Valorization of biomass related substrates into value added chemicals

Hydrogen transfer catalysis

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Hydrogen transfer catalysis

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Hydrogen transfer catalysis

Nitish Kumar Garg

DOCTORAL DISSERTATION

Doctoral dissertation for the degree of Doctor of Philosophy (PhD) at the Faculty of Science at Lund University to be publicly defended on January 26th, 2024 at 09.00 in Lecture Hall KC:B, Kemicentrum

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Hydrogen transfer catalysis

Abstract

In the current global scenario, it is evident that global warming and climate change are primarily driven by emissions stemming from the utilization of fossil fuels. Yet, if we look around, most of what we see is made from or linked to fossil fuels and it clearly shows our over-dependency on fossil fuels and hence there is a significant need to develop alternate sources of energy and raw materials to tackle these problems. One such alternative to fossil fuels is biomass-based resources however, biomass comes with its own set of challenges, including an abundance of functional groups present in biomass and hence finding new ways to reduce those functional groups in biomass has been a hot topic for chemical researchers in the last decade. This thesis shares the same objective, aiming to convert chemicals derived from biomass into value-added products.

In chapter 2, a new and efficient hydrosilylation strategies have been developed to selectively defunctionalize biomass derived levulinic acid into various bio-chemicals and bio-fuels such as gamma-valerolactone, 1,4-pentanediol, 2-pentanol, 2-methyltetrahydrofuran and C-5 hydrocarbons using cost-effective and non-toxic silanes and the commercially available $B(C_6F_5)_3$ as catalyst at room temperature. In chapter 3, attention is directed towards the N-methylation of amines and nitro compounds, a process traditionally accomplished using toxic methylating agents that produce substantial waste. Conversely, within our methodology, the use of methanol as a C1 source for N-methylation is employed through borrowing hydrogen pathways, resulting in the generation of solely water as the byproduct. In chapter 4, C-C and C-N bond forming reactions were performed directly from less-toxic alcohols as substrates without using any transition metal-based catalysts.

Key words: Biomass, levulinic acid, hydrosilylation, borrowing-hydrogen, N-alkylation.

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MADE IN SWEDEN

Half of the chemistry that we know today is probably wrong,
we just don't know which half.

Unknown Indian Professor

Table of Contents

Abstract

In the current global scenario, it is evident that global warming and climate change are primarily driven by emissions stemming from the utilization of fossil fuels. Yet, if we look around, most of what we see is made from or linked to fossil fuels and it clearly shows our over-dependency on fossil fuels and hence there is a significant need to develop alternate sources of energy and raw materials to tackle these problems. One such alternative to fossil fuels is biomass-based resources however, biomass comes with its own set of challenges, including an abundance of functional groups present in biomass and hence finding new ways to reduce those functional groups in biomass has been a hot topic for chemical researchers in the last decade. This thesis shares the same objective, aiming to convert chemicals derived from biomass into value-added products.

In chapter 2, a new and efficient hydrosilylation strategies have been developed to selectively defunctionalize biomass derived levulinic acid into various bio-chemicals and bio-fuels such as gamma-valerolactone, 1,4-pentanediol, 2-pentanol, 2-methyltetrahydrofuran and C-5 hydrocarbons using cost-effective and non-toxic silanes and the commercially available $B(C_6F_5)_3$ as catalyst at room temperature. In chapter 3, attention is directed towards the N-methylation of amines and nitro compounds, a process traditionally accomplished using toxic methylating agents that produce substantial waste. Conversely, within our methodology, the use of methanol as a C1 source for N-methylation is employed through borrowing hydrogen pathways, resulting in the generation of solely water as the byproduct. In chapter 4, C-C and C-N bond forming reactions were performed directly from less-toxic alcohols as substrates without using any transition metal-based catalysts.

Popular science

In the fight against climate change, switching from fossil fuels to renewable energy sources has become essential on a worldwide scale. Scientists and industries are increasingly focusing on biomass-derived chemicals as a cleaner, greener alternative to conventional fossil fuels for the daily needs of sustainable energy and raw materials. Biomass is a renewable resource that can be used to create a variety of chemicals and fuels. It is obtained from organic materials like plant and agricultural waste. We can greatly lower our carbon footprint, mitigate greenhouse gas emissions, and pave the road for a more sustainable and environmentally friendly future by using these biomass derived alternatives. There are many ways of utilizing biomass derived chemicals but we have primarily employed two strategies to utilize biomass-derived chemicals. The first strategy involves designing innovative methods to transform biomass into valuable chemicals typically derived from fossil fuels. Our primary focus has been on lignocellulosic biomass, one of the most abundant organic resources on earth. We have developed novel approaches to convert this biomass into various bio-based chemicals and biofuels, including hydrocarbons and other fuel additives.

The second strategy we have employed involves using sustainable and less toxic alcohols as primary reagents for significant catalytic transformations. Biomass-based alcohols present a viable alternative that has the potential to revolutionize our energy and raw material needs in a sustainable way. These alcohols, derived from renewable sources such as agricultural waste offer an environmentally beneficial alternative to typical fossil fuels. A well-known example of this is the production of bio-ethanol through fermentation of biomass and the world needs more such methods to produce other kinds of alcohols from biomass on a larger scale. The versatility of these alcohols allows for their applications in various industries, including pharmaceuticals, plastics, and renewable energy. In this thesis, we have mainly focused on developing ways to better utilize these alcohols by converting them into raw materials and intermediates that are present in various industrial and pharmaceutical products. Through these efforts, we aim to move one step closer to building a sustainable future.

List of papers

Paper I

Efficient conversion of biomass derived levulinic acid to γ-valerolactone using hydrosilylation

N. K. Garg, V. Schmalz, M. T. Johnson and O. F. Wendt. *Eur. J. Org. Chem.,* 2021, 5243-5247.

Paper II

Selective valorization of bio-derived levulinic acid and its derivatives into hydrocarbons and biochemicals using hydrosilylation

N. K. Garg, M. Tan, M. T. Johnson and O. F. Wendt. *Chem. Eur. J.,* 2023, 29, e202300119.

Paper III

Ruthenium NNN-based pincer complexes with dual metal ligand cooperation as catalysts for *N*-methylation of anilines and nitroarenes under air

N. K. Garg, Y. Goriya, S. Manojveer, O. F. Wendt and M. T. Johnson (*Submitted manuscript)*

Paper IV

Highly efficient base catalyzed *N*-alkylation of amines with alcohols and β-alkylation of secondary alcohols with primary alcohols

N. K. Garg, M. Tan, M. T. Johnson and O. F. Wendt. *ChemCatChem,* 2023, e202300741.

Publications not included in this thesis:

Paper V

Mononuclear Iron (III) Complex with Unusual Temperature Change of Color and Magneto-Structural Properties: Synthesis, Structure, Magnetization, Multi-frequency ESR and DFT Study

N. K. Garg, Y. Goriya, M. Seetharaman, S. Muratović, D. Pajić, M. Cetina, I. Petreska, Y. Krupskaya, V. Kataev, M. T Johnson, O. F. Wendt and D. Žilić. *Dalton. Trans.,* 2022, 51, 2338-2345.

Paper VI

Ligand-Promoted [Pd]-Catalyzed α-Alkylation of Ketones through a Borrowing-Hydrogen Approach

S. Manojveer, **N. K. Garg**, Z. Gul, A. Kanwal, Y. Goriya, and M. T. Johnson, *ChemistryOpen,* 2023**,** 12, e202200245

Author’s contribution to the papers

Paper I

I planned and performed most of the experimental work and also wrote the manuscript.

Paper II

I planned and performed most of the experimental work and also wrote the manuscript.

Paper III

The project was initiated and planned by Dr. Yogesh Goriya, focusing solely on anilines as substrates. I subsequently optimized the experimental conditions and expanded the scope to include nitro arenes as well. I also determined the crystal structure of the ligand and conducted all the necessary control experiments. Additionally, the manuscript was written by me.

Paper IV

I planned and performed most of the experimental work and also wrote the manuscript.

Abbreviations

GVL	Gamma-valerolactone
LA	Levulinic acid
VA	Valeric acid
HMF	Hydroxymethylfurfural
2-MTHF	2-Methyltetrahydrofuran
2-P	2-Pentanol
1-P	1-Pentanol
AL	Alkyl levulinate
EL	Ethyl levulinate
ML	Methyl levulinate
PET	Polyethylene terephthalate
BH	Borrowing-Hydrogen
FAL	Furfuryl alcohol
1,4-PD	1,4-Pentanediol
PMHS	Polymethylhydrosiloxane
TMDS	Tetramethyldisiloxane
TM	Transition metals
TON	Turnover number
TOF	Turnover frequency
MPV	Meerwein–Ponndorf–Verley
RT	Room temperature
MLC	Metal ligand cooperation
NMR	Nuclear magnetic resonance
THF	Tetrahydrofuran

1. General introduction

1.1 Fossil fuels and problems associated with them

Global warming and the climate crisis are undeniably among the most significant challenges faced by the present generation, primarily driven by our excessive reliance on fossil fuels. Nonetheless, it is noteworthy that a significant portion of the world's transportation fuels and industrial chemicals still originates from fossil fuel-based sources. This is further underscored by a report from the U.S. Department of Energy, which forecasts a substantial growth of up to 48% in global energy demand by the year 2040.[1-3]

Nevertheless, it is common knowledge that the combustion of fossil fuels results in the emission of CO_2, thereby increasing the climate crisis (Figure 1.1). As a result, the task of developing renewable resources for both energy and raw materials has emerged. This endeavor is crucial to reduce our reliance on petroleum and mitigate the far-reaching consequences of global warming. While various energy sources like solar, wind and nuclear energy offer solutions to the energy crisis, we still heavily rely on fossil fuels for raw material production. It stands as one of the most significant challenges of the 21st century and has prompted chemical researchers around the globe to seek out alternative approaches that are more sustainable.[4-6]

Figure 1.1: Fossil fuel emissions that can shape the future climate.

1.2 Can biomass replace fossil fuels?

As the complete dependence on fossil fuels for everyday needs is deemed unsustainable, a solution that has been proposed involves the utilization of renewable resources derived from biomass as an alternative to fossil fuels. These biomass-derived resources hold the capacity to serve as substitutes for meeting both energy and raw material requirements. Fuels derived from biomass maintain a carbon-neutral status, given that they are produced from CO_2 that has already been absorbed from the atmosphere by trees. Therefore, employing biomass for the generation of energy and raw materials has the advantage of not engendering additional emissions on a net basis. This renders it a prospective measure in addressing the challenge of global warming however, it is important to keep in mind that the land use for bio based energy will compete with the land use for food. [4, 7, 8]

There are several methods by which biomass can be utilized as an alternative to fossil fuels. As direct replacements for petrol and diesel, biomass can be converted into liquid biofuels like bioethanol and biodiesel and countries like India are investing a lot on bioethanol production. Biomass can be gasified to create syngas, which can then be refined to create synthetic natural gas or other fuels. Additionally, the anaerobic digestion of biomass results in the production of biogas, primarily made of methane and ideal for the production of heat and power.[9-11]

Indeed, the question arises: if biomass holds the potential to combat global warming, why hasn't it been widely adopted? The answer lies in the complexity of biomass. Biomass contains numerous functional groups that must be selectively reduced to yield valuable products. This process demands time and energy, making it less efficient when compared to the cost-effectiveness of fossil fuel’s based raw materials and energy. Therefore, there's an urgent necessity to pioneer novel and efficient approaches for biomass conversion into value-added chemicals, aiming to minimize fossil fuel usage. Centuries ago, humanity developed a method for ethanol production from biomass and looking ahead, our goal should be to continue this tradition of innovation by creating high-efficiency techniques for biomass utilization in the future.[12, 13]

1.3 Potential of lignocellulosic biomass

Lignocellulosic derived biomass stands as the most abundant organic resource on earth. It is widespread across the globe with an annual production of roughly 1.3 billion tons, primarily in the form of agricultural waste. Consequently, the potential exists for lignocellulosic derived biomass to function as a substitute for fossil fuels and petroleum in the generation of bio-based fuels and raw materials. It is noteworthy that lignocellulose does not engage in competition with the food industry, and its availability is readily apparent within various waste streams such as agriculture, forestry, and the paper industry.[14-17] Lignocellulose is predominantly composed of three key constituents, namely cellulose, hemicellulose, and lignin as shown in figure 1.2. In the last decade, a lot of research has been focused on the valorization of lignocellulosic biomass into bio-fuels and bio-chemicals.[9] For example, furfural has gained substantial interest in the production of bio-based terephthalic acid and scaling up this process efficiently could have a profound impact, especially given the extensive global use of PET plastic.[18]

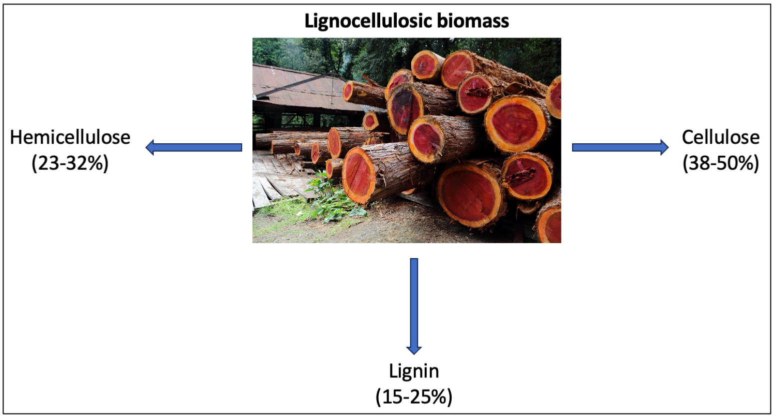


Figure 1.2: Lignocellulosic biomass and its components[19]

1.3.1 Hemicellulose and cellulose (Paper 1 and 2)

Hemicellulose and cellulose, two components of lignocellulosic biomass, have numerous general applications. Hemicellulose is used to make biomaterials such as biodegradable films, coatings, and packaging, which contributes to eco-friendly alternatives. It is also useful in the biofuel business because it can be fermented into ethanol, encouraging green energy sources.[20]

On the other hand, cellulose, being a fundamental component of paper, plays a crucial role in the paper and pulp industry, facilitating the production of this common material. Cellulose fibres, which are frequently sourced from wood or cotton, are used in the textile industry to generate fabrics.[21]

The hemicellulose and cellulose present in the lignocellulosic derived biomass are converted into many other biochemicals such as furfural, HMF, alkyl levulinates, LA etc. These chemicals have enormous number of usages in various different fields, for example, HMF can be used in polymer industries to make bio-based polymers and alkyl levulinates have applications in the fragrance industries.[22-24]

1.3.2 Conversion of cellulose/hemicellulose into levulinic acid (LA)

LA is an excellent platform chemical and it can be easily derived from readily available cellulose and hemicellulose (Figure 1.3). Due to its outstanding properties, LA has also been considered among the top 12 chemical building blocks from biomass by U.S. department of energy in 2004.[25] The synthesis of LA from cellulose and hemicellulose is an essential step in biomass conversion technologies, as LA is a valuable platform chemical that can be used as a precursor for a variety of products, including biofuels, solvents, and pharmaceutical intermediates.[26, 27] Chapter 2 of this thesis primarily focuses on utilizing LA as a fundamental building block for the synthesis of various value-added chemicals.

