, 1H), 7.26-7.29 (m, 3H), 7.20-7.22 (m, 1H), 7.14-7.17 (m, 2H), 2.93-3.09 (m, 3H), 2.31 (s, 3H), 1.19 (d, J = 6.8 Hz, 3H). $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$): δ 187.9, 148.3, 138.9, 138.0, 133.5, 133.3, 133.1, 132.8, 130.1, 129.3, 128.4, 127.02, 126.97, 34.7, 33.2, 22.1, 21.5. HRMS (ESI) m/z calcd for $C_{19}H_{19}O$ $(M+H)^+$: 263.1430, found: 263.1438.

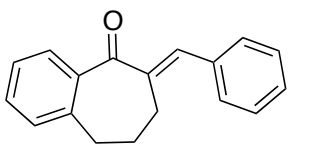
(*E*)-2-(furan-2-ylmethylene)-4-methyl-3,4-dihydronaphthalen-1(2*H*)-one (4.3g): Yellow oil. (Olefination:alkylation ratio = 95:5). Yield (102 mg, 86%). IR (DCM): 2960, 2923, 2866, 1691, 1667, 1478, 1458, 1314, 1264, 1018, 789, 757 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 8.09-8.11 (m, 1H), 7.65 (s, 1H), 7.57 (d, J = 1.6 Hz, 1H), 7.49-7.51 (m, 1H), 7.30-7.37 (m, 2H), 6.71 (d, J = 3.6 Hz, 1H), 6.51-6.53 (m, 1H), 3.17-3.36 (m, 3H), 1.33 (d, J = 7.2 Hz, 3H). $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$): δ 187.5, 152.7, 148.7, 144.5, 133.4, 132.7, 130.6, 128.4, 127.1, 127.0, 124.0, 116.7, 112.3, 34.2, 33.0, 22.4. HRMS (ESI) m/z calcd for $C_{16}H_{15}O_2$ $(M+H)^+$: 239.1067, found: 239.1051.



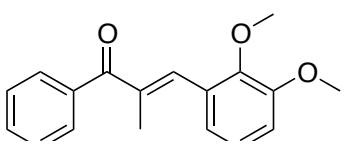
(*E*)-2-(2-ethylbutylidene)-7-methoxy-3,4-dihydronaphthalen-1 (2*H*)-one (4.3h): Colorless oil. (Olefination:alkylation ratio = 95:5). Yield (76 mg, 59%). IR (DCM): 2959, 2926, 2872, 2853, 1675, 1604, 1495, 1462, 1422, 1321, 1285, 1249, 1036, 764 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.61 (d, J = 2.8 Hz, 1H), 7.15 (d, J = 8.4 Hz, 1H), 7.04 (dd, J_1 = 8.4 Hz, J_2 = 2.8 Hz, 1H), 6.65 (d, J = 10.8 Hz, 1H), 3.85 (s, 3H), 2.87-2.90 (m, 2H), 2.76-2.79 (m, 2H), 2.24-2.33 (m, 1H), 1.53-1.58 (m, 2H), 1.30-1.40 (m, 2H), 0.86 (t, J = 7.6 Hz, 6H). $^{13}C\{^{1}H\}$ NMR (100.6 MHz, $CDCl_3$): δ 187.6, 158.7, 144.8, 136.6, 135.5, 134.6, 129.6, 121.3, 110.5, 55.7, 42.0, 28.7, 28.0, 26.6, 12.1. HRMS (ESI) m/z calcd for $C_{17}H_{23}O_2$ $(M+H)^+$: 259.1693, found: 259.1693.



(*E*)-6-benzylidene-6,7,8,9-tetrahydro-5*H*-benzo[7]annulen-5-one (4.3i): Yellow oil. (Olefination:alkylation ratio = 65:35). Yield (75 mg, 61%). IR (DCM): 2936, 2860, 1665, 1493, 1450, 1297, 1266, 1252, 1210, 971, 766, 744 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.78 (s, 1H), 7.72 (d, J = 8.4 Hz, 1H), 7.42-7.45 (m, 2H), 7.34-7.40 (m, 3H), 7.28-7.31 (m, 2H), 7.14 (d, J = 7.6 Hz, 1H), 2.84 (t, J = 6.8 Hz, 2H), 2.54 (t, J = 7.2 Hz, 2H), 2.54 (m, 2H). $^{13}C\{^{1}H\}$ NMR (100.6 MHz, $CDCl_3$): δ 198.2, 139.8, 138.9, 138.2, 138.0, 135.9, 132.6, 129.6, 129.3, 129.1, 128.8, 128.7, 127.2, 31.8, 26.8, 25.0. HRMS (ESI) m/z calcd for $C_{18}H_{17}O$ $(M+H)^+$: 249.1274, found: 249.1264.

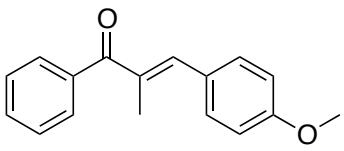


(*E*)-3-(2,3-dimethoxyphenyl)-2-methyl-1-phenylprop-2-en-1-one (4.3j): Colorless

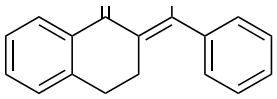


oil. (Olefination:alkylation ratio = 96:4). Yield (100 mg, 71%). IR (DCM): 1225, 1078, 1032, 1014, 795, 759 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.80 (d, J = 7.6 Hz, 2H), 7.54 (t, J = 7.2 Hz, 1H), 7.45 (t, J = 7.2 Hz, 2H), 7.36 (s, 1H), 7.10 (t, J = 8.0 Hz, 1H), 7.02 (d, J = 7.6 Hz, 1H), 6.94 (d, J = 8.4 Hz, 1H), 3.87 (s, 3H), 3.74 (s, 3H), 2.18 (s, 3H). $^{13}C\{^1H\}$ NMR (100.6 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. HRMS (ESI) m/z calcd for $C_{18}H_{18}O_3Na$ $(M+Na)^+$: 305.1148, found: 305.1139.

(*E*)-3-(4-methoxyphenyl)-2-methyl-1-phenylprop-2-en-1-one (4.3k): Colorless oil. (Olefination:alkylation ratio = 96:4). Yield (110 mg, 87%). IR (DCM): 3057, 2929, 2839, 1667, 1640, 1602, 1510, 1490, 1456, 1318, 1297, 1254, 1176, 1030, 1014, 755 cm^{-1}. ^1H 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). $^{13}C\{^1H\}$ NMR (100.6 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. HRMS (ESI) m/z calcd for $C_{17}H_{17}O_2$ $(M+H)^+$: 253.1223, found: 253.1228.



(*E*)-2-benzylidene-3,4-dihydronaphthalen-1(2*H*)-one[20] (**4.2a-D**): White solid. (Olefination:alkylation ratio = 86:14). Yield (74 mg, 64%). IR (DCM): 3056, 3023, 2931, 2844, 1667, 1602, 1493, 1455, 1443, 1299, 1247, 1223, 1156, 1023, 788, 745, 707 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 8.05 (d, J = 8.0 Hz, 1H), 7.79 (s, 1H), 7.25-7.42 (m, 7H), 7.16 (d, J = 7.2 Hz, 1H), 3.05 (t, J = 6.8 Hz, 2H), 2.86 (t, J = 6.4 Hz, 2H). $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$): δ 188.0, 143.3, 136.8, 136.0, 135.9, 135.6,



135.5, 133.5, 133.3, 129.9, 128.6, 128.3, 127.1, 28.9, 27.2. HRMS (ESI) m/z calcd for $C_{17}H_{14}DO$ $(M+H)^+$: 236.1180, found: 236.1183.

Mechanistic Studies for the α- Alkenylation of Ketones:

Experimental Procedure for Scheme 4.5a:

A Schlenk flask (25 mL) was equipped with a stir bar, catalyst **4.1** (0.0015 mmol), Cs_2CO_3 (0.025 mmol), tetralone (0.5 mmol), *tert*-amyl alcohol (1.5 mL), primary alcohol (0.6 mmol) and Hg (2.5 mmol) under nitrogen atmosphere in a glove box. The reaction flask was taken out of the glove box, equipped with a condenser and solution was heated at 135 °C (oil bath temperature) with stirring in an open system under argon flow for 24 h. After completion of reaction, the reaction mixture was filtered through a pad of Celite to remove the mercury metal. After filtration the solvent was evaporated under reduced pressure and 0.5 mmol of internal standard (toluene) was added into the reaction mixture and then diluted with 1.0 mL of acetone. An aliquot of the solution was passed through a small Celite plug and analyzed by GC. The solvent was evaporated under reduced pressure and crude reaction mixture was purified by column chromatography over silica-gel (60-120 mesh) using ethyl acetate /pet ether mixture as an eluent. The conversion of tetralone was calculated using GC analysis and yield of pure product **4.2a** was determined after column chromatography.

