

Design of heterogeneous metal catalysts for organic synthesis

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Design of heterogeneous metal catalysts for organic synthesis

PhD dissertation by Niklas Rosendal Bennedsen



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August 2020

Preface

The results presented in this dissertation represents the accumulated work of my PhD carried out at the Center for Catalysis and Sustainable Chemistry (CSC) at the Department of Chemistry, Technical University of Denmark (DTU), from September 2017 to August 2020. The work was conducted under the supervision of Professor Søren Kegnæs and co-supervised by Assistant Professor Søren Kramer and Senior Researcher Jerrik Mielby. The project was financially supported by Independent Research Fund Denmark grant no. 6111-00237 (Danmarks Frie Forskningsfond, DFF). A three month external stay was done at the International Iberian Nanotechnology Laboratory (INL) in Braga, Portugal, from April 2019 to July 2019 where I had the opportunity to work under the supervision of Dr. Yury Kolenko and Dr. Laura Salonen in the field of covalent organic frameworks (COFs).

This dissertation covers five different projects, which can be divided into two different topics focusing on either nanoparticle based catalysts (chapter 2-4) or porous organic polymers (POPs) as part of the active catalyst (chapter 5-8). A short introduction to each topic is given before the different projects are presented. The projects have resulted in three peer-reviewed publications in scientific journals that are presented in the Appendix with their front pages. Furthermore, two manuscripts have been submitted and another is currently in progress. The synthetic procedures are described in the end of each project. Some figures, schemes, and tables are adapted or directly copied from these publications with corresponding references. If no reference is provided, the figure, scheme, or table is made exclusively for the dissertation.

Chapter 1 gives a short general description of catalysis and heterogeneous catalysis. In **chapter 2**, the use of nanoparticles as the active phase in heterogeneous catalysis is described and the aims of the two projects using nanoparticles are presented. **Chapter 3** covers the continuation of my Master's Thesis where a novel method to synthesize alloy Co/Ni nanoparticles is developed by using a metal organic framework (MOF) as sacrificial precursor. The alloy material is assessed in the hydrosilylation of ketones. In **Chapter 4**, the α -alkylation of ketones with alcohols is optimized and its versatility is being studied with a commercially available Pd/C catalyst. Additionally, the reaction pathway is elucidated by *in*-situ infrared (IR) spectroscopy and stoichiometric tests. **Chapter 5** is the first chapter about POPs and gives a general introduction to them, their properties, and how these properties can be used in catalytic processes. Moreover, the aims of the projects using POPs as part of the active catalyst are presented. **Chapter 6** describes the use of a polyphenylene (PP) based POP in the hydrogenation of CO₂ to formic acid. In **Chapter 7**, a chiral POP is synthesized and assessed in the asymmetric C(sp³)-H functionalization of 3-arylpropanamides. **Chapter 8** covers the use of bipyridine (bpy) based POPs used for the direct C(sp²)-H borylation of arenes. In **Chapter 9**, the dissertation ends with a summary for all the projects and an overall conclusion.

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A special thanks to Dr. Yury Kolenko for allowing me to join his group at INL for three months. It was a fantastic experience that I will never forget. Thanks to Dr. Laura Salonen for her amazing supervision during my stay at INL and her scientific input. For the rest of the people I met there, thank you for your kindness and for giving me an extraordinary experience.

I would like to thank my friends and family who have always been there to fill my life with more than just chemistry. I am really grateful for your company. You have always been the best excuse not to be in the laboratory. Last but not least, I would like to show my gratitude to my lovely girlfriend, Sarah, for her compassion, understanding, and full support throughout the whole period. After a long and exhausting

day, you have always been able to put a smile on my face and you have always believed in me, even when I did not. I am lucky to have you in my life and I cannot wait to see what the future holds for us.

Abstract

The chemical industry is the world's largest industry and produces a variety of chemical products - from fuels and plastics to life-supporting pharmaceuticals. In this industry, catalysts play an indisputable role as it is estimated that up to 90% of all processes today utilize catalysts to a certain extent. The most frequently used type is heterogeneous catalysts where their inherent properties provide cheaper and more sustainable setups. Yet, classical heterogeneous catalysts are still not that common in the synthesis of fine-chemicals as pharmaceuticals due to their lack of selectivity commonly connected with this type of catalysis. Thus, designing and synthesizing novel heterogeneous catalysts with high selectivity are very attractive in organic chemistry.