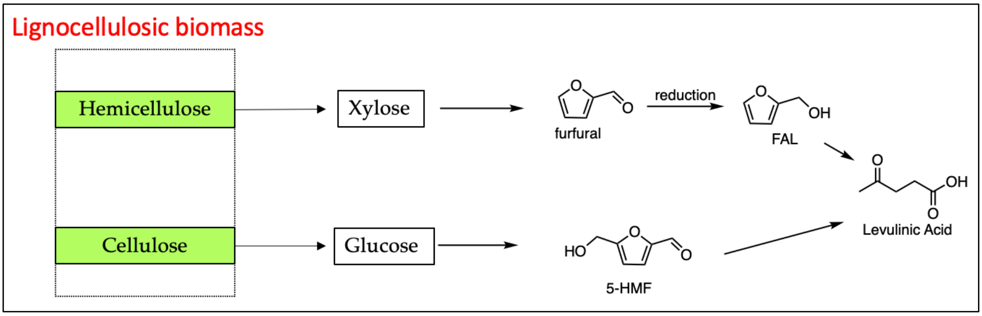


Figure 1.3: Conversion of lignocellulosic biomass to levulinic acid

1.3.3 Lignin

Another useful part of lignocellulosic biomass is lignin, which is a complex organic polymer comprising of various aromatic units.[28] Lignin contains about 30% of all non-fossil based carbon on earth and it can be a great alternative to fossil fuels for the production of sustainable energy and raw materials if we can develop efficient ways to convert lignin into value-added chemicals. Lignin can be employed in a variety of applications such as biofuels, biomaterials, carbon fibre production and because of its versatility, lignin is a great resource for sustainable and eco-friendly solutions in a variety of industries.[28-30]

1.3.4 Aromatic alcohols from lignin (Paper 4)

Depolymerization of lignin produces several aromatic alcohols, which are regarded as a sustainable source of chemicals for a number of reasons.[31] Firstly, they can be produced using renewable resources such as biomass, agricultural waste, and carbon dioxide, minimising dependency on finite fossil fuels. Furthermore, the manufacturing of alcohol from renewable sources results in lower carbon emissions. Many alcohols are biodegradable, reducing their environmental impact. Their adaptability allows for a wide range of applications in pharmaceuticals, cosmetics, agriculture, and renewable energy, thereby aiding sustainable solutions.[32]

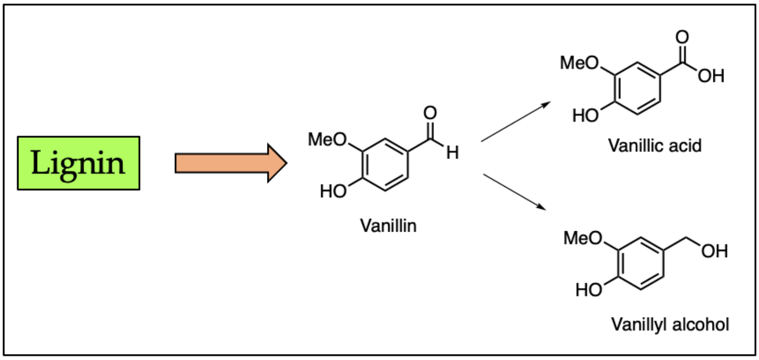
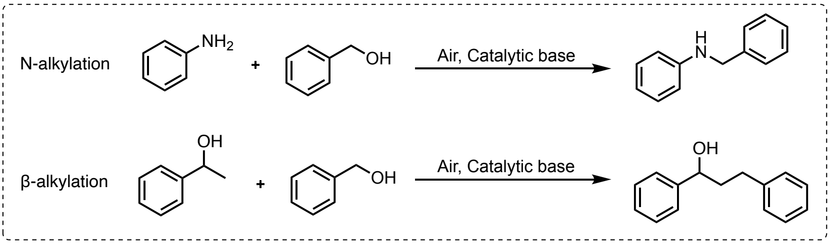


Figure 1.4: Conversion of lignin to vanillin and its derivatives.

An excellent example of an aromatic alcohol derived from lignin is vanillin. Approximately 20,000 tons of vanillin is manufactured annually, with about 15% sourced from lignin, accounting for approximately 3,000 tons per year and vanillin can also be converted into many other useful chemicals (Figure 1.4).[33] This indicates that if we can develop the right process, it is indeed possible to produce other such aromatic alcohols from biomass which can further reduce our dependency on fossil fuels.

In today's world, aromatic compounds find applications in a wide range of products, from pharmaceuticals to everyday items and a fundamental step in the production of these aromatic compounds involves creating new C-C and C-N bonds.[34] The derivation of nearly all these aromatic compounds at present originates from fossil-based resources, with these processes frequently involving the utilization of diverse toxic reagents and resulting in the generation of substantial waste. A sustainable solution could potentially arise through the substitution of these toxic reagents with bio-derived alcohols. The development of innovative methodologies to harness the potential of aromatic alcohols derived from lignin stands as a key avenue in realizing this sustainable solution.[31] Chapter 4 of the thesis is dedicated to the synthesis of numerous such C-C and C-N bonds using aromatic alcohols as reagents, a process that traditionally relied on toxic reagents like alkyl halides. Notably, unlike most of the previous literature in this area, our approach eliminates the necessity for any transition metal-based catalyst, as it effectively operates using only base as the catalyst (Scheme 1.1).

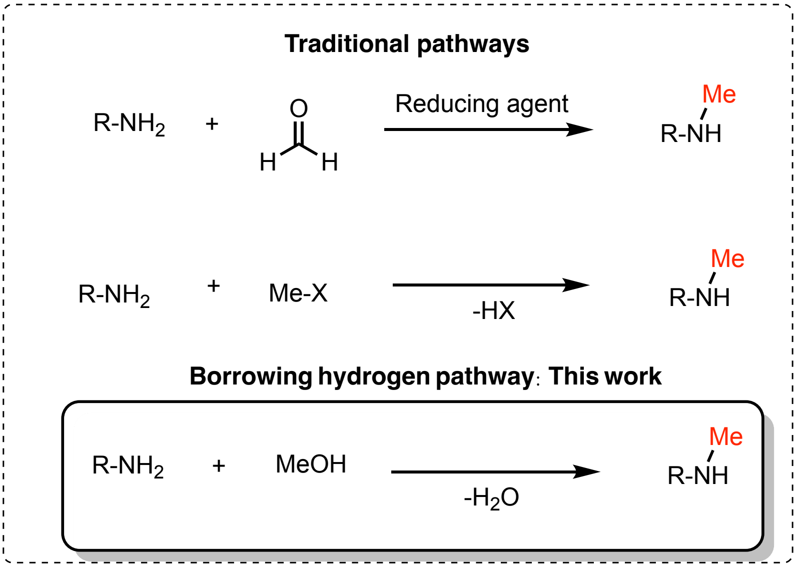


Scheme 1.1: Base catalyzed synthesis of C-N and C-C bonds (Paper 4).

1.4 Methanol and its potential as a C-1 source (Paper 3)

Methanol, also known as wood alcohol, finds application in many industries due to its versatile properties. Every year, around 100 million tons of methanol is produced worldwide, with demand increasing by the day.[35] Methanol is an important feedstock in the chemical industry for the production of formaldehyde, acetic acid, and other compounds. It is commonly used as a solvent for paints, varnishes, and inks, as well as in biodiesel manufacturing and as an antifreeze agent. Methanol is seen as a promising alternative fuel in the energy sector, where it can be used directly or transformed into hydrogen for fuel cells. [36] Currently, methanol is mainly produced using fossil-based resources but its production from biomass is also becoming popular. In future, the production of bio-based methanol is only going to increase to create a sustainable society.[37]

Industrially, methanol is a highly valuable chemical and apart from its other uses, it can be a great source of C1 molecule for many bulk and fine chemicals.[38] An example of this is N-methylation of amines with methanol as a C1 source.[39] N-methyl amines find several applications across industries. They serve as essential building blocks in the manufacture of pharmaceuticals and agrochemicals, which are used to protect crops. Additionally, they are utilized in dyes, pigments, rubber industry as accelerators and surfactants.[40] Traditionally, N-methylation was achieved using methylating agents like methyl iodide or dimethyl sulfate, or through reductive methylation with formaldehyde along with a reducing agent (Scheme 1.2).[41] Diazomethane is another reactive methylating agent used for N-methylation. However, these methods use toxic reagents and generate stoichiometric amounts of waste. Chapter 3 of the thesis focuses on creating an efficient approach for using methanol as a C1 source for the N-methylation of amines and nitro arenes. This is achieved through the development of a unique ruthenium NNN-based pincer complex, which serves as a catalyst for the N-methylation process using the BH method, resulting in the formation of water as the sole byproduct (Scheme 1.2).



Scheme 1.2: Methodologies for the synthesis of N-methyl amines.

1.5 Outline of the thesis

The thesis is aimed at harnessing diverse substrates derived from biomass, particularly chemicals originating from lignocellulosic biomass, to facilitate the generation of value-added chemicals to reduce our over-dependency on fossil fuels. This was done by developing novel catalytic strategies based on hydrosilylation and borrowing hydrogen methodologies.

In chapter 2, valorization of lignocellulosic biomass derived LA into various value-added chemicals was performed using hydrosilylation. The strategy selectively defunctionalizes biomass derived LA and its derivatives into value-added chemicals such as GVL, 1,4-pentanediol, 2-pentanol, 2-MTHF and even to C-5 hydrocarbons using cost-effective and non-toxic silanes and the commercially available catalyst $B(C_6F_5)_3$ at room temperature. Furthermore, various control experiments and kinetic studies were performed to get further insight of the reaction mechanism.

In chapter 3, a highly efficient phosphine free ruthenium-based pincer complex was developed with the potential of dual MLC and it was further used as a catalyst for the synthesis of various N-methylamines from anilines and nitroarenes using methanol as a C1 source with only catalytic amounts of base via borrowing hydrogen pathway.

In chapter 4, we have explored two catalytic transformations generally carried out with the BH methodology i.e., N-alkylation of amines with alcohols and β-alkylation of secondary alcohols with primary alcohols. Our findings reveal that these reactions can be executed with remarkable efficiency, with only catalytic amounts of base under the presence of air without any reliance on transition metal-based catalysts. Furthermore, to gain deeper insights into the underlying mechanistic pathways of these C-N and C-C bond-forming reactions, a series of control experiments were performed.

2. Valorization of biomass using hydrosilylation (Paper 1 and 2)

2.1 Introduction

2.1.1 Levulinic acid (LA): a chemical building block from biomass

Over the past few decades, there has been a notable surge in interest towards sustainable chemistry, primarily due to the depletion of fossil resources, the degradation of the environment, and the compelling necessity to shift towards alternatives that are both sustainable and environmentally friendly. Among the many chemicals being considered for this positive change, LA has captured significant attention due to its adaptable applications and its capacity to effectively tackle numerous urgent worldwide challenges.[42, 43]

LA can be easily derived from lignocellulosic biomass through tandem dehydration and hydrolysis as shown in figure 1.3 and has tremendous potential due to its efficient and economic production from renewable biomass, making it a sustainable platform chemical. LA has also been considered among the top 12 chemical building blocks from biomass by U.S. department of energy.[25]

LA is utilised as a precursor in the production of pharmaceuticals, plasticizers, and a variety of other additives.[44] The most common usage of LA is in the synthesis of aminolevulinic acid, a biodegradable herbicide widely used throughout South Asia. Another important application of levulinic acid is in cosmetics. Ethyl levulinate, a main derivative of LA, is widely used in perfumes and fragrances.[45] The global LA market is expected to touch around 71 million dollars by 2027 and especially in the last decade, a lot of work has been done for the valorization of LA into various value-added chemicals.[46, 47] LA can be upgraded into various biochemicals such as gamma-valerolactone, 2-methyltetrahydrofuran, valeric acid, 1,4-pentanediol, 2-pentanol, alkanes, alkenes etc. as shown in figure 2.1 and these chemicals can be further used as biofuels or biochemicals. [22] [48, 49]

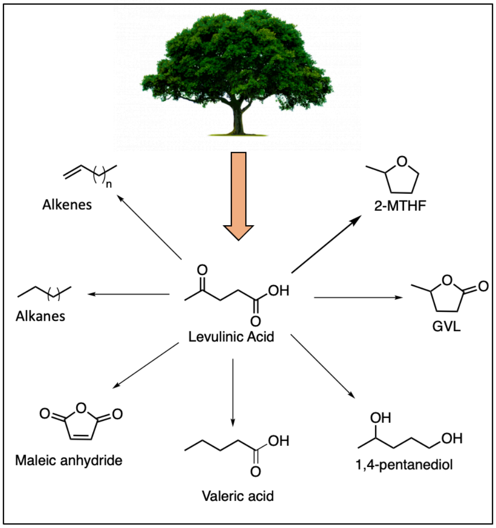


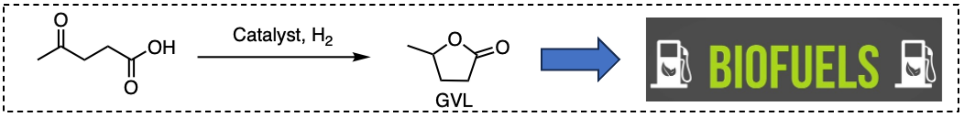
Figure 2.1: Conversion of LA into various value-added chemicals.