Experimental Procedure for Scheme 4.5b:

To an oven dried Schlenk tube Cs_2CO_3 (0.025 mmol), tetralone (0.5 mmol), *tert*-amyl alcohol (1.5 mL) and benzaldehyde (0.6 mmol) were added under nitrogen atmosphere in a glove box and equipped with a stir bar. The reaction flask was taken out of the glove box, equipped with a condenser and solution was heated at 135 °C (oil bath temperature) with stirring in an open system under argon flow for 12 h. After

cooling to room temperature, the solvent was evaporated under reduced pressure and 0.5 mmol of internal standard (toluene) was added into the reaction mixture and then diluted with 1.0 mL of acetone. An aliquot of the solution was passed through a small Celite plug and analyzed by GC. The solvent was evaporated under reduced pressure and crude reaction mixture was purified by column chromatography over silica-gel (60-120 mesh) using ethyl acetate /pet ether mixture as an eluent. The conversion of tetralone was calculated using GC analysis and yields of pure product was determined after column chromatography.

Experimental Procedure for Scheme 4.5c:

To an oven dried Schlenk tube catalyst **4.1** (0.0015 mmol), Cs_2CO_3 (0.025 mmol), ketone (0.5 mmol), *tert*-amyl alcohol (1.5 mL) and benzaldehyde (0.6 mmol) were added under nitrogen atmosphere in a glove box and equipped with a stir bar. The reaction flask was taken out of the glove box, equipped with a condenser and solution was heated at 135 °C (oil bath temperature) with stirring in an open system under argon flow for 12 h. The completion of the reaction was monitored from NMR analysis using 1,2-dibromoethane as an internal standard. The solvent was evaporated under reduced pressure and crude reaction mixture was purified by column chromatography over silica-gel (60-120 mesh) using ethyl acetate /pet ether mixture as an eluent. The conversion of tetralone was calculated using NMR analysis and yield of pure product was determined after column chromatography.

Experimental Procedure for Scheme 4.5d:

To an oven dried Schlenk tube catalyst **4.1** (0.0015 mmol), Cs_2CO_3 (0.025 mmol), tetralone (0.5 mmol), *tert*-amyl alcohol (1.5 mL) and benzyl alcohol-d_3 (0.6 mmol, α-D = 87%) were added under nitrogen atmosphere in a glove box and equipped with a stir bar. The reaction flask was taken out of the glove box, equipped with a condenser

and solution was heated at 135 °C (oil bath temperature) with stirring in an open system under argon flow for 12 h. The completion of the reaction was monitored using GC analysis. After cooling to room temperature, the solvent was evaporated under reduced pressure and 0.5 mmol of internal standard (toluene) was added into the reaction mixture and then diluted with 1.0 mL of acetone. An aliquot of the solution was passed through a small Celite plug and analyzed by GC. The solvent was evaporated under reduced pressure and crude reaction mixture was purified by column chromatography over silica-gel (60-120 mesh) using ethyl acetate /pet ether mixture as an eluent. The conversion of 1-tetralone was calculated using GC analysis and yield of pure product was determined after column chromatography.

Experimental Procedure for 1 mmol Scale Reaction

Synthesis of **4.2a**:

A Schlenk flask (25 mL) was equipped with a stir bar, catalyst **4.1** (0.003 mmol), Cs_2CO_3 (0.05 mmol), 1-tetralone (1.0 mmol), *tert*-amyl alcohol (3.0 mL) and benzyl alcohol (1.2 mmol) under nitrogen atmosphere in a glove box. The reaction flask was taken out of the glove box, equipped with a condenser and solution was heated at 135 °C (oil bath temperature) with stirring in an open system under argon flow for 12 h. Upon completion, the crude reaction mixture was purified by column chromatography over silica-gel (60-120 mesh) using ethyl acetate /pet ether mixture as an eluent. The conversion of 1-tetralone and yield of product **4.2a** were 92% and 73% (171 mg), respectively.

X-Ray Analysis of α-Alkenylated Product: Crystals suited for single crystal X-ray diffraction measurements were mounted on a glass fiber. Geometry and intensity data were collected with a Bruker SMART D8 goniometer equipped with an APEXCCD detector and with an Incoatecmicrosource **(Mo-Kα** radiation, λ = 0.71073 Å,

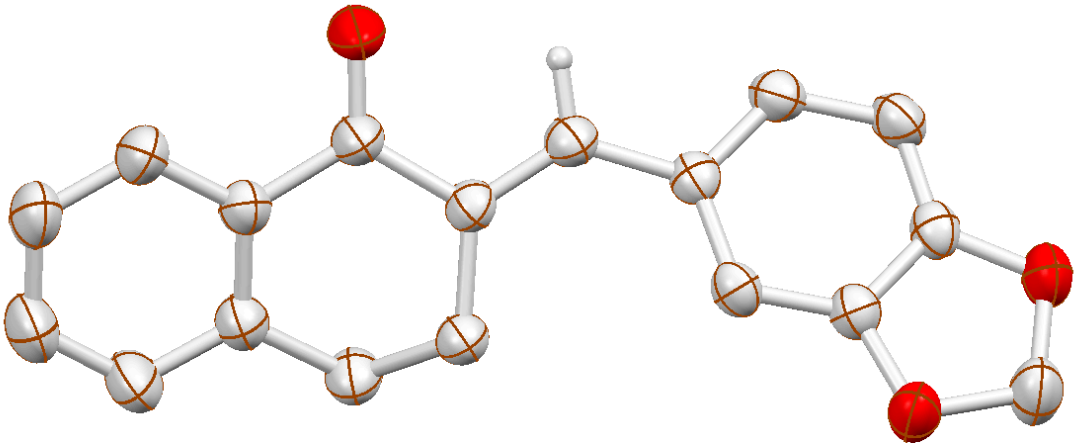
multilayer optics). Temperature was controlled using an Oxford Cryostream 700 instrument. Intensities were integrated with SAINT+[24] and corrected for absorption with SADABS.[25] The structure was solved by direct methods and refined on F^2 with SHELXL-97[26] using Olex-2[27] software.

Crystal Data of α-Alkenylation Product 4.2g: $C_{18}H_{14}O_3$, yellow solid, M = 278.29 gm/mol, monoclinic with space group P 1 21/c 1, a = 13.5024(4) Å, b = 11.7642(3) Å, c = 8.58460(10) Å, α = 90°, β = 95.067(2)°, γ = 90°, V = 1358.29(6) $Å^3$, Z = 4, F(000) = 584, μ-(CuK_α) = 0.748 mm^{-1}, $2\theta_{max}$ = 153.0260, ρ_{calcd} = 1.361 g/cm^3, T = 293(2) K, 10496 Reflections collected (6.572° ≤ 2Θ ≤ 153.026°), 2770 unique, R_1 = 0.0664, WR_2 = 0.2000 (all data). Residual electron density max/min = 0.302/-0.292e.$Å^{-3}$. The structure has been deposited at the CCDC data center and can be retrieved using the deposit number **CCDC 1905606**

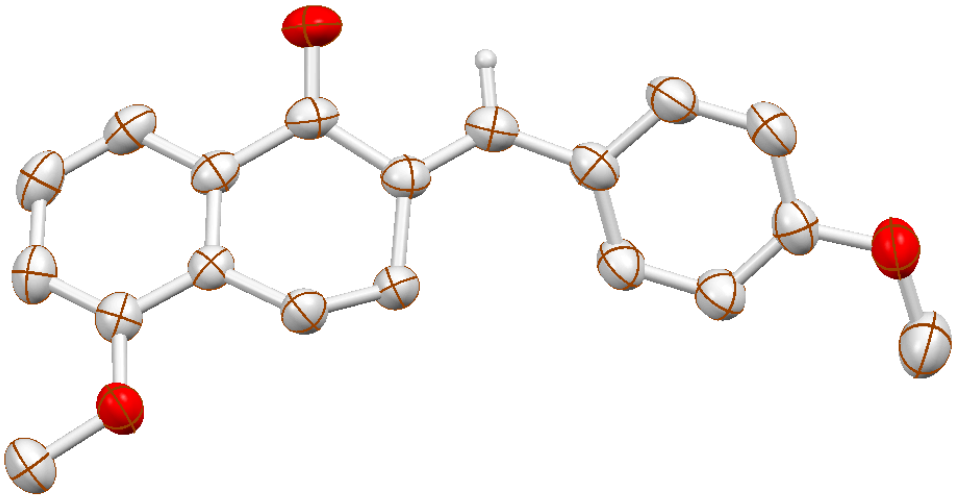
Crystal Data of α-Alkenylated Product 4.3a: $C_{19}H_{18}O_3$, clear white, M = 276.44 gm/mol, monoclinic with space group P 1 21/c 1, a = 14.7747(3) Å, b = 7.7514(2) Å, c = 13.0463(3) Å, α = 90°, β = 94.115(2) °, γ = 90°, V = 1490.27(6) $Å^3$, Z = 4, F(000) = 624, μ-(CuK_α) = 0.703 mm^{-1}, $2\theta_{max}$ = 152.6660, ρ_{calcd} = 1.232 g/cm^3, T = 294.8 (3) K, 9486 Reflections collected (12.012° ≤ 2Θ ≤ 152.666°), 3041 unique, R_1 = 0.0706, WR_2 = 0.1644 (all data). Residual electron density max/min = 0.405/-0.706 e.$Å^{-3}$. The structure has been deposited at the CCDC data center and can be retrieved using the deposit number **CCDC 1905607**