This dissertation includes five different projects aiming to improve heterogeneous catalysis by designing, synthesizing, and/or optimizing (novel) catalytic systems and evaluating them in organic synthesis relevant for the industry. A short introduction has been made for each topic in order to present the industrial relevance and some of the potential challenges. For all projects, the heterogeneous nature of the catalysts has been assessed and possible limitations have been investigated and presented.

The first project focused on the synthesis of cobalt/nickel alloy nanoparticles encapsulated in nitrogendoped carbon. The material was made by using ZIF-67 as a sacrificial precursor that after impregnation with nickel and carbonization created the alloyed Co/Ni nanoparticles. The material was tested as a catalyst in the hydrosilylation of ketones where the catalyst was easily reused due to its magnetic properties. However, the alloyed nanoparticles did agglomerate during the recycling, which decreased the catalytic activity. Nevertheless, the alloy material was able to hydrosilylate a variety of ketones with moderate success.

In the second project, the α -alkylation of ketones with alcohols using a commercially available palladium on carbon as heterogeneous catalyst was investigated. The simple and easy accessible palladium catalyst showed excellent performance compared to other heterogeneous palladium systems as the reaction could be carried out under mild reaction conditions and with high substrate tolerance. The reaction pathway was elucidated by *in-situ* IR spectroscopy and stoichiometric tests where the results matched the hydrogen borrowing mechanism seen for many homogeneous catalytic systems.

In the third project, PP-based POPs were synthesized, which acted as heterogeneous ligands that were capable of hydrogenating CO_2 to formic acid (FA) in the presence of iridium. The process is highly attractive as it can enable the use of H_2 as a renewable energy source. A POP incorporated with bpy ligands showed the most promising results yielding a TON value above 20,000. The origin of the catalytic activity was evaluated by a filtration experiment, using homogeneous iridium complexes or nanoparticles of iridium as the active catalyst, and other relevant control experiments. The tests indicated that the incorporation of the bpy ligand into the POP enhanced the catalytic performance beyond making recovery and recycling easier.

The fourth project described POP-based catalytic systems as well. However, the application was very different as the POPs were polystyrene (PS)-based providing swelling properties to the materials. The POPs' ability to swell were exploited to mimic homogeneous catalytic systems in the challenging asymmetric C(sp³)-H functionalization of 3-arylpropanamides using an auxiliary methodology. The enantioselectivity was achieved by incorporating chiral phosphoramidite into the POP, which in the presence of palladium showed to have good catalytic performance providing up to 70% yield and 86%

enantiomeric excess (ee). Even though no metal leaching was observed, the system showed diminishing catalytic performance during reuse due to the formation of metal nanoparticles and ligand oxidation.

In the fifth project, the borylation of arenes using a POP-based system was examined. The borylation reaction represents a strong and widely used tool to gain access to key building blocks in organic synthesis. The catalytic system was made *in*-situ by mixing $[Ir(cod)Cl]_2$ with a bpy-based PS-POP using the arene as solvent. The system was capable of borylating two times for each B_2pin_2 making the transformation highly atom efficient. Various arenes were tested and showed high influence on steric effects in term of both activity and regioselectivity. The reaction pathway was examined using competition studies, isotope labeling, and other relevant test. The results from the different arenes and mechanistic tests matched strongly with an Ir(III)/Ir(V) catalytic cycle.

Resumé

Den kemiske industri er verdens største industri og fremstiller mange forskellige kemiske produkter – alt lige fra brændstof og plastik til livsvigtig medicin. I denne industri spiller katalysatorer en uundværlig rolle, da det anslås, at op til 90% af alle processer i dag anvender katalyse i en vis grad. Den mest anvendte type er heterogen katalyse med dens unikke egenskaber, som gør reaktionerne billigere og mere bæredygtige. Alligevel bruger man ikke klassiske heterogen katalysatorer til at fremstille finkemikalier som f.eks. medicin pga. den manglende selektivitet, som ofte er forbundet ved disse systemer. Det er derfor utrolig attraktivt at designe og fremstille nye heterogene katalysatorer med høj selektivitet.