2.2 What has been already done with LA?

2.2.1 Valorization of LA using hydrogenation

Recently, there has been significant attention directed towards the valorization of LA and it has mainly been accomplished with hydrogenation i.e., in the presence of hydrogen and a catalyst, typically derived from transition metals. However, these procedures demand harsh reaction conditions, including elevated temperatures and pressures. Below are a few highlighted instances of value-added chemicals generated from LA through hydrogenation, accompanied by their respective applications.[1]

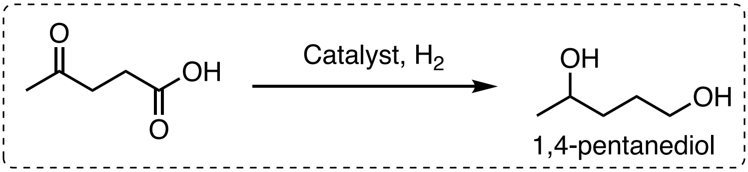
2.2.2 Conversion of LA to GVL



Scheme 2.1: Conversion of LA to GVL with hydrogenation

Catalytic reduction of LA to the non-toxic and water-miscible GVL is an important process as GVL is a versatile compound with applications in multiple fields. It serves as a green solvent, offering an eco-friendly alternative for various chemical processes. GVL is also explored as fuel additive and in biofuel production due to its high energy density and it also finds potential in pharmaceuticals, polymers, and personal care products (Scheme 2.1).[49] Hydrogenation of LA to GVL has been previously done with both homogeneous and heterogeneous catalysis. For example, Beller and coworkers reported ruthenium-triphos-based catalytic system for the production of GVL at 140 °C and 80 bar H_2 yielding up to 95% under solvent-free conditions,[50] and Fischmeister and coworkers reported the GVL production using iridium sandwich type homogeneous catalyst getting turnover numbers (TONs) as high as 174000.[51] Several heterogeneous catalysts have also been explored, for example, Jagadeesh and coworkers reported cobalt based nanoparticles as catalysts for the conversion of LA to GVL.[52] These are just some examples from the literature and many such examples of LA to GVL conversion are available in the literature underscoring the significance of this transformation.

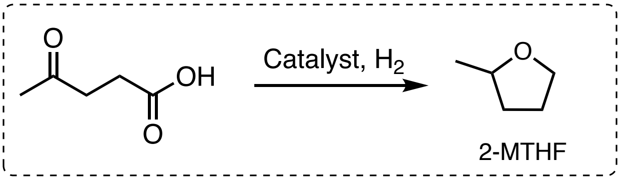
2.2.3 Conversion of LA to 1,4-pentanediol (1,4-PD)



Scheme 2.2: Conversion of LA to 1,4-PD with hydrogenation

LA or alkyl levulinates can also be converted to valuable 1,4-PD (Scheme 2.2). Recently, 1,4-PD has been considered for applications in polymer chemistry as a bio-based monomer along with its use in fragrances and synthetic lubricant industry.[53] 1,4-PD can also be converted into valuable pentadiene.[54] Most strategies for the production of 1,4-PD from biomass comprise of heterogeneous hydrogenation and all the available methodologies to synthesize 1,4-PD operates at very high temperatures and pressures and the commercial cost of 1,4-PD is expensive making it less feasible as a biochemical. Following are some selected examples from the literature for the conversion of LA to 1,4-PD. Cui *et al.* reported the hydrogenation of LA into 1,4-PD using Ru–MoO_x/activated carbon catalyst in a continuous fixed-bed reactor getting yields up to 96% under mild reaction conditions (70 °C and 4MPa H_2).[55] Recently, Dong and coworkers reported nitrogen doped carbon nanotube confined CuCo nanoalloy based catalyst for the hydrogenation of LA to 1,4-PD getting yields up to 87.8%.[56]

2.2.4 Conversion of LA to 2-MTHF



Scheme 2.3: Conversion of LA to 2-MTHF with hydrogenation

Due to its distinctive combination of properties such as the capacity to dissolve a wide variety of compounds, low toxicity, and a reduced boiling point, 2-MTHF holds significance as both a crucial solvent and an intermediate across diverse industries. It is frequently adopted as an environmentally friendlier substitute for conventional solvents like THF and dichloromethane and the United States Department of Energy has also granted approval for the incorporation of 2-MTHF as a gasoline additive.[57] 2-MTHF is usually synthesized from furfural however, its synthesis from LA has also grabbed significant attention in past few years. Following are some selected examples from the literature for the conversion of LA to 2-MTHF. For example, Miller and coworkers have reported N-triphos based ruthenium complexes as catalysts for the production of 2-MTHF and Kaneda and coworkers reported a one-pot synthesis of MTHF from LA using a Pt−Mo/H-β catalyst in water giving 2-MTHF with yields up to of 86%.[58, 59]

2.2.5 Conversion of LA/GVL to hydrocarbons

Hydrocarbons have an enormous number of applications in our society and synthesizing them from biomass has the potential to reduce our dependency on fossil fuels. Also, the circular economy is supported by biomass-derived hydrocarbons, which have a variety of uses as fuels, solvents, and chemical intermediates. Both homogeneous and heterogeneous hydrogenation has been explored for the valorization of lignocellulosic biomass derived chemicals into hydrocarbons. For example in 2005, Dumesic and coworkers reported the production of liquid alkenes having carbon atoms from C_7-C_{15} from biomass derived carbohydrates.[60] In 2010, the same group reported the conversion of GVL into liquid alkenes via a butene intermediate by combining the decarboxylation and oligomerization strategies.[61] Recently, GVL has also been investigated as a source for bio-derived pentane synthesis. For example, Yan and coworkers reported converting GVL to biofuels pentyl valerate and pentane with yields of 60.6% and 22.9%, respectively, using a bifunctional Pd/HY catalyst[62] and Gu, Ding and coworkers reported converting GVL to pentane with yields of up to 93.5% using a Co/HZSM-5 bifunctional catalyst.[63]

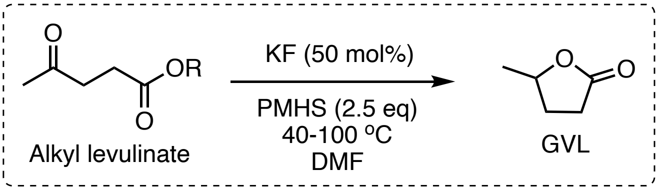
2.2.6 Concluding remarks on the conversion of biomass to hydrocarbons

While significant advancements have been outlined in the preceding section, the conversion of biomass into hydrocarbons still generally remains a less economically viable process in comparison to obtaining them from fossil fuels. In addition, numerous research groups worldwide are actively working on devising novel methodologies for utilizing CO_2 as a carbon source to produce hydrocarbons and if humanity can successfully achieve this transformation in an economically sustainable and scalable manner, it has the potential to be a game-changer in the battle against climate change.[64, 65]

2.3 Valorization of LA using hydrosilylation

Silicon is the second most abundant element in the earth's crust and there are substantial number of organosilicon compounds integrated into our everyday life. Among many other methods available for the formation of the organosilicon compounds, catalytic hydrosilylation has been considered the best method so far as it is a safer and relatively milder method.[66] Considering the benefits of hydrosilylation, it also has the potential to upgrade biomass in large quantities for the production of value-added chemicals. Also, hydrosilylation can utilize silanes such as polymethylhydrosiloxane (PMHS) and tetramethyldisiloxane (TMDS) that are cheap and non-toxic large-scale byproducts of the silicone industry.[67] Following are some selected examples from the literature where hydrosilylation was utilized for the valorization of lignocellulosic biomass into bio-chemicals.

2.3.1 Conversion of LA to GVL with hydrosilylation

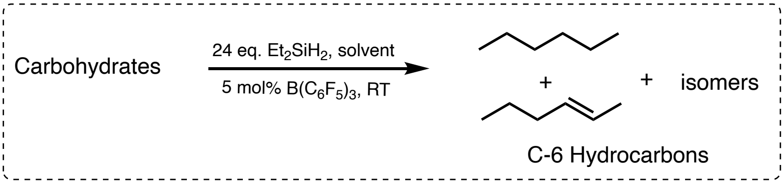


Scheme 2.4: Conversion of LA to GVL using hydrosilylation

Despite the fact that hydrosilylation is a well-established technique, we discovered that it has rarely been utilized for the valorization of levulinic acid to GVL. Yang and coworkers, for example, reported a recyclable hydrosilylation method for the conversion of alkyl levulinates to GVL employing PMHS and KF as catalysts

(Scheme 2.4).[68] In 2019, the same group reported the conversion of alkyl levulinates to GVL using tetrabutylammonium fluoride (TBAF) as a catalyst and PMHS as silane; however, very high catalyst loadings were used.[69]

2.3.2 Conversion of biomass to hydrocarbons with hydrosilylation



Scheme 2.5: Conversion of carbohydrates into C-6 hydrocarbons

Hydrosilylation has rarely been utilized for the valorization of lignocellulosic biomass to hydrocarbons. For examples, in 2013, Gagné and coworkers used an iridium pincer catalyst to convert silyl-protected sugars into a mixture of hexane isomers.[70] In 2014, the same group reported the valorization of carbohydrates into hydrocarbons by utilizing $B(C_6F_5)_3$ as a catalyst and Et_2SiH_2 as silane although high catalyst loading of 5 mol% was used for the reaction (Scheme 2.5).[71] In 2014, Cantat and coworkers reported the reduction of oxalic acid to ethane using hydrosilylation at room temperature using $B(C_6F_5)_3$ as catalyst.[72] Notably, hydrosilylation has never been used for the valorization of levulinic acid into hydrocarbons.

2.3.3 Our goal

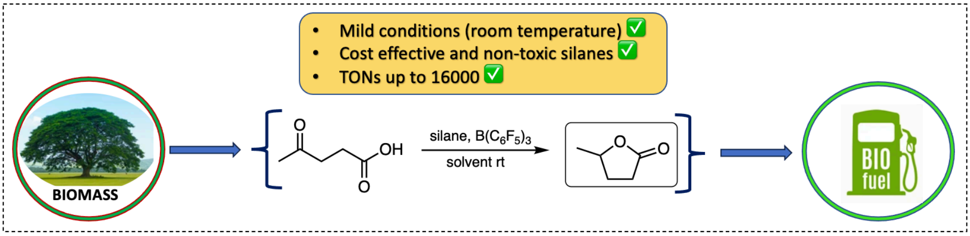
Although several strategies for valorizing LA and its derivatives existed in the literature, the majority of them necessitated elevated temperatures and pressure. Furthermore, many of the existing strategies could only produce a specific value-added chemical from LA, such as GVL, 2-MTHF, or 1,4-PD. Our objective was to establish a novel hydrosilylation-based methodology for LA valorization, characterized by milder reaction conditions, and the capacity to produce multiple value-added chemicals from a single starting material. Furthermore, we aimed to explore the reduction outcomes of LA between hydrosilylation and previously reported hydrogenations and also to investigate the reactivity differences among various silanes such as PMHS, TMDS and Et_3SiH in the valorization of LA and its derivatives.

2.4 Summary of paper 1: Conversion of levulinic acid to GVL using hydrosilylation

2.4.1 Motivation behind the work

Although GVL is a valuable chemical derived from biomass, its conversion from LA has primarily relied on hydrogenation, which typically demands elevated temperatures and pressures. Surprisingly, despite the extensive use of hydrosilylation in chemistry, we discovered that the conversion of LA to GVL had never been attempted through hydrosilylation. This piqued our interest, and our objective became exploring the development of a novel hydrosilylation-based methodology for the conversion of LA to GVL under milder conditions. After going through the literature on hydrosilylation, we found that $B(C_6F_5)_3$ as catalyst can be the right candidate for this work as it has been previously used for many different transformations such as hydrosilylation, deoxygenation, boration and hydrogenation among others.[73] As the catalytic system of $B(C_6F_5)_3$ and silane has been utilized multiple times by the researchers for many interesting transformations, we were curious to check its reactivity with levulinic acid.

After optimizing the reaction conditions, it was found that $B(C_6F_5)_3$ as catalyst can efficiently catalyze the conversion of LA to GVL at room temperature. The lewis acid system enabled the use of cost effective and non-toxic silanes (such as PMHS and TMDS) and a very low catalyst loading was achieved (Scheme 2.6).[74]

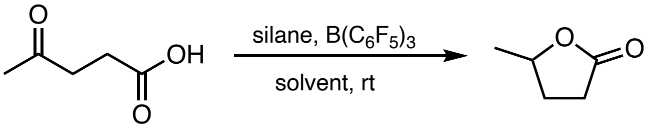


Scheme 2.6. Conversion of LA to GVL using hydrosilylation. [19]

Different silanes were tested for the conversion of LA to GVL and TMDS was found be the most effective with TONs as high as 16000 as shown in table 2.1 (entry 3). Other silanes were also investigated for the conversion, including Et_3SiH and Ph_2SiH_2, which provided excellent yields despite requiring higher catalyst loadings (entries 4-7). Gratifyingly, Et_3SiH gave 80% yields when water was employed as the solvent, and PMHS gave 50% yield with a mixture of water and CH_2Cl_2 (entries 5 and 8). These results show that drying of reagents and solvents is not necessary. The best solvent for the conversion, out of a number of others tested, was CH_2Cl_2

which is a limitation of this work considering the toxicity and poor environmental performance associated with chlorinated solvents. However, with only a 0.5 mol% catalyst loading, other solvents like acetonitrile, toluene, and benzene also demonstrated fair-to-good yields with PMHS (entries 9–12). Notably, the reaction only requires one step to complete and no further workup is required to cleave the silyl ether intermediate.