Figure 4.1 ORTEP Structure of (a) (*E*)-2-(benzo[*d*][1,3]dioxol-5-ylmethylene)-3,4-dihydronaphthalen-1(2*H*)-one (**4.2g**.) and (b) (*E*)-5-methoxy-2-(4-methoxybenzylidene)-3,4-dihydronaphthalen-1(2*H*)-one **(4.3a)** Ellipsoids are Drawn with 50% Probability

(a)



(b)



NMR Spectra of Complexes and α-Alkenylation of Ketone Products:

Figure 4.2 ^{1}H NMR spectrum of (4-Ph)Tr(NHP(iPr)$_2$)$_2$ **(L4)**:

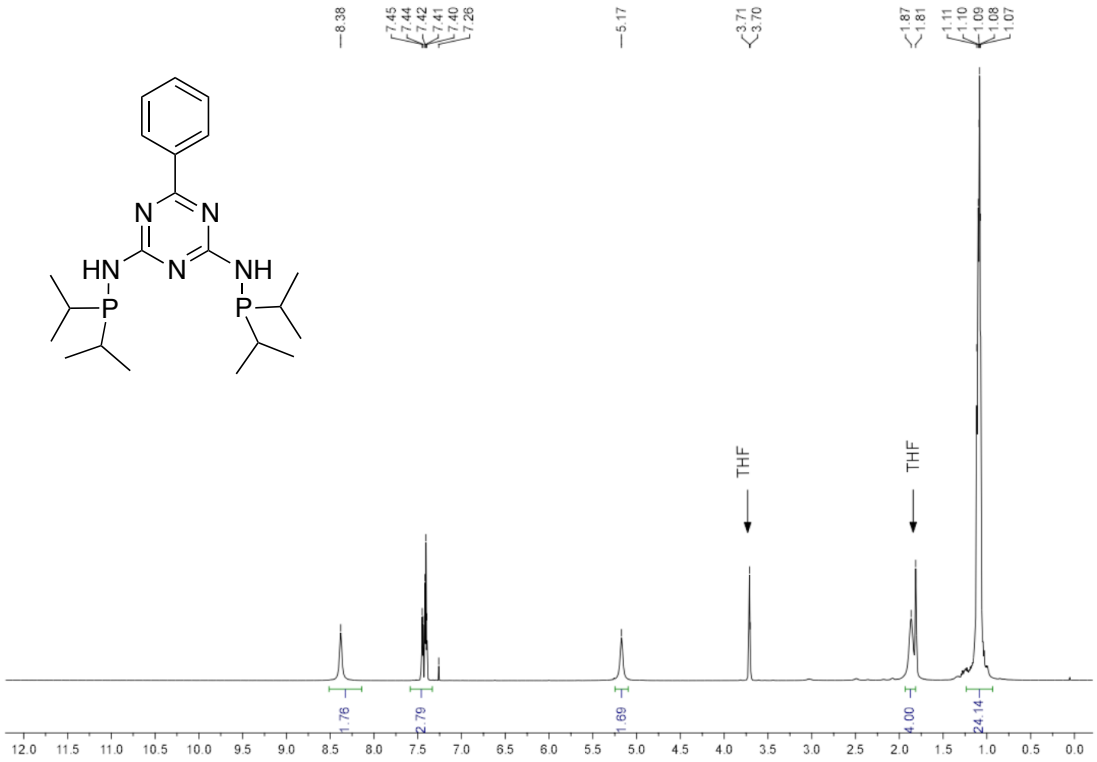


Figure 4.3 ^{1}H NMR spectrum of [(4-Ph)Tr(NHP(iPr)$_2$)$_2$Mn(CO)$_2$Br] (**Catalyst 3.1**):

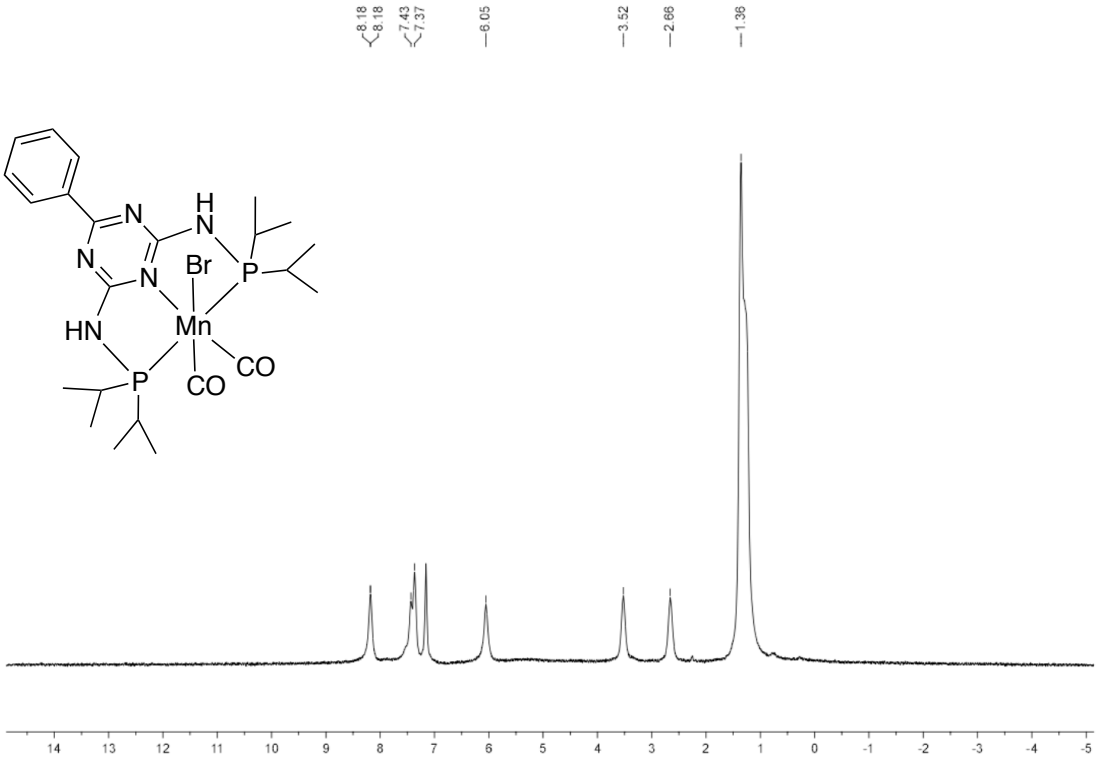


Figure 4.4 ^{31}P NMR spectrum of [(4-Ph)Tr(NHP(iPr)2)2Mn(CO)2Br] (**Catalyst 3.1**):

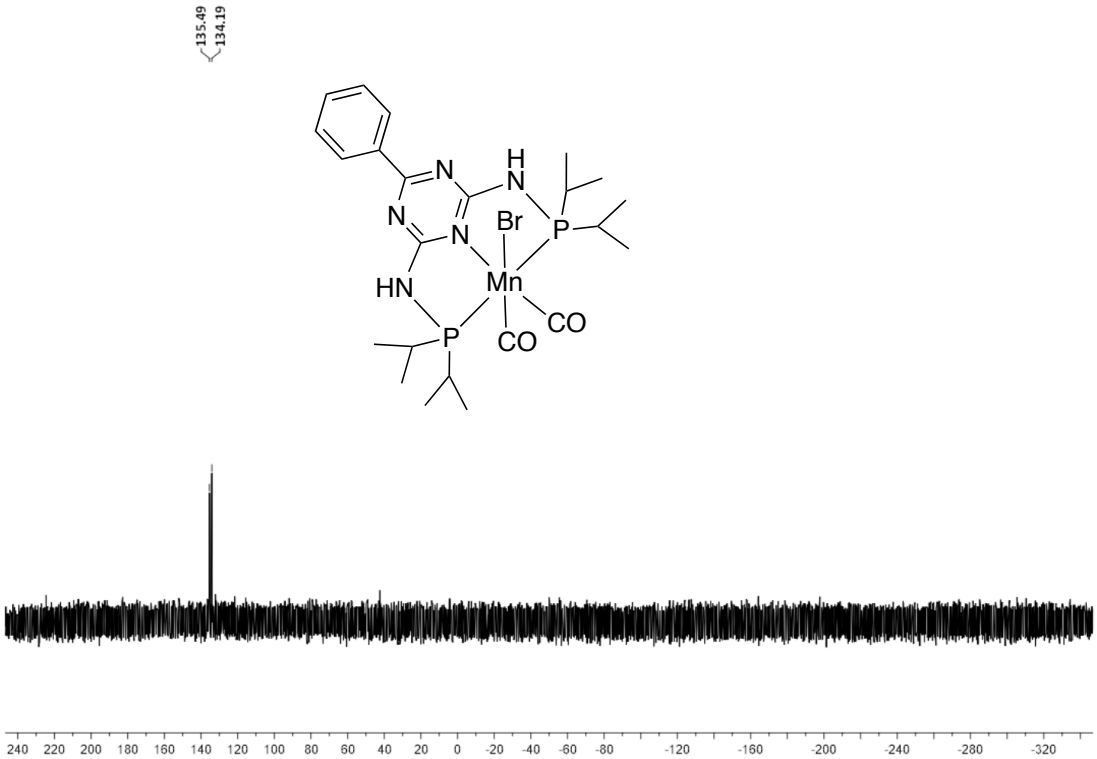


Figure 4.5 ^{1}H NMR spectrum of [(4-Me)Tr(NHP(iPr)$_2$)$_2$] **(L5)**:

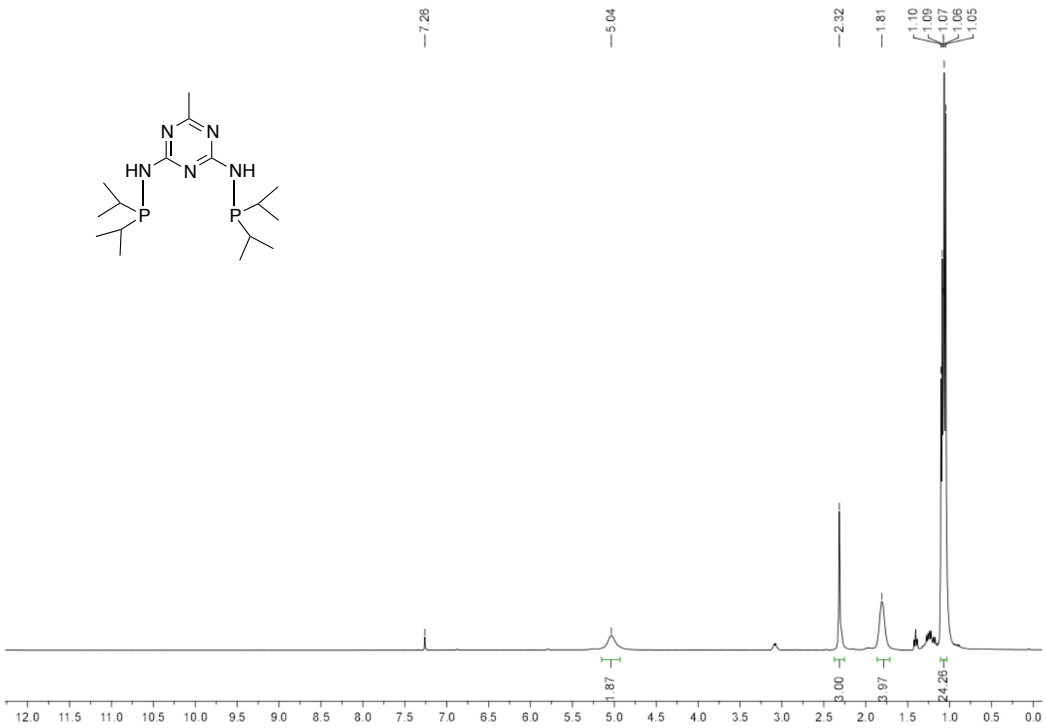


Figure 4.6 ^{1}H NMR spectrum of [(4-Me)Tr(NHP(^{i}Pr)$_2$)$_2$Mn(CO)$_2$Br] **(Catalyst 4.1)**:

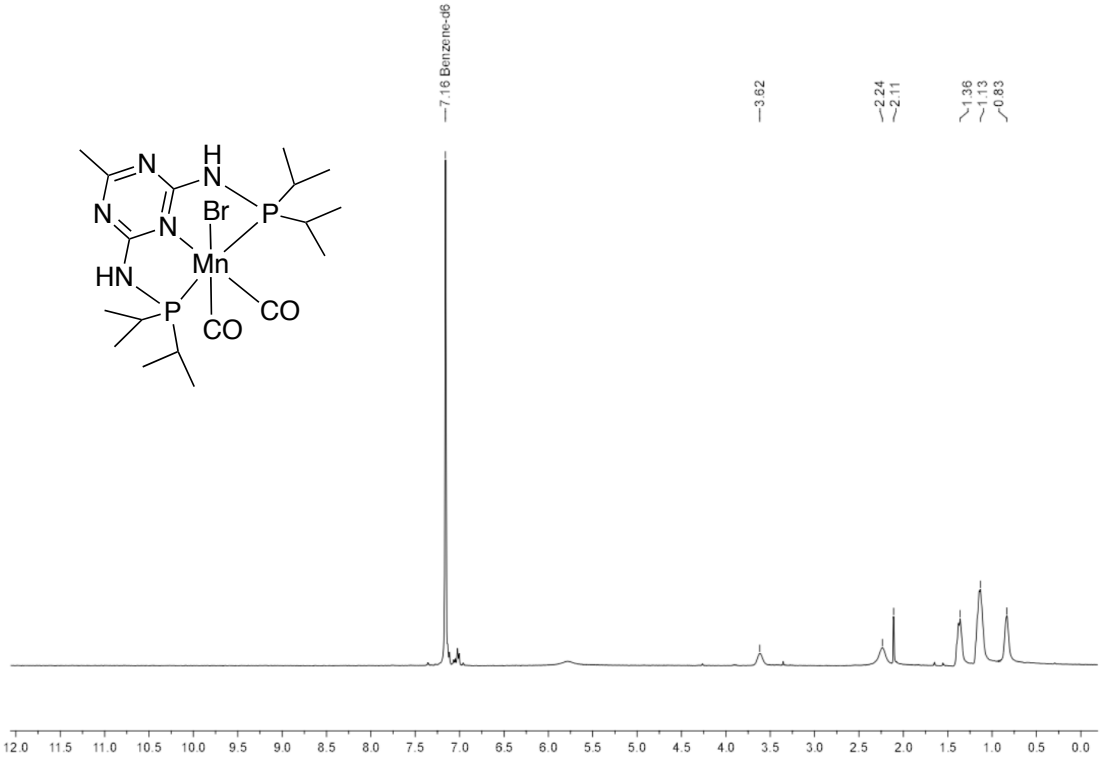


Figure 4.7 ^{31}P NMR spectrum of [(4-Me)Tr(NHP(^{i}Pr)$_2$)$_2$Mn(CO)$_2$Br] (**Catalyst 4.1**)

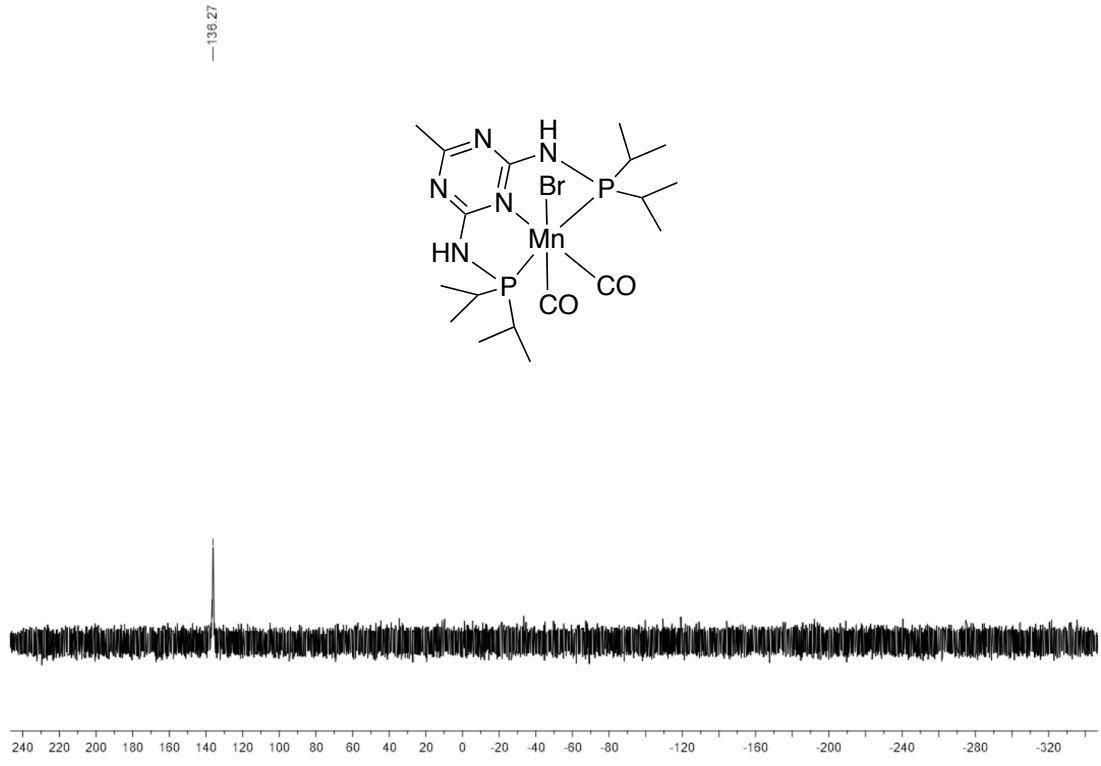


Figure 4.8 [1]H NMR spectrum of (*E*)-2-benzylidene-3,4-dihydronaphthalen-1(2*H*)-one **(4.2a)**:

Figure 4.9 [13]C NMR spectrum of (*E*)-2-benzylidene-3,4-dihydronaphthalen-1(2*H*)-one **(4.2a)**:

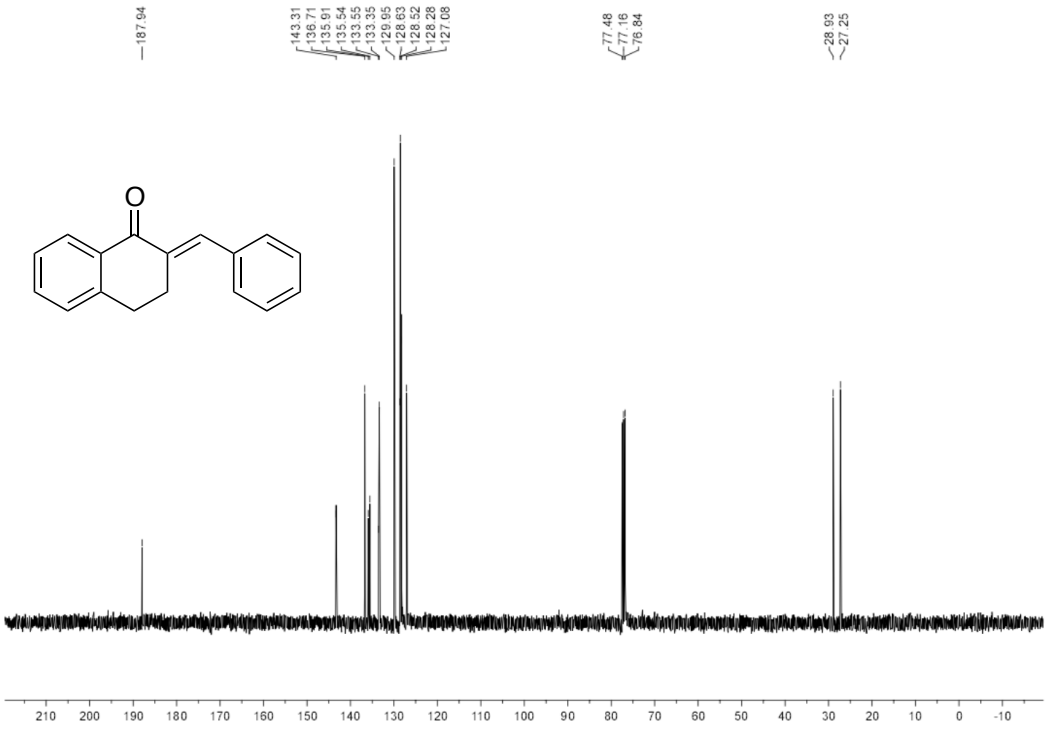


Figure 4.10 ^{1}H NMR spectrum of (E)-2-(2-methylbenzylidene)-3,4-dihydronaphthalen-1(2H)-one **(4.2c)**:

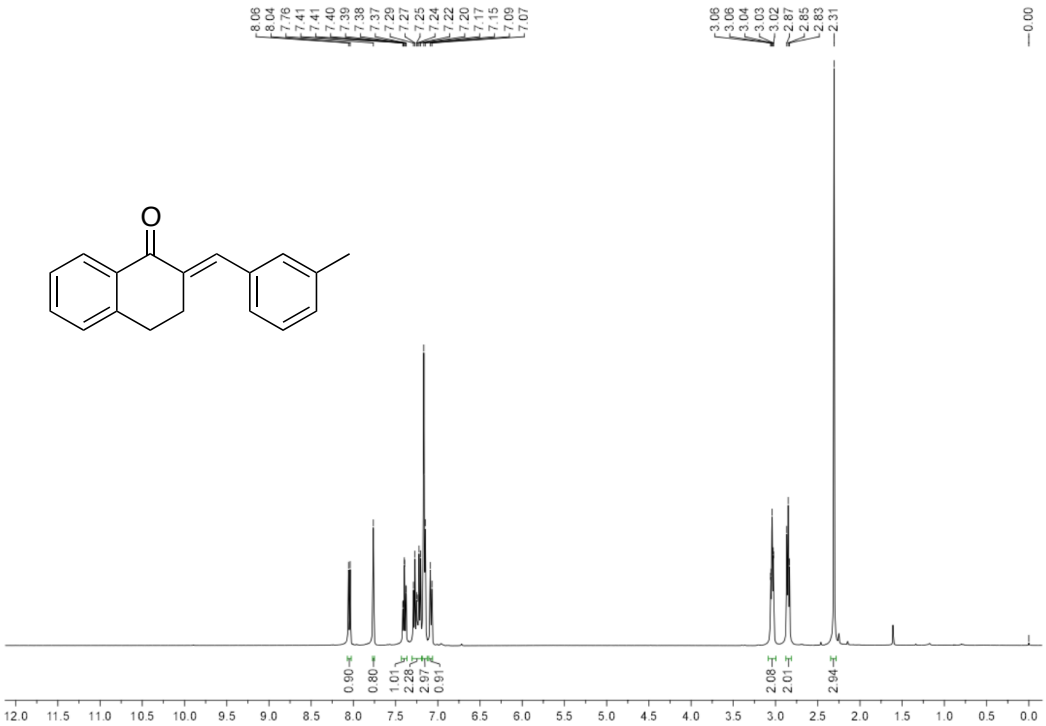


Figure 4.11 ^{13}C NMR spectrum of (E)-2-(3-methylbenzylidene)-3,4-dihydronaphthalen-1(2H)-one **(4.2c)**:

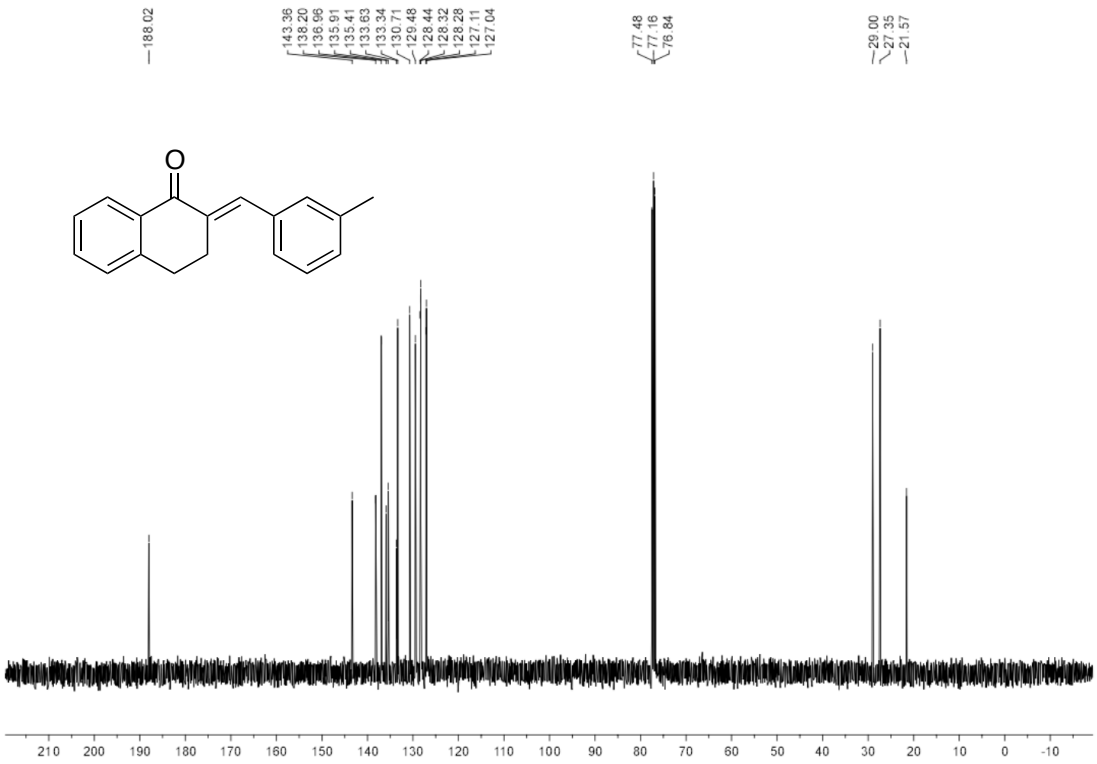


Figure 4.12 ^{1}H NMR spectrum of (E)-2-(furan-2-ylmethylene)-3,4-dihydronaphthalen-1(2H)-one **(4.2l)**:

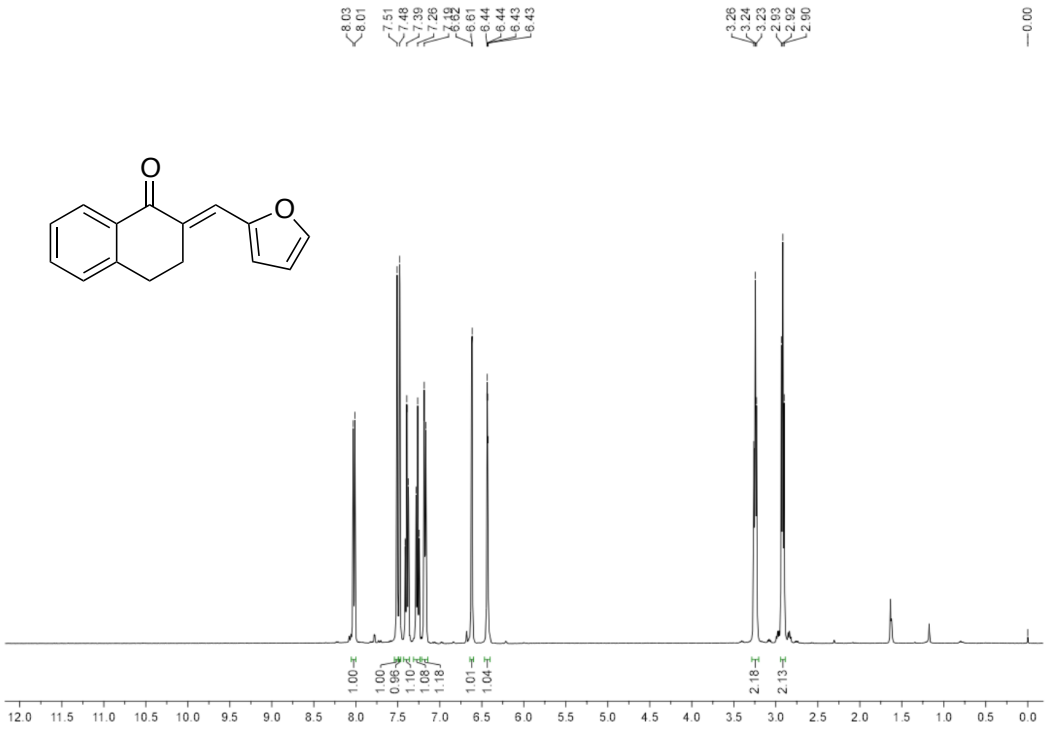


Figure 4.13 ^{13}C NMR spectrum of (E)-2-(furan-2-ylmethylene)-3,4-dihydronaphthalen-1(2H)-one **(4.2l)**:

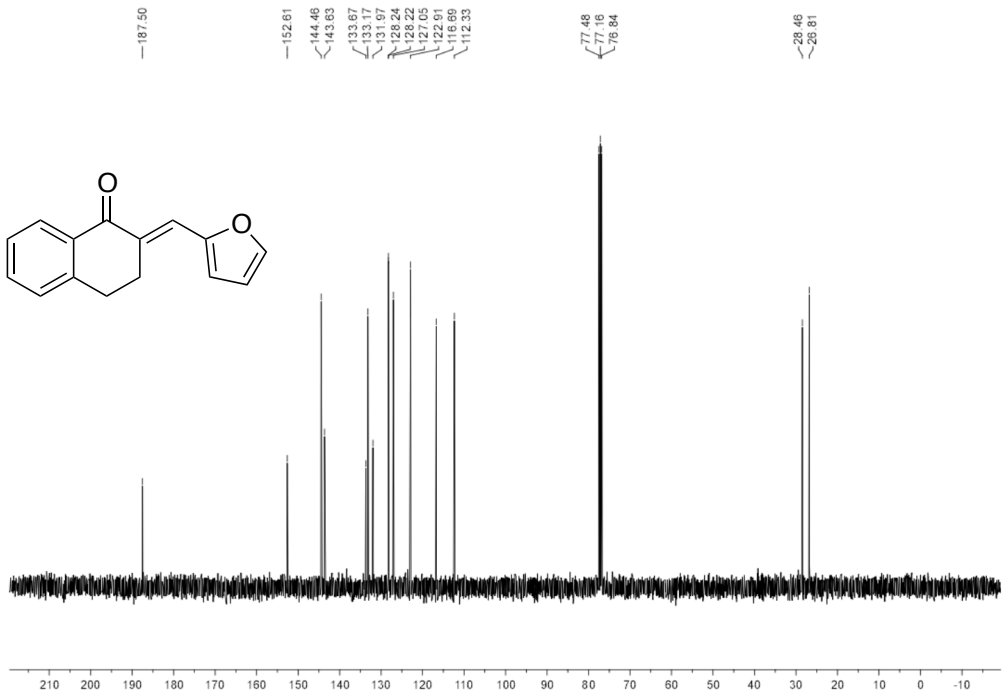


Figure 4.14 ^{1}H NMR spectrum of (E)-2-(2-ethylbutylidene)-3,4-dihydronaphthalen-1(2H)-one **(4.2n)**:

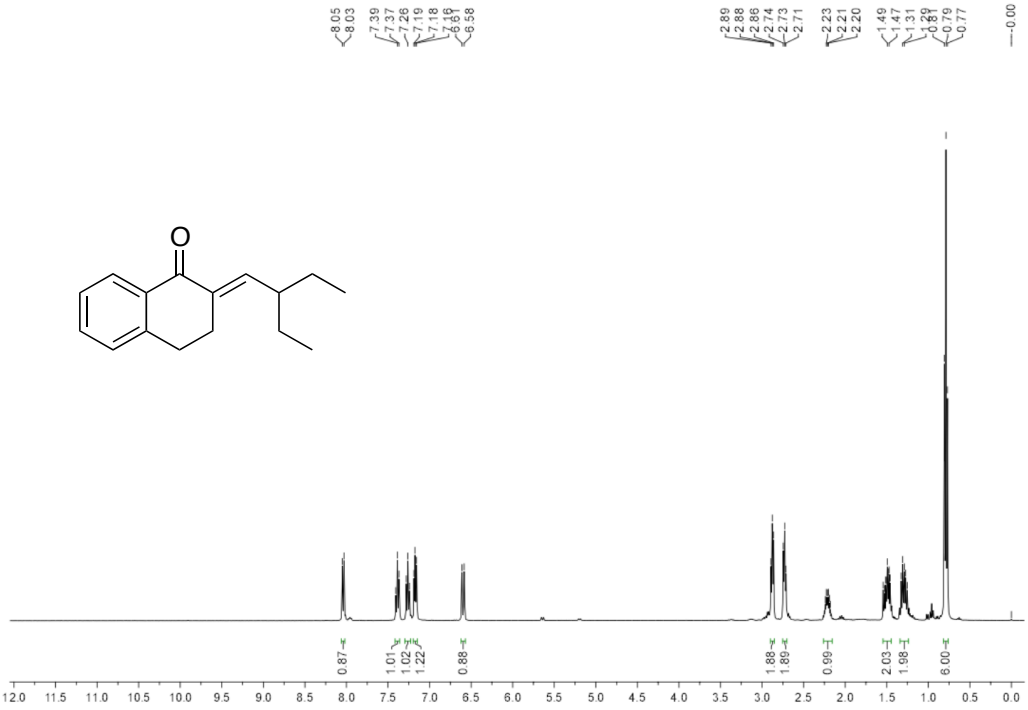


Figure 4.15 ^{13}C NMR spectrum of (E)-2-(2-ethylbutylidene)-3,4-dihydronaphthalen-1(2H)-one **(4.2n)**:

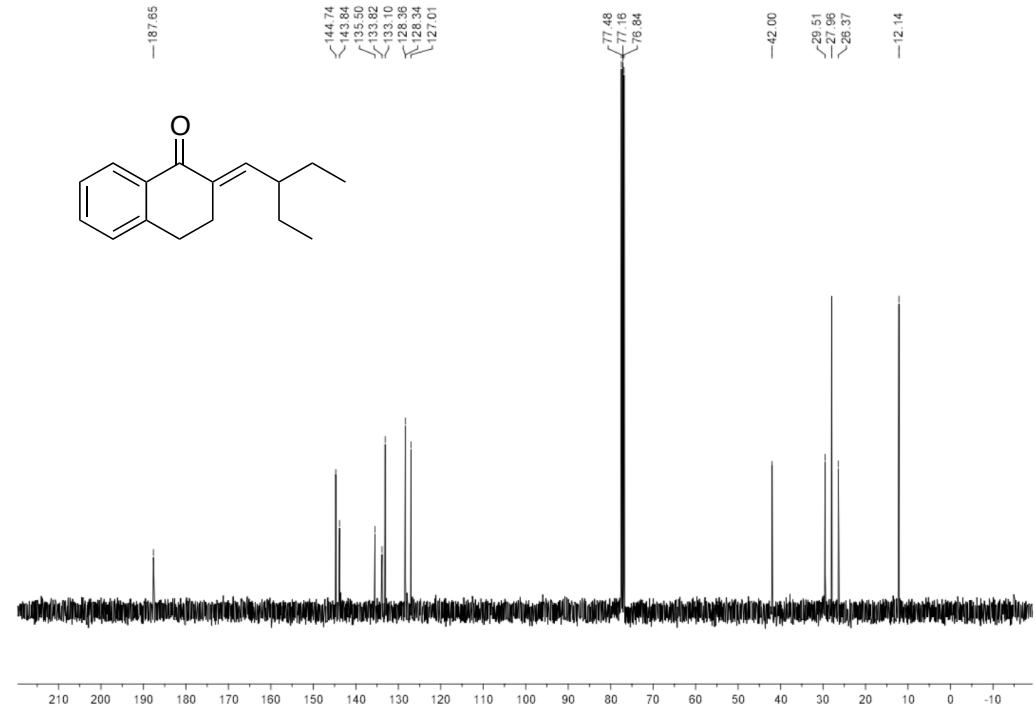


Figure 4.16 ^{1}H NMR spectrum of (*E*)-2-(3,4-dimethoxybenzylidene)-6-methoxy-3,4-dihydronaphthalen-1(2*H*)-one **(4.3b)**:

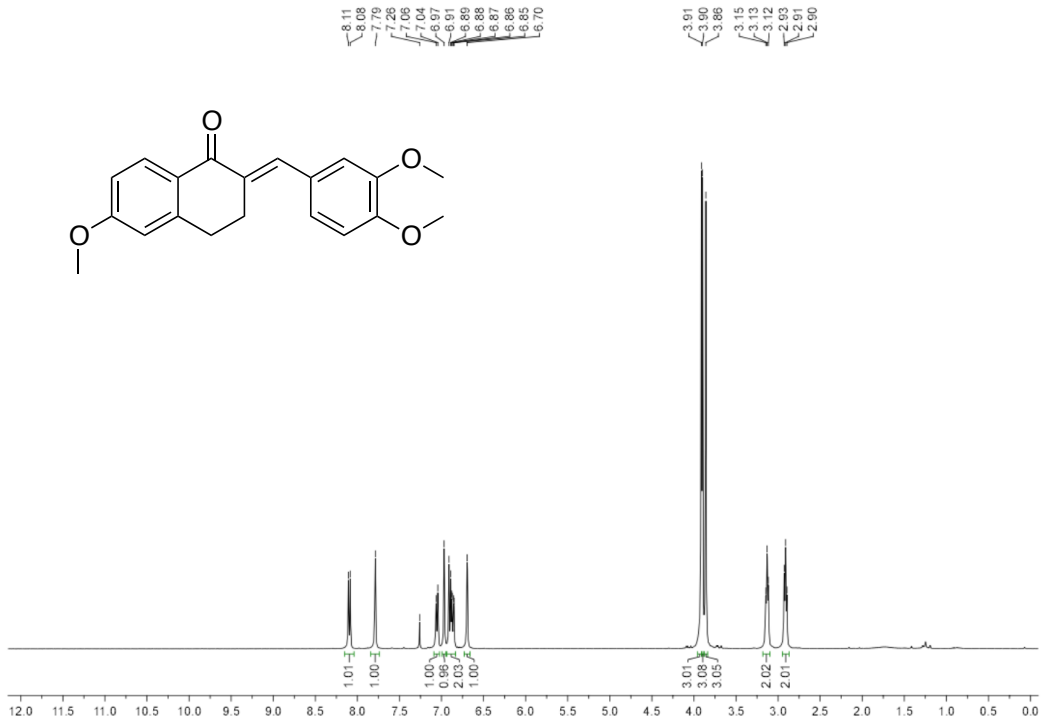


Figure 4.17 ^{13}C NMR spectrum of (*E*)-2-(3,4-dimethoxybenzylidene)-6-methoxy-3,4-dihydronaphthalen-1(2*H*)-one **(4.3b)**:

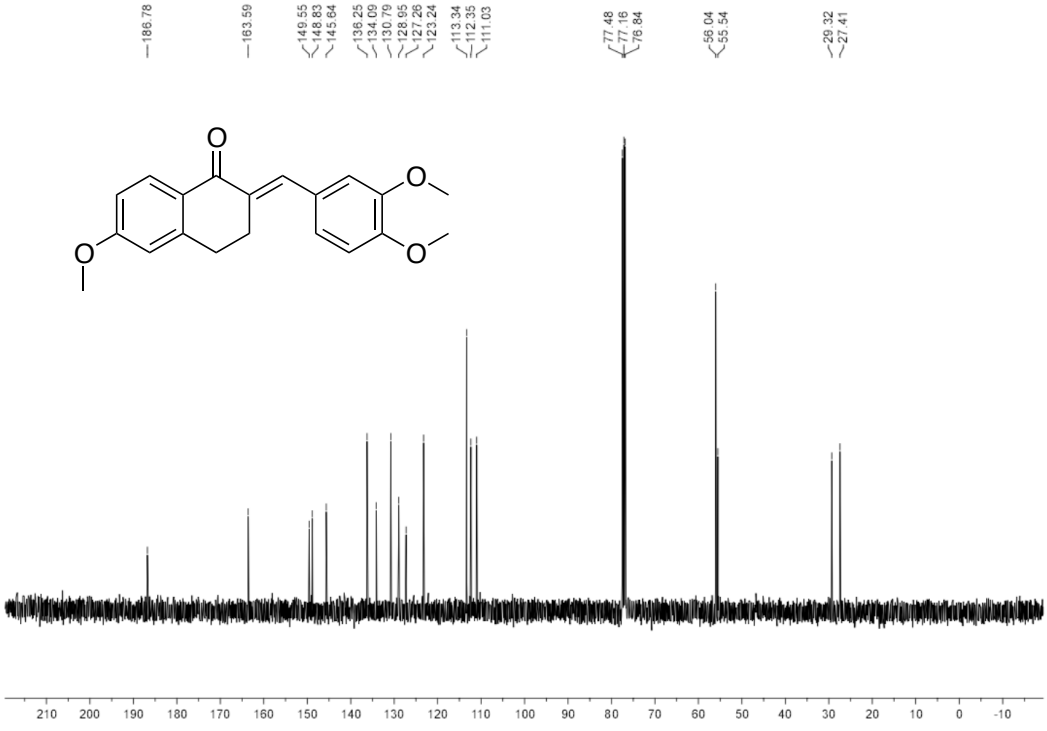


Figure 4.18 ^{1}H NMR spectrum of (*E*)-3-(2,3-dimethoxyphenyl)-2-methyl-1-phenylprop-2-en-1-one **(4.3j)**:

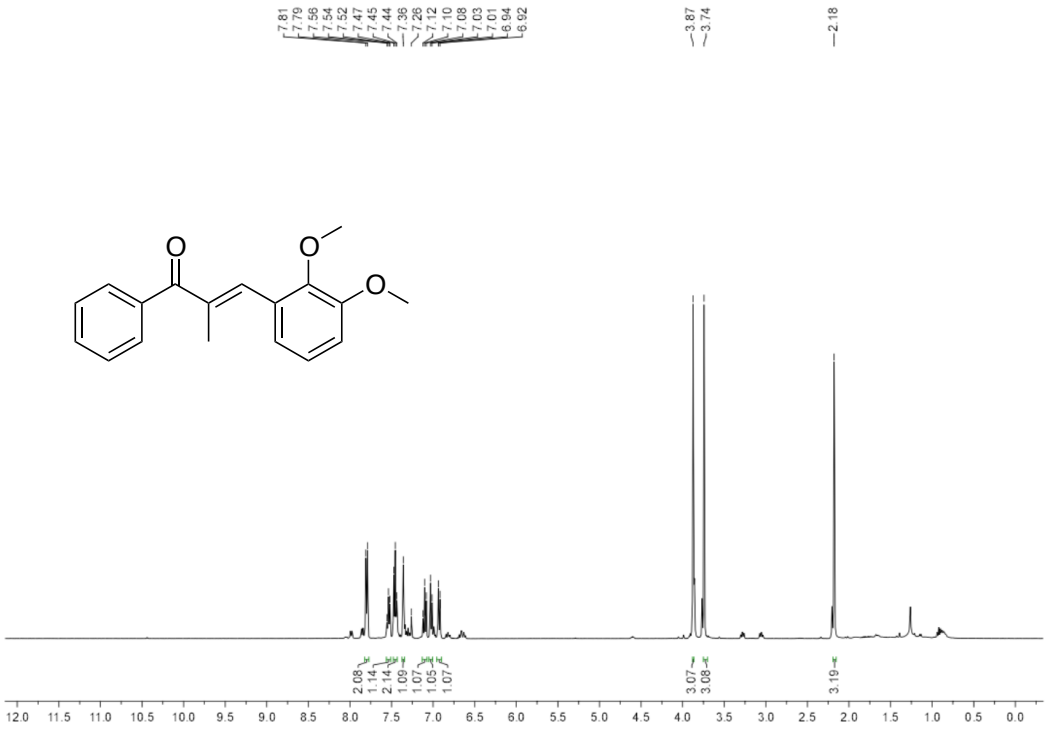


Figure 4.19 ^{13}C NMR spectrum of (*E*)-3-(2,3-dimethoxyphenyl)-2-methyl-1-phenylprop-2-en-1-one **(4.3j)**:

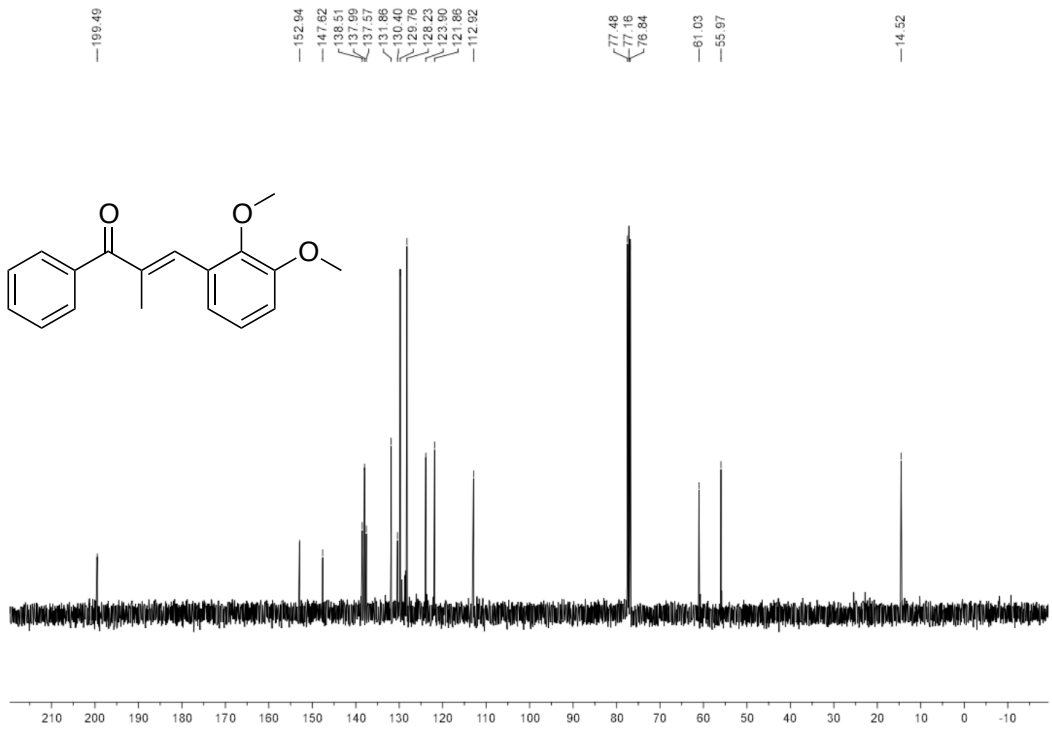
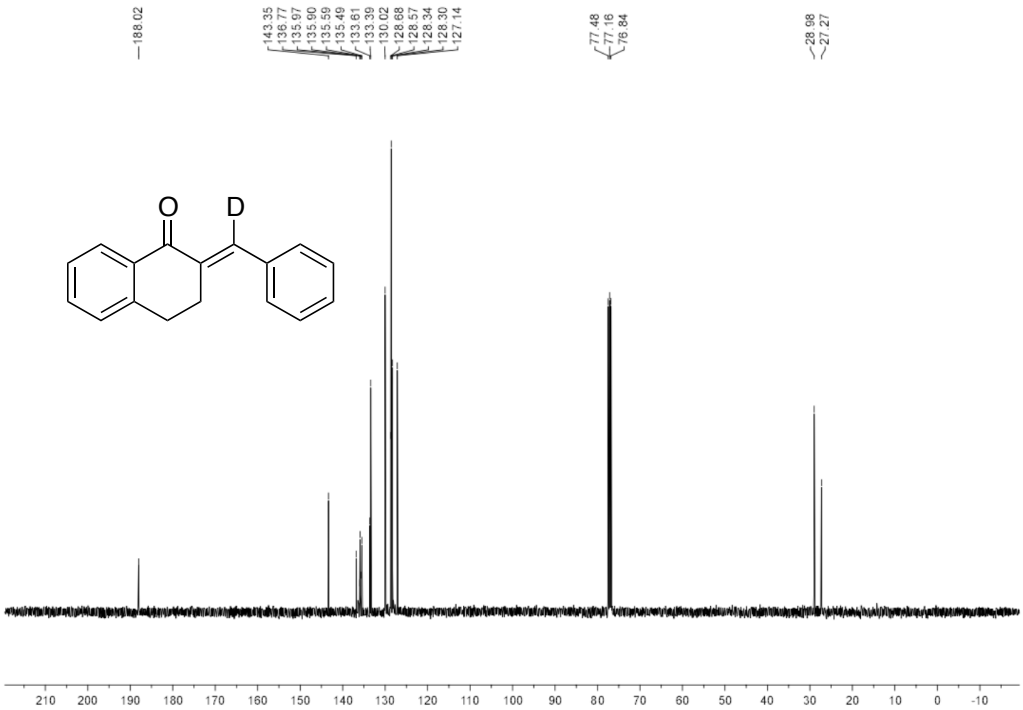


Figure 4.20 [1]H NMR spectrum of (*E*)-2-benzylidene-3,4-dihydronaphthalen-1(2*H*)-one **(4.2a-D)**:

Figure 4.21 [13]C NMR spectrum of (*E*)-2-benzylidene-3,4-dihydronaphthalen-1(2*H*)-one **(4.2a-D)**:



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Thesis Highlight

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Thesis Title: Catalysis by Iron and Manganese Pincer Complexes
Discipline: Chemical Sciences **Sub-Area of Discipline:** Organometallic Chemistry
Date of viva voce: 27/05/2020

In recent year pincer complexes have the ability to uncover the unusual reactivity with high selectivity in catalysis to provide various organic transformations. The discovery of Metal-Ligand Cooperation (MLC) in tridentate pincer complexes opened a new class of bond activation mode and consequently, an assortment of small molecules have been activated and utilized efficiently to provide benevolent routes in organic transformations. Homogeneous catalysis using more abundant, non-toxic, inexpensive and environmentally benign first row transition metals such as iron and manganese catalysts are particularly desirable.

Here, thesis mainly provides a detailed study on the design, synthesis and catalytic applications of iron and manganese pincer complexes. The types and chemistry of iron and manganese pincer complexes including metal-ligand cooperation and their application in sustainable catalysis are introduced in the first chapter. Simple di(aminomethyl)pyridine ligated iron-pincer complexes were synthesized, which have been demonstrated to catalyzed the regioselective [2+2+2] cyclotrimerization of terminal and internal alkynes to 1,2,4-trisubstituted benzene molecules and hexa-substituted benzene compounds.

In chapter 3 and 4 of the thesis encompasses on efficient protocol of alcohol feedstock as alkylating partner. Manganese pincer complexes catalyzed cross-couplings of ketones and secondary alcohols with primary alcohols were developed in which a range of alpha-alkylated ketone products were obtained. Challenging α-ethylation of ketones is also attained using ethanol as an alkylating reagent. With slight modification of catalyst structure and reaction conditions we have obtain the selective alpha-alkenylation (unsaturated alkenylation) of ketones using primary alcohols. Remarkably, water and liberated hydrogen are the only byproduct in these catalytic processes. Mechanistic studies indicated that these catalytic transformations proceed through O−H bond activation of alcohols via dearomatization−aromatization metal-ligand cooperation operative in catalysts leading to the oxidation of alcohols.

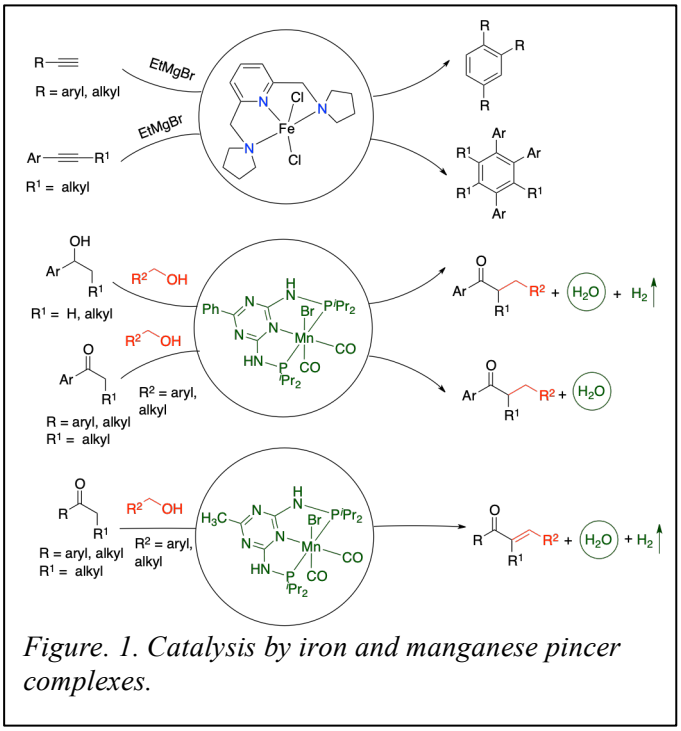

Figure. 1. Catalysis by iron and manganese pincer complexes.