Denne afhandling består af fem forskellige projekter, der forsøger at forbedre heterogen katalyse ved at designe, syntetisere og/eller optimere (nye) katalytiske systemer samt evaluere dem i organisk syntese relevant for industrien. Hvert projekt indledes med en kort introduktion, hvor den industrielle relevans og eventuelle udfordringer præsenteres. I alle projekter undersøges katalysatorens natur og eventuelle begrænsninger er blevet undersøgt og italesat.

Det første projekt fokuserer på dannelsen af kobolt/nikkel legerede nanopartikler, som er indkapslet i nitrogen-holdigt carbon. Materialet blev fremstillet ved at bruge ZIF-67 som udgangsstof, der efter en imprægnering og carbonisering dannede de ønskede legerede nanopartikler. Det legerede materiale blev testet som en katalysator i hydrosilyleringen af ketoner, hvor det viste sig, at den nemt kunne genanvendes på grund af dens magnetiske egenskaber. Nanopartiklerne dannede dog agglomerater under genanvendelsen, hvilket gjorde, at den katalytiske aktivitet faldt over tid. På trods af dette var det legerede materiale dog stadig i stand til at hydrosilylere forskellige ketoner med udmærket succes.

I det andet projekt undersøges α -alkyleringen af ketoner med alkoholer, som er katalyseret af kommerciel tilgængelig palladium på carbon. Den simple og lettilgængelige palladiumkatalysator viste fremragende katalystiske egenskaber i forhold til andre palladium-baseret katalytiske systemer, da reaktionen forløb under milde reaktionsbetingelser og med høj tolerance for forskellige substrater. Reaktionsmekanismen blev belyst ved hjælp af *in-situ* IR spektroskopi og støkiometriske forsøg, hvor resultaterne passer med en "hydrogen borrowing pathway", som er kendt for mange homogene katalytiske systemer.

I det tredje projekt fremstilles polyphenylen (PP)-baseret porøse organiske polymerer (POPs), der blev anvendt som heterogene ligander. I forsøgene var de heterogene ligander i stand til at hydrogenere CO₂ til myresyre ved tilstedeværelsen af iridium. Denne proces er meget attraktiv, da den kan gøre anvendelsen af H₂, som en vedvarende energikilde, mulig. En PP POP inkorporeret med bipyridin (bpy) ligander viste de mest lovende resultater med en TON-værdi på over 20.000. Baggrunden for den katalytiske aktivitet blev undersøgt med et filtreringsforsøg, brug af homogene iridiumforbindelser eller nanopartikler af iridium som katalysator samt andre relevante kontrolforsøg. Udover at gøre opsamlingen og genanvendelsen nemmere indikerede forsøgene, at inkorporeringen af bpy ind i POP'en forbedrede de katalytiske egenskaber.

Det fjerde projekt beskriver også POP baseret katalytiske systemer, dog er anvendelsen betydelig anderledes, da POP'erne er polystyren (PS)-baseret. Det gav materialerne "swelling"-egenskaber, som blev udnyttet til at efterligne homogene katalytiske systemer i den udfordrende asymmetriske C(sp³)-H funktionaliseringen af 3-arylpropanamider. Den enantiomeriske selektivitet stammede fra inkorporeringen af kirale phosphoramiditer i POP'en, som ved tilstedeværelsen af palladium viste gode katalytiske egenskaber med op til 70% udbytte og 86% enantiomerisk overskud (ee). Selvom der ikke

forekom udvaskning af metal, så viste systemet en faldende katalytisk præstation ved genanvendelse pga. forekomsten af nanopartikler og oxidation af liganden.