Table 2.1. Hydrosilylation of levulinic acid to GVL.[a]

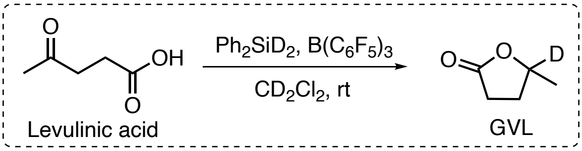


Entry	Silane (eq)	$B(C_6F_5)_3$ [mol%]	Solvent	Yield, Conversion [%][b] (TON)
1	PMHS (2)	0.1	CH_2Cl_2	85, 95 (850)
2	TMDS (1)	0.05	CH_2Cl_2	97, 100 (1940)
3	TMDS (1)	0.005	CH_2Cl_2	80, 86 (16000)
4	Et_3SiH (1.5)	0.1	CH_2Cl_2	94, 100 (940)
5	Et_3SiH (3)	1	H_2O	80, 94 (80)
6	Et_3SiH (1.5)	0.5	$CDCl_3$	94, 100 (188)
7	Ph_2SiH_2 (1)	0.5	$CDCl_3$	93, 100 (186)
8	PMHS (2)	1	CH_2Cl_2/H_2O[c]	50, 62 (50)
9	PMHS (2)	0.5	Benzene	71, 89 (142)
10	PMHS (2)	0.5	Toluene	55, 83 (110)
11	PMHS (2)	0.5	CH_3CN	50, 88 (100)
12	PMHS (2)	0.5	Pentane	20, 45 (40)

[a] Reaction conditions: In a round bottom flask, solvent and catalyst were added followed by the addition of silane and levulinic acid and the reaction was stirred for 8 hours. [b] Yield and conversion were determined by ^1H NMR of the crude reaction mixture with respect to 1,3,5-trimethoxybenzene as internal standard. All reactions were repeated at least twice to ensure reproducibility. [c] CH_2Cl_2 and H_2O were used in a ratio of 1:1 (v/v).

2.4.2 Deuterium labelling studies

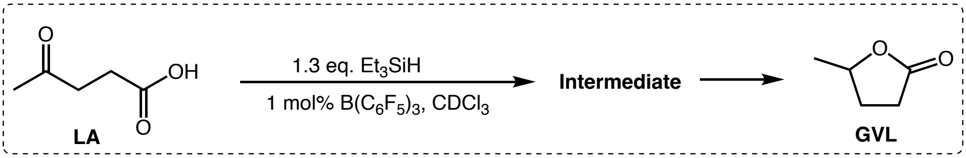
Deuterium labelling studies were performed using Ph_2SiD_2 as silane to incorporate deuterium in the GVL confirming the role of hydrosilylation in the GVL formation (Scheme 2.7).



Scheme 2.7: Deuterium labelling studies for the conversion of LA to GVL.

2.4.3 Mechanistic studies

To gain further insight of the reaction mechanism, a reaction was performed with LA and 1.3 eq. Et_3SiH using 1 mol% of $B(C_6F_5)_3$ in a J. Young NMR tube (Scheme 2.8). The reaction was monitored using in-situ ^{1}H NMR spectroscopy and the concentration vs time graph can be seen in figure 2.2. It can be clearly seen in the concentration profile that LA is consumed very early in the reaction and there is a significant concentration of the intermediate throughout the reaction.



Scheme 2.8: LA to GVL conversion inside J. Young NMR tube.

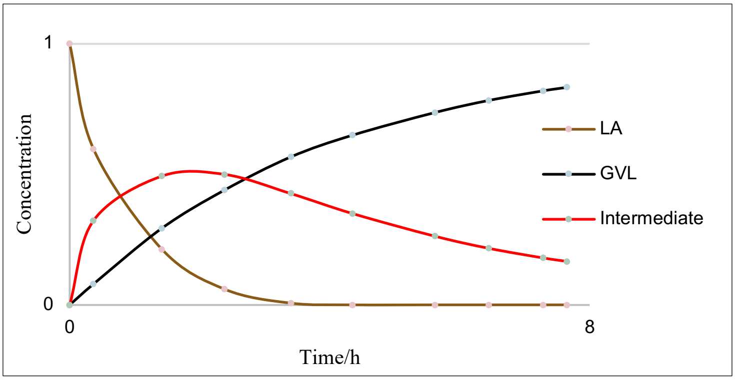
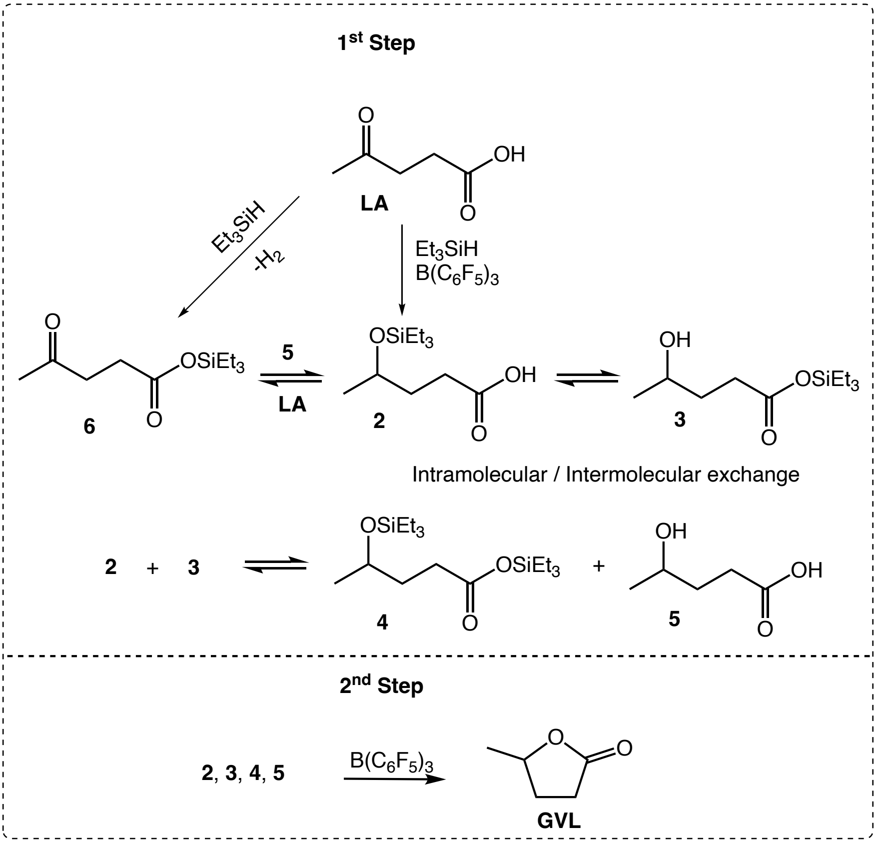


Figure 2.2: Reaction profile for the conversion of LA to GVL.

It is worth noting that the conversion of LA to GVL involved five distinct intermediates, making the reaction mechanism particularly intriguing. Initially, hydrosilylation happens on the keto group of LA to form the intermediate **2** which can further cyclize into GVL (Scheme 2.9). However, ^{1}H NMR spectroscopy showed that **2** is not the sole intermediate in the reaction and four other intermediates similar to **2** are also involved. We attributed this to the exchange of the silyl group in both intermolecular and intramolecular fashion as shown in the scheme 2.9. Interestingly, the concentration of the intermediates was found to be dependent on the amount of silane used in the reaction. Using 0.9 eq. of silane (Et_3SiH) resulted in higher concentration of monosilylated intermediates **2** and **3** and in contrast using 2.5 eq. of Et_3SiH resulted in higher concentration of bissilylated intermediate **4.** Furthermore, control experiments were performed with acetic acid and acetone as substrates to confirm the same behavior of silyl exchange.



Scheme 2.9. Mechanism of LA to GVL conversion with all the intermediates involved.

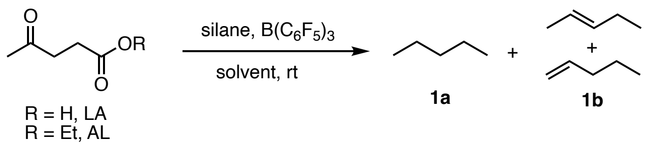
To study the kinetics of LA to GVL conversion, we used the graphical elucidation method proposed by Burés.[75] The kinetics study revealed that in the 1st step, the reaction order is 1 in silane, 1.5 in catalyst $B(C_6F_5)_3$ and a negative order of -1 was observed with respect to LA (Scheme 2.9). In the second step, it was observed that the order with respect to $B(C_6F_5)_3$ had changed to 1. Notably, our kinetics studies pointed towards the Lewis acid activation of both the carbonyl group and the silane contrary to previous findings by Piers and coworkers as they proposed a mechanism where the carbonyl group is not activated by the borane based on the fact that they found a rate law which was first order on $B(C_6F_5)_3$. Based on the higher reaction order in catalyst as compared to Piers previous observation, our mechanism differs in that it proposes activation also of the ketone.[76, 77]

2.5 Summary of paper 2: Selective valorization of LA and its derivatives into hydrocarbons and biochemicals

2.5.1 Conversion of biomass to C-5 hydrocarbons

After the conversion of LA to GVL, we wanted to explore the conversion of LA into other value-added chemicals and we became curious to explore our novel hydrosilylation methodology for the complete defunctionalization of LA to C-5 hydrocarbons. The production of C-5 hydrocarbons from biomass presents numerous advantages, offering a long-term and sustainable alternative to fossil fuels. With great optimism, we commenced testing various reaction conditions and after optimizing the reaction parameters, we were able to successfully use our hydrosilylation based methodology for the reduction of LA into a mixture of C-5 hydrocarbons at room temperature. Notably, defunctionalization of LA/AL resulted in a mixture of pentane and pentene with pentane being the major product. Different silanes were tested for the process and cost effective TMDS showed the best turnover number and turnover frequency of 1900 and 11400 h^{-1} respectively (Table 2.2, entry 2). Also, toluene was explored as an alternative and greener solvent as compare to chlorinated solvents and excellent yields were achieved although higher catalyst loadings were required (entries 7-10).[78]

Table 2.2. Hydrosilylation of LA and its derivatives into hydrocarbons. [a]



Entry	Substrate	$B(C_6F_5)_3$ (mol %)	Silane (eq.)	Solvent	Yield %[b] (1a/1b)
1[c]	LA	0.1	TMDS (4)	CH_2Cl_2	90 (55/35)
2[c]	EL	0.05	TMDS (4)	CH_2Cl_2	95 (59/36)
3[c]	ML	0.05	TMDS (4)	CH_2Cl_2	94 (58/36)
4[c]	LA	1	PMHS (7)	CH_2Cl_2	60 (37/23)
5[d]	LA	0.5	Et_2SiH_2(4)[e]	$CDCl_3$	84 (56/28)
6[d]	LA	0.5	Ph_2SiH_2(4)[e]	$CDCl_3$	80 (55/25)
7[d]	LA	0.5	TMDS (4)	toluene-d_8	92 (62/30)
8[d]	EL	0.5	TMDS (4)	toluene-d_8	95 (63/32)
9[d]	ML	0.5	TMDS (4)	toluene-d_8	94 (62/32)
10[c]	GVL	0.5	TMDS (3)	toluene	92 (58/34)

[a] Reaction conditions: Solvent and catalyst were taken in a round bottom flask/J. Young NMR tube followed by the addition of substrate and silane for 10-30 minutes in a water bath. [b] Yields were determined by ^1H NMR spectroscopy using mesitylene as internal standard. [c] The reactions were performed with 1 mmol substrate and 5 ml solvent in a round bottom flask. [d] The reactions were performed with 0.2 mmol substrate, 0.5 ml solvent in a J. Young NMR tube. [e] Reactions were performed inside a glove box. AL = alkyl levulinate, EL =. ethyl levulinate.

Furthermore, a wide range of lignocellulosic biomass derived chemicals were explored to expand the substrate scope of our methodology. Using TMDS as silane defunctionalization of substrates such as GVL, valeric acid (VA), 1,4-PD, 2-MTHF, 2-P etc. to the respective hydrocarbons was achieved with very high yields (Figure 2.3). All the reactions were conducted inside a J. Young NMR tube with toluene as solvent at room temperature and analyzed using ^1H NMR spectroscopy.

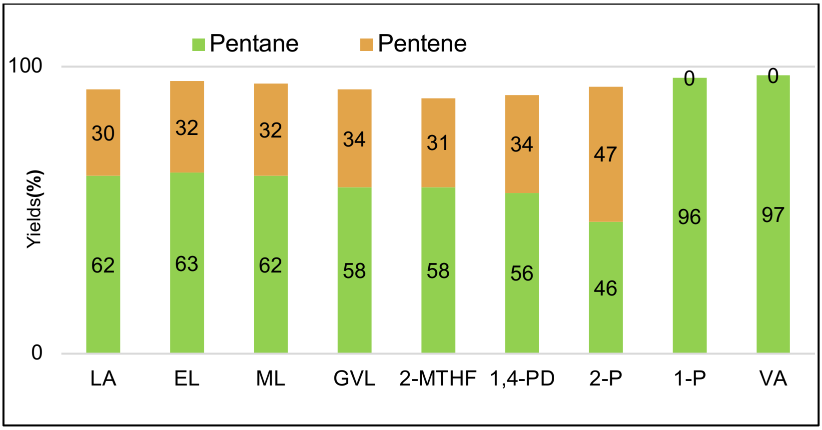
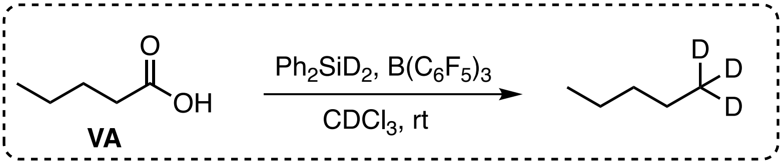


Figure 2.3. Defunctionalization of biomass derived substrates into hydrocarbons.

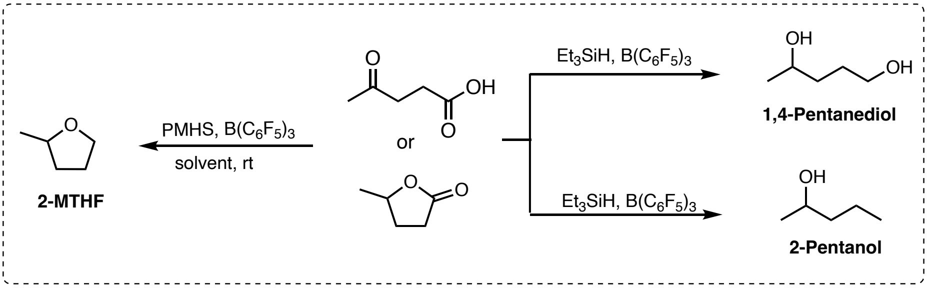
To confirm the role of hydrosilylation in the formation of hydrocarbons, deuterium labelling studies were conducted with VA as substrate and Ph_2SiD_2 as silane and the incorporation of deuterium in the pentane molecule was confirmed by ^1H and ^{13}C NMR spectroscopy (scheme 2.10).



Scheme 2.10. Deuterium labelling studies using valeric acid as substrate.

2.5.2 Conversion of LA/GVL into other value-added chemicals

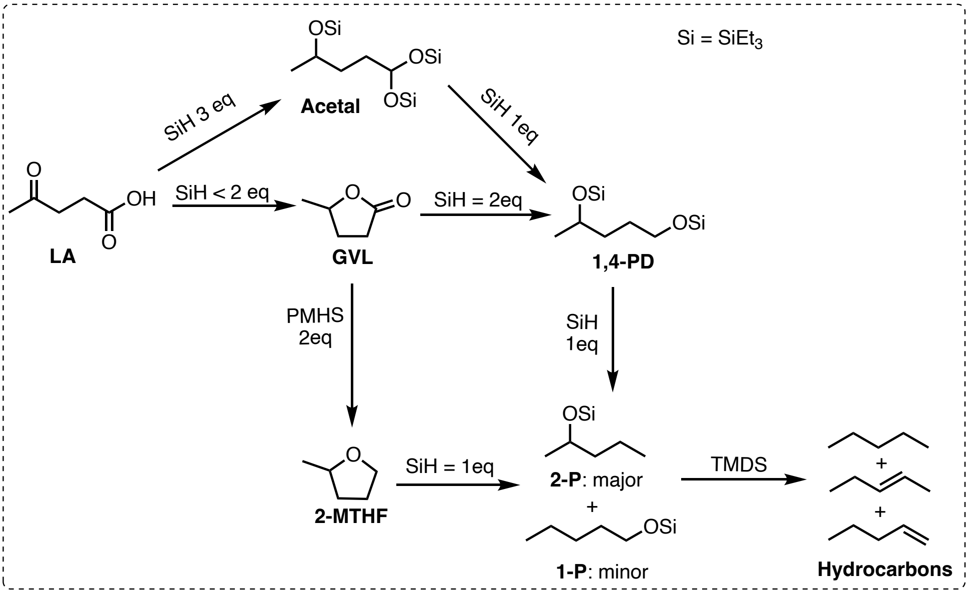
Furthermore, we wanted to explore the valorization of LA into other value-added chemicals and after optimizing the reaction conditions, we were able to tune the reactivity of our methodology for the selective conversion of LA/GVL into different value-added chemicals such as 1,4-PD, 2-P and 2-MTHF at room temperature using $B(C_6F_5)_3$ as catalyst just by changing either the concentration of silane or the silane itself (Scheme 2.11). Utilization of Et_3SiH as silane even under neat conditions selectively defunctionalized LA/GVL into 1,4-PD and 2-P whereas employment of non-toxic PMHS resulted in the formation of 2-MTHF as the sole product. Notably, the conversion of LA to 1,4-PD had never been achieved with hydrosilylation before our work and there is only one example in the literature for the conversion of LA to 2-MTHF with hydrosilylation by Garcia and coworkers using a manganese-based catalyst.[79]



Scheme 2.11: Conversion of LA/GVL into 1,4-PD, 2-P and 2-MTHF.

2.5.3 Mechanistic studies

Scheme 2.12 shows the possible reaction pathway for the conversion of LA to hydrocarbons. As shown in the mechanism of paper 1, the use of less than 2 eq. of silane with LA resulted into GVL as the sole product, it was found that using 3 eq. silane resulted into the acetal intermediate. Furthermore, using 4 eq. of Et_3SiH with LA resulted into the formation of silylated 1,4-PD and interestingly, that process goes via an acetal intermediate and not via GVL. For the hydrosilylation of carboxylic acid, a similar acetal intermediate has been observed many times in the literature.[72, 80, 81] It is interesting to note that depending on the silane employed, two distinct products were seen when GVL was reduced. When utilising Et_3SiH as silane, 1,4-PD was the product whereas using PMHS as silane resulted into 2-MTHF as the product. Furthermore, 1,4-PD or 2-MTHF can be reduced into 2-P and 1-P with former being the major product.[82] Finally, complete defunctionalization can be done into hydrocarbons using silanes such as TMDS, Ph_2SiH_2, Et_2SiH_2 etc.



Scheme 2.12: Stepwise reaction pathway from levulinic acid to hydrocarbons.

2.5.4 Conclusion of paper 1 and 2

In summary, we have developed a new hydrosilylation based methodology for the selective defunctionalization of bio-derived LA into various bio-chemicals such as GVL, 1,4-PD, 2-P, 2-MTHF and even C-5 hydrocarbons using a commercially available metal-free catalyst at room temperature. The utilization of cost-effective silanes, including TMDS, highlights the economic viability and sustainability of the work. Notably, this is the first example of the conversion of LA to GVL, 1,4-PD and even hydrocarbons through hydrosilylation, utilizing non-toxic silanes and a low catalyst loading, achieving exceptional TONs and TOFs. Furthermore, several control experiments and kinetics studies were also performed to shed some light on the mechanism.

3. N-methylation with methanol as a C1 source (Paper 3)

3.1 Introduction

Metal pincer complexes have received significant attention in the last two decades owing to their excellent reactivities for a number of catalytic transformations such as hydrogenation and dehydrogenation reactions. Many of these metal pincer complexes operate via the principle of metal ligand cooperation (MLC), a phenomenon where the ligand contributes directly in the catalysis. This project is about the development of a new class of Ru-NNN based pincer complexes with the potential for dual modes of MLC and the synthesized Ru complexes were further used as catalyst for the N-methylation of anilines and also direct N-methylation of nitro arenes with methanol as a green source of C1 to selectively synthesize N-methylanilines via BH methodology under relatively milder conditions.

3.1.1 Pincer complexes and dual MLC

The groundbreaking research by Moulton and Shaw regarding the metallation of the tridentate PCP ligand using transition metals gave rise to an innovative category of organometallic complexes. These compounds were subsequently termed "pincer complexes" by van Koten.[83-86] These organometallic complexes exhibit distinct structures and reactivity, capturing significant interest in catalytic applications that span a wide array of uses.[87-90] Ligands play a very important role in the pincer complexes to control the reactivity around the metal center and hence developing new ligands or modification of the existing ligands can in principle completely change the reactivity of the metal pincer complex.[91]

Many of these pincer complexes works on the principle of MLC, where both metal and ligands actively participate in the catalysis and particularly, after the pioneering work by Milstein and coworkers on MLC, pincer complexes with MLC have become an important area for researchers.[92-95] Milstein and coworkers had reported the ruthenium PNN based pincer complex as an effective catalyst for multiple catalytic transformations where the pyridyl based metal complex operated via the aromatization/dearomatization MLC strategy and after that many other similar MLC strategies have been reported in the literature.[96, 97]

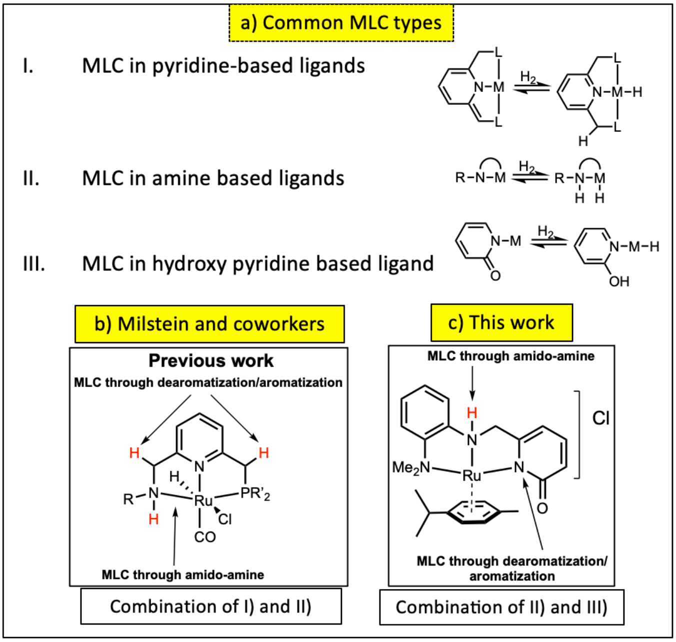


Figure 3.1: a) Common types of MLC, b) Dual MLC reported by Milstein and coworkers and c) This work with dual MLC

Presently, the three most widely recognized forms of MLC include the aromatization/dearomatization of pyridyl-based ligands, as reported by Milstein and coworkers,[94] MLC in the amine based ligands pioneered by Noyori[98, 99] and MLC in the hydroxypyridine based ligands reported by Fujita, Yamaguchi and coworkers also via aromatization/dearomatization as shown in figure 3.1a.[100-103]

However, in 2014, Milstein and coworkers reported a special PNN-based pincer ligand. This ligand was unique because it combined two different MLC pathways into one ligand (Figure 3.1b). This special feature allowed the complex to have dual MLC modes, and as a result, it showed much better catalytic activity. Later on, the same group developed many similar pincer complexes using this dual MLC approach. They found that these complexes performed exceptionally well in multiple catalytic transformations compared to pincer complexes with only one MLC pathway.[104-106]

3.1.2 Our approach

Motivated by the discoveries of Milstein and coworkers, our curiosity led us to explore the dual MLC approach. We integrated the other two MLC types into a single ligand i.e., MLC in amine-based ligands and MLC in hydroxypyridine-based ligands and subsequently synthesized the ruthenium complex of the ligand, as depicted in figure 3.1c. Furthermore, to test the catalytic activity of our novel pincer complex, N-methylation of amines with methanol was chosen as the benchmark reaction.

3.1.3 N-methyl amines (production and uses)

N-methylation involves the addition of a methyl group to the nitrogen atom of an organic compound such as aniline and is an essential part in the process of making several fine chemicals, including pharmaceuticals, dyes and agricultural chemicals.[87] Historically this synthesis has been done using relatively expensive and environmentally hazardous chemicals such as methylating agents like methyl iodide or dimethyl sulfate, or via reductive methylation with formaldehyde along with a reducing agent. Diazomethane is another reactive methylating agent used for N-methylation (Figure 3.2a). However, most of these methylating agents are toxic in nature and also produces stoichiometric amounts of waste.

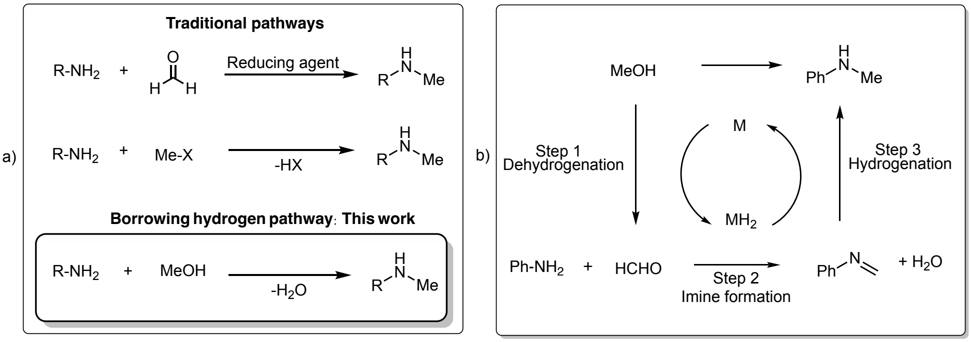


Figure 3.2: a) Methodologies for the synthesis of N-methyl amines, b) Mechanism of the N-methylation of amines with methanol with the BH approach.

As opposed to the traditional mono-amination methods, the BH approach uses methanol as an inexpensive C1 source to form the new C-N bonds generating only water as byproduct with transition metal-based catalysts.[41] The BH method is highly selective in mono-methylation and circumvents the very common problem of forming dimethyl amines as the product from mono-methylated amines is more reactive than the starting material. The BH mechanism consists of 3 steps as shown in figure 3.2b. In the first step the methanol gets dehydrogenated into formaldehyde followed by an intermediate reaction to form the imine and the last step is the hydrogenation of imine into the N-methylated product. The role of transition metal-based catalyst is to store the hydrogen after the first step of methanol dehydrogenation and to deliver it back in the last step of imine hydrogenation and this storage of hydrogen in the pincer complex can be done via MLC pathway as shown in figure 3.1a.[107, 108]

3.1.4 Previous works on N-methylation of anilines

Ruthenium complexes as catalysts are well-known for catalyzing such borrowing-hydrogen transformations, including N-alkylation of amines with alcohols and especially after the pioneering work by Watanabe and co-workers in 1988, several transition metal catalyzed N-methylation of alkyl or arylamines with methanol have been reported.[109] Many groups have previously investigated the N-methylation of amines with methanol as a C1 source, primarily using noble metal-based catalysts.[87, 110-124] For example, Kayaki and coworkers published a ruthenium-based catalyst for N-methylation, but the utilized temperature was relatively high at 150 °C. On another front, Chen and coworkers reported the mono-methylation of aniline using a bidentate iridium-based catalyst. More recently, researchers have also utilized first-row transition metal-based catalysts for the N-methylation of amines with methanol.[125-131] For example, Beller and coworkers reported a manganese-based pincer complex as a catalyst with 50 mol% base, while Renaud and coworkers reported an iron-based catalyst with 10 mol% CsOH as the base (Figure 3.3).

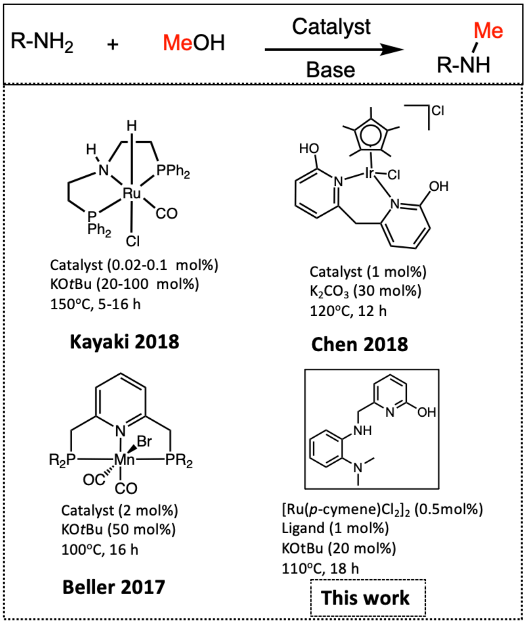


Figure 3.3: Selected examples of N-methylation of amines with methanol

3.1.5 Direct N-methylation of nitro arenes

Aromatic amines are industrially produced via hydrogenation of nitro arenes so the classical synthesis of N-methyl amines goes via two steps i.e., the conversion of nitro arenes to amines and the conversion of amines to N-methyl amines. Therefore, the direct N-methylation of nitroarenes to N-methylamines has gained recent attention for converting the two step process into a single step. The N-methylation of nitrobenzene using methanol as a C1 source has been investigated by several groups, employing both noble and non-noble transition metal-based catalysts.[113, 115-118, 121, 132, 133] For example, Kundu and coworkers reported a ruthenium pincer complex as catalyst with 100 mol% NaOMe as base and recently, Balaraman and coworkers reported manganese PNP based pincer complex as catalyst for the N-methylation of nitroarene at 150 °C with 50 mol% Cs_2CO_3 as base.[134] (Figure 3.4) However, a prevalent challenge in most of the reported N-methylation methods for nitroarenes is the necessity for stoichiometric amounts of base or elevated temperatures to achieve satisfactory yields. Additionally, many catalytic complexes utilize expensive ligands, often containing phosphine groups, which not only incur high costs but are also susceptible to oxidation. To tackle these problems, we became curious to test our novel ruthenium complex with nitrogen based ligand for the direct N-methylation of nitro arenes.