Det femte projekt omhandler boryleringen af arener med et POP-baseret katalytisk system. Boryleringensreaktionen repræsenterer et stærkt og meget anvendt redskab til at fremstille vigtige udgangsstoffer i organisk syntese. Det katalytiske system blev dannet *in-situ* ved at blande [Ir(cod)Cl]₂ med en bpy-baseret PS-POP ved brug af arenen som solvent. Systemet var i stand til at borylere to gange per B₂pin₂, hvilket gør reaktionen utrolig atomeffektiv. Forskellige arener blev testet, og det viste sig, at sterik havde stor indflydelse på både aktivitet og regioselektivitet. Reaktionsmekanismen blev også undersøgt vha. konkurrence studier, isotop mærkning og andre relevante forsøg. Resultaterne fra de forskellige arener og de mekanistiske forsøg underbygger kraftigt en Ir(III)/Ir(V) katalytisk cyklus.

Graphical abstracts





Chapter 4: α -Alkylation of ketones with alcohols using Pd nanoparticles



Chapter 6: Formation of formic acid by a polyphenylene-based catalyst



Chapter 7: Asymmetric C(sp²)-H functionalization by chiral porous organic polymer



Chapter 8: Direct C(sp²)-H borylation of arenes with porous organic polymers



Abbreviations

ΔG	Gibbs Free Energy
AIBN	Azobisisobutyronitrile
BHT	3,5-Di- <i>tert</i> -butyl-4-hydroxytoluene
BINAP	2,2'-bis(diphenylphosphino)-1,1'- binaphthalene
BINOL	1,1'-Bi-2-naphthol
bpy	Bipyridine
^t BuPS	<i>tert</i> -Butylpolystyrene
COD	1,5-cyclooctadiene
COF	Covalent Organic Framework
СР	Cross-polarization
dba	Dibenzylideneacetone
DMF	Dimethylformamide
dppBz	1,2-bis(diphenylphosphino)benzene
dppe	1,2-bis(diphenylphosphino)ethane
DVB	Divinylbenzene
Ea	Activation Energy
EDTA	Ethylenediaminetetraacetic Acid
EDX	Energy Dispersive X-Ray
EtOAc	Ethyl Acetate
EtOH	Ethanol
ee	Enantiomeric Excess
EPR	Electron Paramagnetic Resonance
eV	Electron Volt
FA	Formic Acid
fcc	Face-Centered Cubic
HPLC	High Performance Liquid Chromatography
ICP	Induced Coupled Plasma
IR	Infrared

KIE	Kinetic Isotope Effect
LOHC	Liquid Organic Hydrogen Carrier
MAS	Magic Angle Spinning
MeOH	Methanol
MOF	Metal-Organic Framework
NC	Nitrogen-Doped Carbon
NMP	N-Methyl-2-pyrrolidone
NMR	Nuclear Magnetic Resonance
OES	Optical Emission Spectroscopy
pin	Pinacol
Phen	Phenanthroline
POP	Porous Organic Polymer
PP	Polyphenylene
PS	Polystyrene
Salen	N,N'-Ethylenebis(salicylimine)
SAMC	Single Atomic Metal Catalyst
SBU	Secondary Building Unit
SEM	Scanning Electron Microscopy
STEM	Scanning Transmission Electron Microscopy
TBDMS	tert-Butyldimethylsilyl
TEM	Transmission Electron Microscopy
TEMPO	2,2,6,6-Tetramethylpiperidine 1-oxyl
TGA	Thermal Gravimetric Analysis
THF	Tetrahydrofuran
TOF	Turn-Over Frequency
TON	Turn-Over Number
XPS	X-Ray Photoelectron Spectroscopy
XRD	X-Ray Diffraction
XRF	X-Ray Fluorescence
ZIF	Zeolitic Imidazolate Framework

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1 General introduction to catalysis

1.1 Introduction to catalysis

Catalysis is an important research area as catalysts play a fundamental role in many critical processes including the production of plastics, life-supporting pharmaceuticals, fuels, fertilizers etc. The importance of catalysis can be exemplified in the formation of ammonia by the Haber Bosch process. The ammonia is used for the production of fertilizers applied in agriculture, which is believed to help feed up to 50% of the world's population.¹ Moreover, it is estimated that up to 90% of all chemical processes in the industry utilize a catalyst.² These examples amplify the role that catalysis has and will most likely continue to possess in the future especially with an increasing need for more sustainable solutions and applications.^{3–}