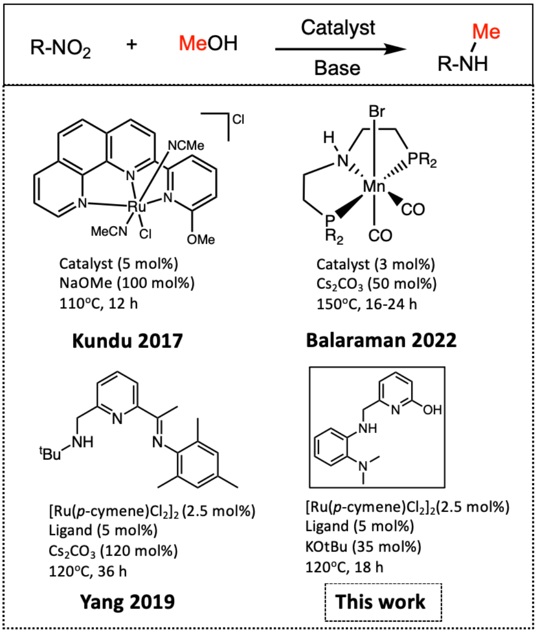


Figure 3.4: Selected examples N-methylation of nitro arenes with methanol.

3.2 Summary of paper 3: Ruthenium NNN-based pincer complexes with the potential of dual metal ligand cooperation as catalysts for N-methylation of anilines and nitroarenes under air

We started our investigation by synthesizing the ligand **L1** and **L2** where two types of MLC strategies were combined together into one ligand i.e., MLC in amido/amine and MLC in hydroxypyridine/pyridone as shown in figure 3.5 and both **L1** and **L2** can potentially have dual MLC pathway. Having the desired ligand in hand, we were curious to explore its reactivity for N-methylation reactions using methanol as a C1 source. At the start of our investigation, we tested both the ligands *in situ* along with different commercially available ruthenium precursors as catalyst for N-methylation of aniline as shown in table 3.1 and after optimizing the reaction conditions it was found that **L1** is more efficient than **L2** and subsequently **L1** was chosen for further reactions (entries 2 and 3). Furthermore, after optimizing several reaction parameters, the best reaction conditions were found to be 20 mol% of KOtBu at 110 °C for 18h with a catalyst loading of $[Ru(p\text{-cymene})Cl_2]_2$ (0.5 mol%) and **L1** (1 mol%) giving 98% yields (entry 4).

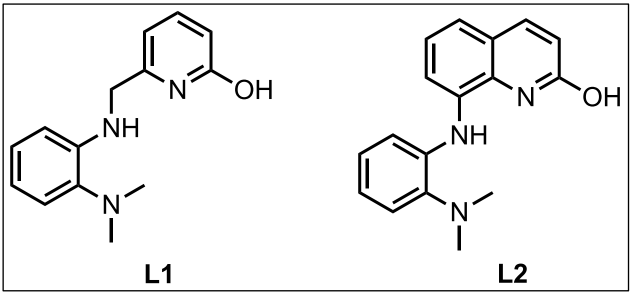
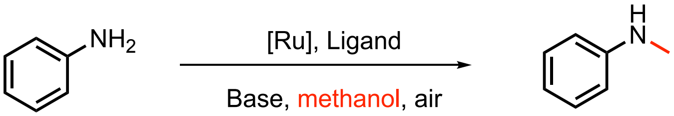


Figure 3.5: Ligands synthesized in this work with the potential of dual MLC.

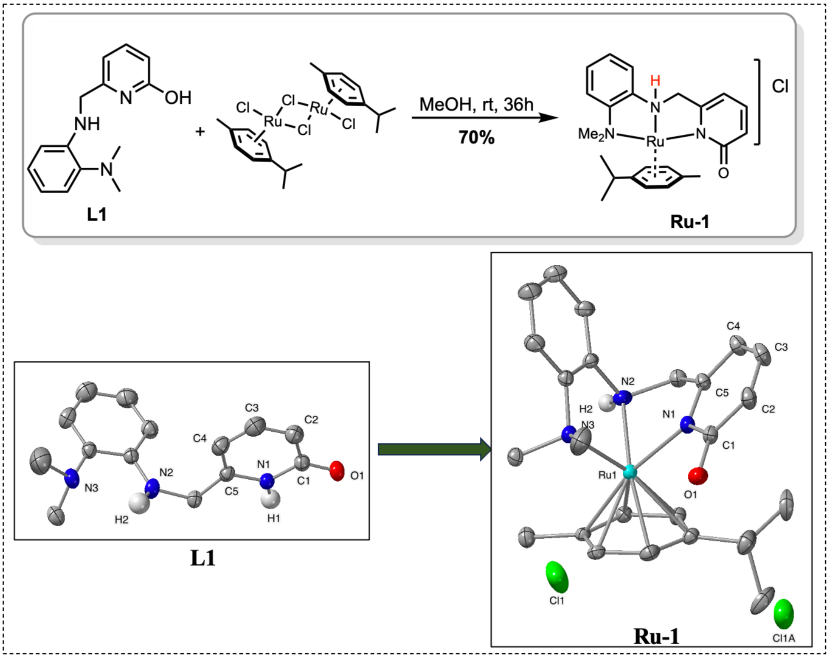
Table 3.1: Optimization of Ru-catalyzed N-methylation of aniline with methanol



Entry	Ru precursor (mol%) + Ligand (mol%)	Base (mol%)	Temp.(°C)	Yields%
1	$[\mathrm{Ru}(p\text{-cymene})\mathrm{Cl_2}]_2$ (0.5) + L-1 (1)	KOtBu (20)	80	38%
2	$[\mathrm{Ru}(p\text{-cymene})\mathrm{Cl_2}]_2$ (0.5) + L-1 (1)	KOtBu (20)	100	91%
3	$[\mathrm{Ru}(p\text{-cymene})\mathrm{Cl_2}]_2$ (0.5) + L-2 (1)	KOtBu (20)	100	63%
4	$[\mathrm{Ru}(p\text{-cymene})\mathrm{Cl_2}]_2$ (0.5) + L-1 (1)	KOtBu (20)	110	98%
5	$[\mathrm{Ru}(p\text{-cymene})\mathrm{Cl_2}]_2$ (0.25) + L-1 (0.5)	KOtBu (20)	110	67%
6	$[\mathrm{Ru}(p\text{-cymene})\mathrm{Cl_2}]_2$ (0.5) + L-1 (1)	KOtBu (10)	110	55%
7	$\mathrm{Ru(PPh_3)_3Cl_2}$ (0.5) + L-1 (1)	KOtBu (20)	110	39%
8	$\mathrm{RuCpCl(PPh_3)_2}$ (0.5) + L-1 (1)	KOtBu (20)	110	54%
9	$[\mathrm{Ru}(p\text{-cymene})\mathrm{Cl_2}]_2$(0.5) + terpyridine (1)	KOtBu (20)	110	70%
10	$[\mathrm{Ru}(p\text{-cymene})\mathrm{Cl_2}]_2$ (0.5) + L-1 (1)	NaOMe (20)	110	82%
11	$[\mathrm{Ru}(p\text{-cymene})\mathrm{Cl_2}]_2$ (0.5) + L-1 (1)	KOH (20)	110	87%
12	$[\mathrm{Ru}(p\text{-cymene})\mathrm{Cl_2}]_2$ (0.5) + L-1 (1)	NaOH (20)	110	77%
13	$[\mathrm{Ru}(p\text{-cymene})\mathrm{Cl_2}]_2$ (0.5) + L-1 (1)	$\mathrm{K_2CO_3}$ (20)	110	88%
14	Ru-1 (1 mol%)	KOtBu (20)	110	94%
15	$[\mathrm{Ru}(p\text{-cymene})\mathrm{Cl_2}]_2$ (0.5)	KOtBu (20)	110	44%
16	-	KOtBu (20)	110	ND

We then prepared and isolated the complex of **L1** and $[\mathrm{Ru}(p\text{-cymene})\mathrm{Cl_2}]_2$ to check its reactivity for N-methylation of amines. The molecular structures of the ligand **L1** and its ruthenium complex **Ru-1** is shown in scheme 3.1. **L1** contains the 2-hydroxypyridine functional group which can tautomerize into 2-pyridone and in the crystal structure of the ligand **L1**, the 2-pyridone motif was observed whereas in the **Ru-1** complex, nitrogen N1 was found to be coordinated as an anionic ligand after the extraction of hydrogen H1 from the ligand and nitrogen N2 was found to be coordinated as a neutral ligand.

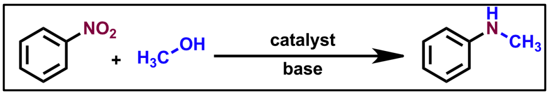
Furthermore, when 1 mol% of **Ru-1** was used as a catalyst in the reaction, 94% yield of N-methyl aniline was observed which is comparable to using [Ru(*p*-cymene)Cl_2]$_2$ precursor and ligand (**L1**) (entry 14) and hence we continued using the ruthenium precursor and ligand in all our further reactions. Having the optimal reaction conditions in hand, we then moved to expand the scope of the novel methodology by investigating the broad range of aniline derivatives for the N-methylation with methanol and observed good to excellent yields. The substrate scope can be found in the attached manuscript at the end of this thesis.



Scheme 3.1: Synthesis of the complex **Ru-1** along with molecular structures of **L1** and **Ru-1**.

After getting encouraging results with N-methylation of amines, we then moved to investigate the direct conversion of nitrobenzene to N-methyl amine and after optimizing the various reaction parameters such as temperature, base loading and catalyst loading, the best conditions were found to be nitrobenzene (0.1 mmol), base (35 mol%), ruthenium precursor (2.5 mol%) and ligand (5 mol%) in methanol at 120 °C for 18h. (entry 4, table 3.2). After finding the optimum reaction conditions, we then moved to explore the substrate scope of our methodology with various derivatives of nitro benzene and observed good to excellent yields and the substrate scope can be found in the attached manuscript.

Table 3.2. Optimization of Ru-catalyzed N-methylation of nitrobenzene with methanol



Sr No.	Ru precursor (mol%) + Ligand (mol%)	Base (mol%)	Temperature (°C)	Yields %
1	[Ru(*p*-cymene)Cl$_2$]$_2$ (1) + L-1 (2)	KOtBu (20)	110	28%
2	[Ru(*p*-cymene)Cl$_2$]$_2$ (1) + L-1 (2)	KOtBu (35)	110	39%
3	[Ru(*p*-cymene)Cl$_2$]$_2$ (2.5) + L-1 (5)	KOtBu (35)	110	83%
4	[Ru(*p*-cymene)Cl$_2$]$_2$ (2.5) + L-1 (5)	KOtBu (35)	120	92%
5	[Ru(*p*-cymene)Cl$_2$]$_2$ (2.5) + L-1 (5)	KOtBu (50)	120	93%
6	[Ru(*p*-cymene)Cl$_2$]$_2$ (2.5) + L-1 (5)	KOtBu (25)	120	63%
7	[Ru(*p*-cymene)Cl$_2$]$_2$ (2.5)	KOtBu (35)	120	37%
8	[Ru(*p*-cymene)Cl$_2$]$_2$ (2.5) + L-1 (5)	-	120	-
9	Ru-1 (5 mol%)	KOtBu (35)	120	87%
10	[Ru(*p*-cymene)Cl$_2$]$_2$ (2.5) + L-1 (5)	NaOMe (35)	120	79%
11	[Ru(*p*-cymene)Cl$_2$]$_2$ (2.5) + L-1 (5)	KOH (35)	120	84%
12	[Ru(*p*-cymene)Cl$_2$]$_2$ (2.5) + L-1 (5)	NaOH (35)	120	77%

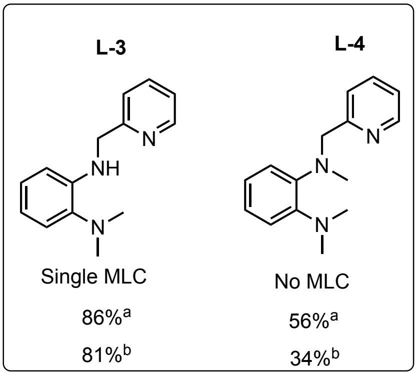
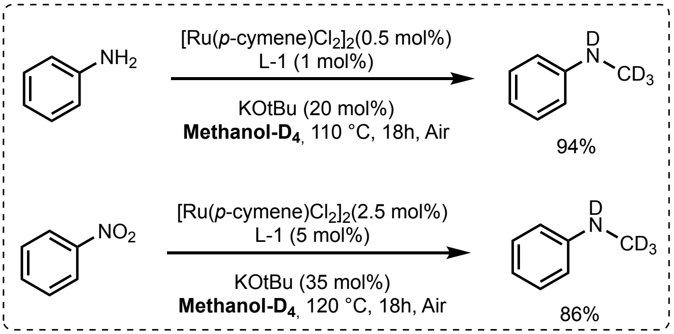


Figure 3.6: Other ligands synthesized for the work and their yields with N-methylation of (a) aniline and (b) nitrobenzene

Furthermore, to probe the role of a dual MLC pathway in our system, we synthesized the ligands **L3** and **L4** to selectively have either single MLC or no MLC pathway in the ligand (Figure 3.6). The ligand **L3** does not have the hydroxypyridine functional group and hence **L3** lack the ability of dual MLC and can only have single MLC pathway. In case of **L4**, neither hydroxypyridine nor N-H group is present so **L4** cannot potentially operate via MLC. We then tested the ligands **L3** and **L4** for both N-methylation of aniline and nitrobenzene using our optimized reaction conditions. **L3** and **L4** gave 86% and 56% yields for aniline and 81% and 34% yields for nitrobenzene respectively. This clearly suggests that having dual MLC route have significant effect on the reactivity as both **L3** and **L4** gave much lower yields than **L1**.

Furthermore, to demonstrate the role of methanol in N-methylation, deuterium labelling studies were conducted with CD_3OD serving as both the solvent and the reagent for both aniline and nitrobenzene as substrates under the respective optimized conditions, as depicted in scheme 3.2, resulting in high conversion to deuterated N-methylaniline in both reactions.



Scheme 3.2: Deuterium labelling experiments.

3.3 Conclusion

In summary, we have synthesized a new class of ruthenium pincer complexes capable of dual MLC pathways and the complexes can be used to selectively mono-methylate a range of aniline and nitro benzene derivatives. Both the transformations were conducted using catalytic amounts of base without using inert atmosphere Also, **Ru-1** is a NNN based pincer complex making it easier to handle as it does not oxidize over time and is less expensive to synthesize in comparison to commonly used PNP pincer complexes. Furthermore, deuterium labelling studies were conducted to shed some light on the mechanism and to show the involvement of dual MLC in the methodology.

4. Base catalyzed C-N and C-C coupling reactions (Paper 4)

4.1 Introduction

As mentioned in the chapter 1, lignocellulosic biomass comprises three primary constituents: cellulose, hemicellulose and lignin. This chapter is dedicated to an exploration of the valorization of lignin-derived chemicals. Lignin can be broken down (depolymerized) into smaller aromatic compounds and this can be done using a variety of chemical methods. In the future, if a transition towards greater utilization of biobased resources is considered, the development of improved methods for the treatment of alcohols becomes especially crucial and some examples of bio-based alcohols are shown in figure 4.1. These alcohols, being the most prevalent precursors derived from biomass, possess the potential to be further transformed into biofuels and various valuable bulk and fine chemicals.[135]

In this chapter, we have utilized several aromatic alcohols for the production of various important C-N and C-C bonds via BH strategy. Notably, these reactions were generally carried out with transition metal-based catalysts along with stoichiometric/catalytic amounts of base however, we were able to perform the same transformation with just catalytic amounts of base without using any transition metal under closed air conditions.

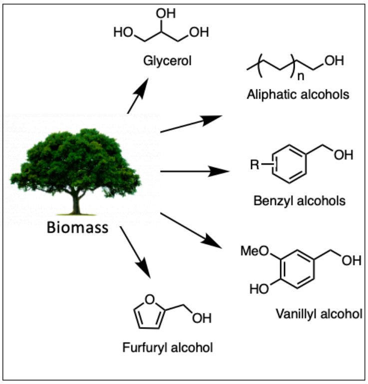


Figure 4.1: Alcohols derived from biomass

4.2 Importance of C-N and C-C bond forming reactions

C-N and C-C bond forming reactions play an important role in our everyday lives as they are abundant in biologically active natural compounds and have a wide range of uses in pharmaceuticals, agrochemicals and material chemistry.[136] The 2010 Nobel Prize in Chemistry was awarded for palladium-catalyzed C-C cross-coupling reactions. These reactions hold significant importance as C–C bond forming reactions are fundamental in organic chemistry. Even today, numerous palladium-catalyzed reactions continue to be employed in the pharmaceutical industry for the creation of novel C-N and C-C bonds.[137] Figure 4.2 depicts various drug molecules that incorporate such C-N bonds into their structural frameworks. Many of these drugs serve as crucial components of our well-being that we depend on regularly.[41, 138]

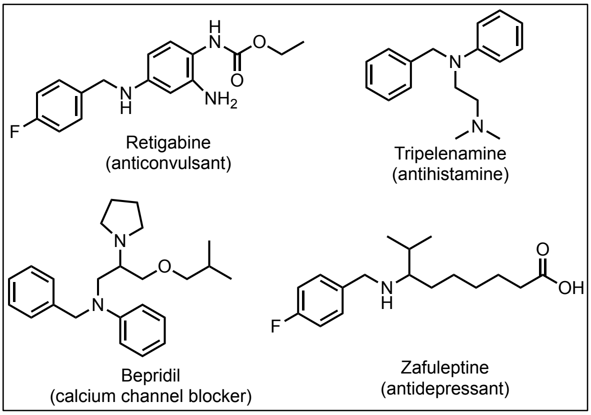


Figure 4.2. Various drug molecules with C-N bonds which could be synthesized by N-alkylation of amines.

4.3 Borrowing hydrogen approach

Among the most promising methods for their synthesis is the borrowing hydrogen approach, wherein sustainable and abundant alcohols serve as coupling reagents to furnish these C-N and C-C bonds.[139, 140] One significant advantage of this technology is its environmental friendliness, as it replaces harmful alkyl halides with alcohols as alkylating agents. Furthermore, these reactions have good atom economy, resulting in water as the sole byproduct, which adds to their attraction. A catalytic process is involved in the BH pathway for these N-alkylation and C-alkylation reactions as shown in figure 4.3. For the N-alkylation reaction, the primary alcohol is first oxidised to an aldehyde generating hydrogen molecule followed by the formation of an imine intermediate and finally, the hydrogen produced in the first step of alcohol dehydrogenation is transferred to the imine, yielding the N-alkylated amine product.[138, 141] Whereas, in the β-alkylation reaction, the intermediate reaction is aldol condensation reaction and the final step is the hydrogenation of ketone and C-C double bond using the hydrogen generated in the first step (Figure 4.3).[142]

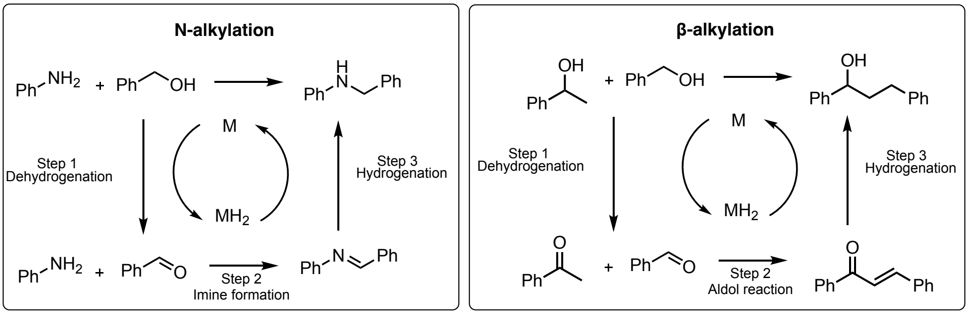


Figure 4.3: Mechanisms of the N-alkylation and β-alkylation reactions with the BH approach.

To extend our work on BH chemistry on N-methylation of amines as discussed in chapter 3, we wanted to expand our methodology of N-alkylation of anilines from methanol to other alcohols such as benzyl alcohol using the same ruthenium-based catalyst **Ru-1**. The similar work on N-alkylation has been previously reported by many groups using TM-based catalysts and some selected examples are shown in figure 4.4.[125, 143-145]

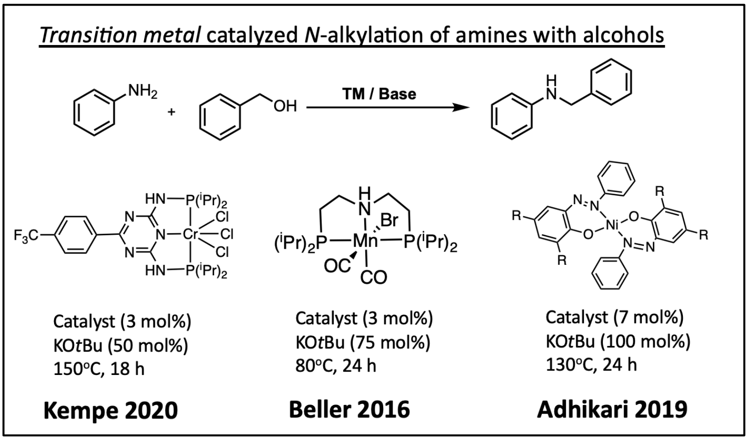
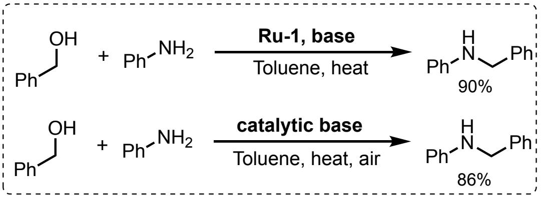


Figure 4.4: Selected examples of TM catalyzed N-alkylation of amines with alcohols.

4.4 Our observation

Motivated by our results for the N-methylation of anilines, we became curious to explore the effectiveness of the **Ru-1** catalyst in the N-alkylation of anilines. The work was started by employing benzyl alcohol and aniline as the substrates, in conjunction with base and **Ru-1** as the catalyst, resulting in high yields of 90% as shown in scheme 4.1. Surprisingly, when a blank reaction was conducted without the **Ru-1** catalyst under closed air conditions, it was observed that the reaction proceeded with similar yields, as illustrated in scheme 4.1. This outcome was very unexpected for us, as it implied that the **Ru-1** complex played no significant role in the reaction, and the reaction effectively proceeded with only base as the catalyst.



Scheme 4.1: Our observation with the N-alkylation reaction with and without using TM based catalyst.

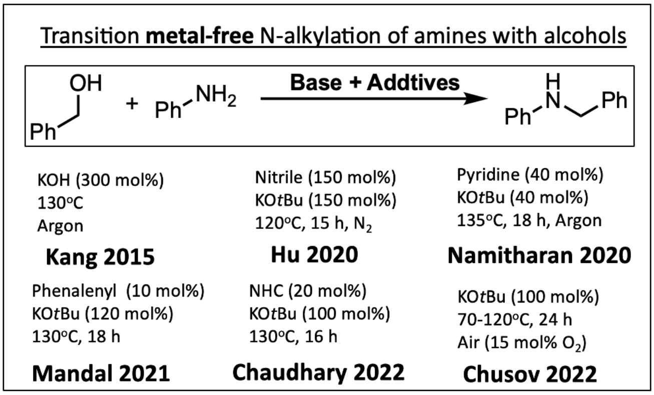


Figure 4.5: Selected examples of TM-free N-alkylation of amines

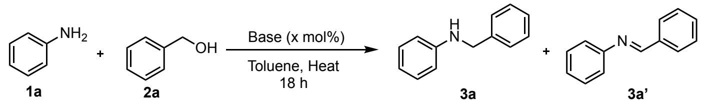
Subsequently, we conducted a review of the existing literature to determine if similar phenomena had been observed previously and our investigation revealed numerous instances of TM-free amination reactions, as depicted in figure 4.5.[146-151] Notably, Chusov and coworkers reported the transformation using only 100 mol% of base and in contrast, many other research groups, as illustrated in figure 4.5, have reported the use of either catalysts or additives, alongside the requirement of 100 mol% base for the same reaction.

Despite the presence of numerous TM-free instances for N-alkylation of amines reported in the literature, these methods often involved the use of additives like pyridine, phenalenyl, NHC or the utilization of stoichiometric amounts of base. This sparked our interest in investigating this crucial transformation using only catalytic amounts of base. Furthermore, the majority of TM-catalyzed or TM-free N-alkylation processes found in literature have employed KOtBu as the base. This raised our curiosity regarding the uniqueness of KOtBu in this context and why it appears to be a prevalent choice for such reactions.

4.5 Summary of paper 4

The N-alkylation reaction was initiated without the involvement of transition metals, and following the optimization of reaction conditions (table 4.1), it was determined that the N-alkylation of amines with alcohols could be achieved with only 25 mol% base under closed air conditions, as illustrated in entry 4 in a 4 mL pressure tube. Notably, use of stoichiometric base and the presence of inert N_2 atmosphere was found to be less effective with our reaction conditions as we got only 49% and 22% yields respectively (entry 7 and 8). Expanding our investigations, we explored various derivatives of aniline and benzyl alcohol under the optimized reaction conditions, resulting into good to excellent yields and the substrate scope table can be found in the attached manuscript.[152] Imine (**3a’**), which is an intermediate in the reaction was observed as a minor product however, it is possible to stop the reaction at imine as recently reported by Kirchner and coworkers using a similar TM-free approach with KOtBu and air.[153]

Table 4.1: Optimization table for base catalyzed N-alkylation of aniline with benzyl alcohol[a]



Entry	Base (mol%)	Temperature(°C)	Reaction conditions	Yields (3a:3a')
1[b]	KOtBu (100)	120	Reflux	31:27
2[b]	KOtBu (25)	120	Reflux	57:20
3	KOtBu (25)	130	Pressure tube (4 ml)	78:1
4	KOtBu (25)	140	Pressure tube (4 ml)	93:3
5	KOtBu (10)	140	Pressure tube (4 ml)	60:10
6	KOtBu (50)	140	Pressure tube (4 ml)	59:1
7	KOtBu (100)	140	Pressure tube (4 ml)	49:1
8[c]	KOtBu (25)	140	Pressure tube (4 ml) in N_2	22:7
9[d]	KOtBu (25)	140	Pressure tube (4 ml)	90:1

[a] Reactions conditions: 0.2 mmol aniline, 0.25 mmol benzyl alcohol, 0.3 ml toluene, base, air, 18 h. Yields were calculated using ^{1}H NMR spectroscopy with respect to mesitylene as internal standard. [b] Reactions conditions: 1 mmol aniline, 1.25 mmol benzyl alcohol, 3 ml toluene, KOtBu (25/100 mol%), air. [c] reaction was performed under N_2 atmosphere. [d] sublimed grade KOtBu (99.99% trace metals basis).

Following a similar line of thought, we got interested in the idea of extending our strategy to encompass other BH type reactions. Our focus turned to the β-alkylation of secondary alcohols with primary alcohols, a pivotal reaction in forming carbon-carbon bonds. Notably, similar to the N-alkylation process, this reaction has predominantly been explored using TM based catalysts and some selective examples are shown in figure 4.6a.[142, 154, 155] The transformation has also been explored without using TM. For example, Crabtree and coworkers reported base mediated β-alkylation of alcohols with 100 mol% base and Xu and coworkers reported aldehyde catalyzed β-alkylation of secondary alcohols with 20 mol% aldehyde and 30 mol% base (Figure 4.6b) and the mechanism reported by Crabtree and coworkers was based on Oppenauer oxidation and MPV reduction.[156, 157]

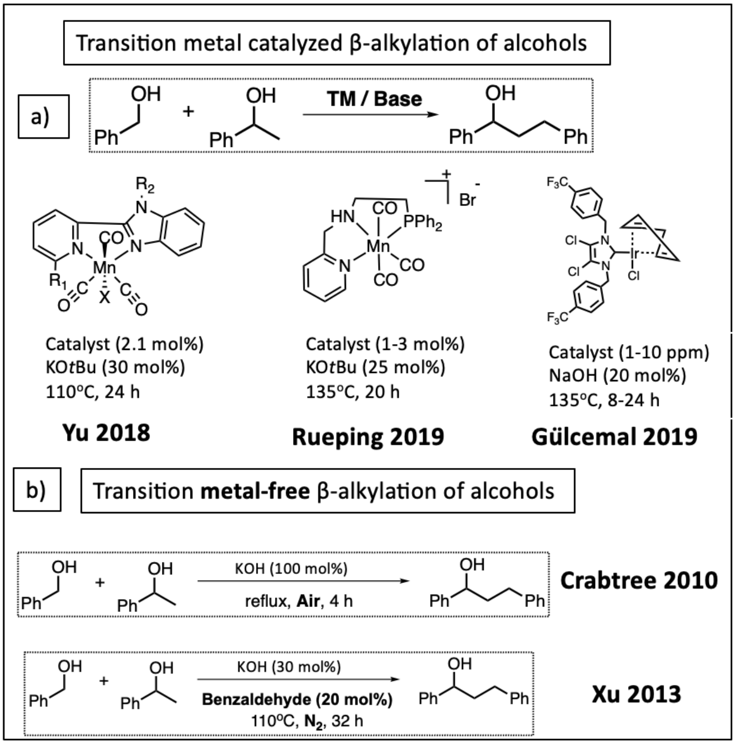
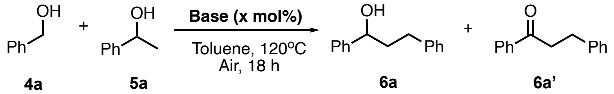


Figure 4.6: Selected examples of β-alkylation of secondary alcohols with primary alcohols from the literature a) with TM based catalyst and b) without TM based catalyst.

Our aim was to execute this reaction without the utilization of any TM based catalyst, relying solely on base as the catalyst. Our investigation began by utilizing benzyl alcohol and 1-phenylethanol as substrates, alongside KOtBu as the chosen base, inside a pressure tube. After optimizing the reaction conditions, it was determined that the reaction could indeed be effectively conducted with a catalytic quantity of base at a temperature of 120°C in a closed air environment, as illustrated in table 4.2. The successful transformation was achieved using only 25 mol% KOH within a 4 mL pressure tube, as demonstrated in entry 4 of the table. Similar to N-alkylation, use of stoichiometric base and the presence of inert N_2 atmosphere was found to be less effective with our reaction conditions. Also, several reactions were performed inside the J. Young NMR tubes to constantly monitor the reactions in-situ by using ^{1}H NMR spectroscopy to better understand the reaction mechanism (entries 9-10).

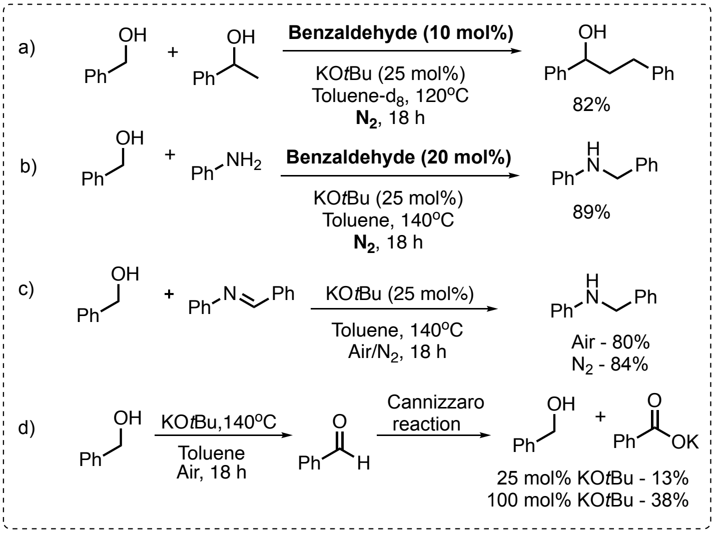
Table 4.2: Optimization table for base catalyzed β-alkylation of 1-phenylethanol with benzyl alcohol[a]



Entry	Base (mol%)	Reaction conditions	Yields (6a:6a')
1	KO*t*Bu (25)	Pressure tube (4 mL)	94:6
2[b]	KO*t*Bu (25)	Pressure tube (4 mL)	16:1
3	KO*t*Bu (100)	Pressure tube (4 mL)	8:0
4	KOH (25)	Pressure tube (4 mL)	98:2
5	KOH (100)	Pressure tube (4 mL)	95:1
6	KOH (200)	Pressure tube (4 mL)	90:0
7	KOH (10)	Pressure tube (4 mL)	20:1
8[c]	KOH (25)	Reflux	47:45
9[d]	KOH (25)	J.Y NMR tube under air	98:1
10[d]	KO*t*Bu (25)	J.Y NMR tube under N_2	11:0

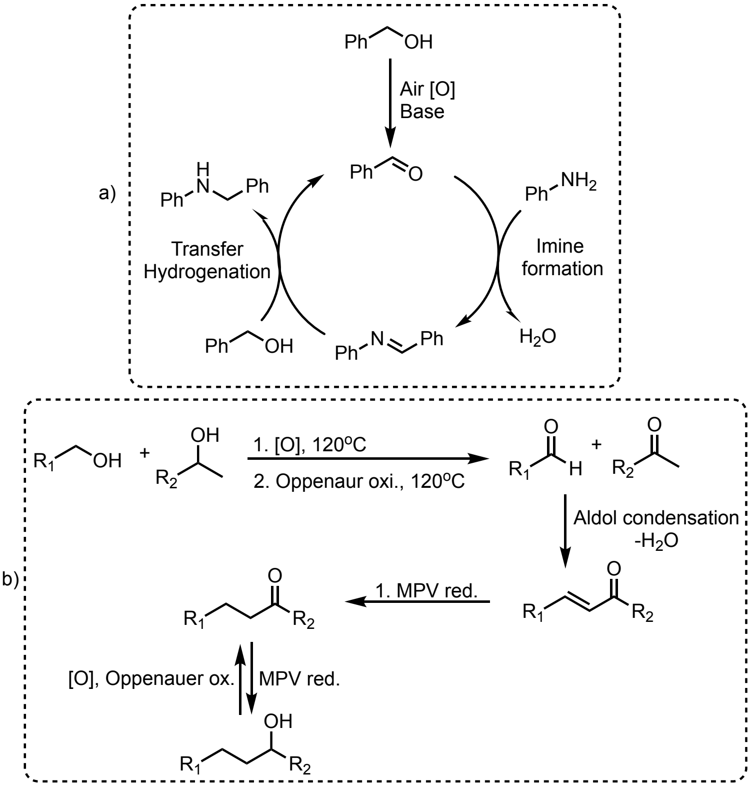
[a] Reactions conditions: 0.2 mmol 1-phenylethanol, 0.25 mmol benzyl alcohol, 0.3 mL toluene, base, air, 18 h, 120°C, yields were calculated using ^{1}H NMR spectroscopy with respect to mesitylene as internal standard. [b] Reaction was performed under N_2 atmosphere. [c] Reactions conditions: 1 mmol 1-phenylethanol, 1.25 mmol benzyl alcohol, 3 mL toluene, KOH (25 mol%), air. [d] Reactions were performed inside J. Young NMR tube with toluene-d_8 as solvent.

A particularly intriguing aspect we discovered concerning both N-alkylation and β-alkylation reactions is the essential role of air in the reaction. However, it is worth noting that we are not the pioneers in observing this phenomenon, as several other research groups have documented similar behavior prior to our own investigation.[151, 156, 158] We believe that the role of air is to oxidize a small amount benzyl alcohol into benzaldehyde in the presence of air and the benzaldehyde further drives the reaction forward by transfer hydrogenation which was further confirmed after performing some control experiments as shown in scheme 4.2.[157]



Scheme 4.2: Control experiments

Scheme 4.2a and 4.2b shows that both the reactions can be performed equally well under inert atmosphere in the presence of catalytic amounts of benzaldehyde without air. Scheme 4.2c shows that benzyl alcohol can hydrogenate imine into the product amine via transfer hydrogenation and at last we have also shown that oxidation of benzyl alcohol to benzaldehyde is indeed possible with just base and air without using any other additive and the aldehyde can further convert into benzoate via Cannizzaro side reaction.[159] The primary factor contributing to the reduced efficacy of the reaction with stoichiometric base is likely the increased dominance of the Cannizzaro side reaction in presence of stoichiometric base and the aldehyde generated through the oxidation of benzyl alcohol is consumed rapidly via the Cannizzaro reaction in case of stoichiometric base as compare to catalytic base.



Scheme 4.3: Proposed mechanisms for base catalyzed a) N-alkylation of amines with alcohols and b) β-alkylation of secondary alcohols with primary alcohols.

Based on our results and previous literature reports we believe that the mechanism for the β-alkylation of secondary alcohols with primary alcohols is based on Oppenauer oxidation and MPV reduction as reported previously in the literature (Scheme 4.3b).[156-158, 160, 161] whereas the proposed reaction mechanism for the N-alkylation of amine is shown in scheme 4.3a.[151, 162]

Discussion

Observing our results, a natural query arises: why have numerous research groups reported the same reaction utilizing TM based catalysts in combination with catalytic/stoichiometric base, whereas we accomplished it with solely catalytic base under air? A plausible explanation lies in the reaction conditions employed by those groups. Their use of TM complexes likely made their reactions sensitive to air and moisture, potentially hindering their ability to achieve substantial yields in blank reactions due to the absence of air. Furthermore, it is noteworthy that the base-catalyzed reaction is sensitive to reaction parameters such as temperature, volume of air present, and base loadings. However, considering that the reaction necessitates solely a catalytic quantity of the oxidized alcohol, it becomes plausible that the role of the transition metal in various TM catalyzed N-alkylation and β-alkylation reactions reported in the literature could be that of a stoichiometric oxidant that dehydrogenates a small amount of the alcohol to the respective aldehyde and the aldehyde further catalyzes the reaction. Some examples of this can be seen in figure 4.7 where air can be used instead of transition metals to enhance the oxidation, thereby increasing the sustainability of these reactions.

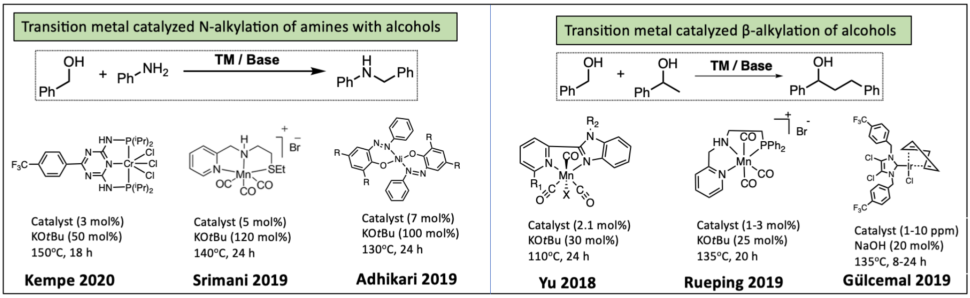


Figure 4.7: Selected examples of N-alkylation of amines and β-alkylation of alcohols from the literature where air could have been used instead of transition metal-based catalysts.[142, 145, 163]

Conclusion

To summarize, we have shown that two important transformations i.e., N-alkylation of amines with alcohols and β-alkylation of secondary alcohols with primary alcohols can be performed with just catalytic amounts of base under closed air vessel without using any transition metals or other additives generating only water as byproduct. The approach demonstrates a broad substrate scope for both the reactions, with yields up to 98%. Furthermore, a sequence of control experiments were systematically performed to get further insight of the reaction mechanism and the proposed reaction mechanism centers around the base mediated oxidation of alcohols to aldehydes under air and the aldehyde further acts as the catalyst in the reaction via transfer hydrogenation.

Future outlook

In chapter 2, levulinic acid and its derivatives were successfully defunctionalized into hydrocarbons like pentane and pentene. The prospect of advancing pentene into higher molecular weight hydrocarbons suitable for transportation fuels captures significant interest, and this can be accomplished through strategies such as alkene metathesis or oligomerization.[164] Furthermore, the exploration of other substrates derived from biomass for the production of hydrocarbons with varying carbon atom counts holds the potential to yield valuable outcomes.

In chapter 3, methanol was employed as the C1 source to achieve the N-methylation of amines and nitro compounds. There lies an interesting opportunity to formulate a comparable methodology for diverse aliphatic alcohols. Furthermore, given the relatively high cost and noble nature of ruthenium, the exploration of the ligand's potential with 3d transition metals like iron and manganese is warranted. Also, the concept of dual metal-ligand cooperation can be harnessed to synthesize other pincer ligands, thus enhancing catalytic efficiency to a great extent for many important catalytic transformations.

In chapter 4, two reactions were explored i.e., N-alkylation of amines with alcohols and β-alkylation of secondary alcohols with primary alcohol which were previously carried out with TM based catalyst and we were able to perform those with catalytic amounts of base under closed air conditions. Hence, exploring additional analogous BH-based reactions using merely catalytic amounts of base in an air environment could give interesting results. Furthermore, throughout this thesis, the reactions were exclusively conducted on a small scale. Nevertheless, there exists significant utility in pursuing further investigations into upscaling these reactions. Additionally, given the considerable importance of these BH reactions, it is recommended that enhanced emphasis be placed on elucidating the mechanisms underlying these TM-free reactions. This could be accomplished through the execution of a more extensive array of control experiments and kinetics studies.

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One challenge facing the current generation is that we don't pick up lessons from our ancestors, assuming they weren't that clever

We think that we have our own views or opinions about things but they are not really our own, they were given to us by the society.

The genuine measure of success shouldn't be tied to acquiring material possessions. To me, true success lies in comprehending and mastering one's emotions

People can be funny; they laugh while thinking about what they wanted a few years ago and then repeat the cycle with their current wishes in the future

-Nitish Kumar Garg

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