One of the earliest definitions of a catalyst was given by Ostwald in 1895.⁷ This definition is still representative today as it defines some of the most important features of a catalyst: "a catalyst accelerates a chemical reaction without affecting the position of the equilibrium". From this definition, it is stated that a catalyst is able to increase (accelerate) a reaction rate by facilitating a lower-energy reaction path compared to a non-catalyzed reaction. This is visualized in Figure 1.1 where the catalyzed reaction (red) has a lower activation energy compared to the non-catalytic one (black). Furthermore, a catalyst does not change the thermodynamics of a reaction as the reactants and products do not change, which are both visualized in the figure but also mentioned in the definition from Ostwald (...without affecting the position of the equilibrium). An important property of a catalyst, which is not described in the definition from Ostwald, is that a catalyst should not be consumed during a reaction as it has to participate in many consecutive cycles. Here, a cycle is described by how the catalyst interacts with a substrate to induce the lower-energy reaction pathway before the catalyst is released/regenerated to participate in a new cycle. The performance of a catalyst is often evaluated on the number of cycles it catalyzes (turn over number, TON) and how fast it carries out these cycles (turn over frequency, TOF).



Reaction Progress

Figure 1.1. Schematic illustration of a reaction diagram of a non-catalyzed and a catalyzed reaction. E_a is the activation energy, ΔG is the Gibbs free energy of the reaction, X and Y are reactants, and Z is the product.⁸

Catalysis has been established as a key factor in the implementation of sustainable and green chemistry. In the 12 principles of green chemistry formulated by Anastas and Warner from the late 1990s, catalysis can both directly and indirectly play a positive role on the principles shown below;^{9,10}

- "It is better to prevent waste than to treat or clean up waste after it is formed."
- *"Synthetic method should be designed to maximize the incorporation of all materials used in the process into the final product."*
- "Energy requirements should be recognized for their environmental and economic impacts and should be minimized. Synthetic methods should be conducted at ambient temperature and pressure."
- "Catalytic reagents (as selective as possible) are superior to stoichiometric reagents."

Based on these statements, catalysis can help the implementation of green and sustainable chemistry as catalysts often decrease the amount of waste generated and increase the atom efficiency of a reaction by removing the requirement of high excess or activated reagents.¹¹ Furthermore, as the use of a catalyst decreases the activation energy, it is possible for the reactions to occur at a lower temperature, which diminishes the requirement of high energy processes. At the same time, catalysts can participate in multiple reaction cycles and are thereby only added in small amounts compared to the use of stoichiometric reagents, which again heavily reduces the waste of the process. Moreover, catalysts can be reused to catalyze the same process over consecutive days or even years. Therefore, the field of catalysis is highly relevant in the implementation of green and sustainable chemistry.

Catalysis is commonly divided into three distinguishable categories: biocatalysis, homogeneous catalysis, and heterogeneous catalysis. The active site of the catalyst defines its type - with active biological substances being a biocatalyst. Active sites in the same phase as the reaction media are known as homogeneous catalysis, while in heterogeneous catalysis, the active sites are in another phase than the reaction media.

1.2 Introduction to heterogeneous catalysis

Heterogeneous catalysis has found the most industrial usage due to the inherent benefits of having the catalytic active phase separated from the reactants and products with the most profound examples being a solid catalyst with either a gaseous- or liquid phase reaction media. The solid catalyst often has an active phase of either metal nanoparticles, a metal complex, acidic or basic sites, which are commonly stabilized on a support material like metal oxide(s), aluminosilicates, or carbon. The heterogeneous nature provides many beneficial features to the catalytic system such as easier recovery and reuse of the catalyst. Other benefits could be easier removal of undesired metallic species from the final product, higher stability, and easier application in different reaction setups (continuous or batch-oriented), which may also lead to favorable economics.^{4,5,12–15} These features highlight the industrial attraction for heterogeneous catalysis. However, the heterogeneity of the catalyst with the presence of different compositions (active phase and support material) provides an increasing complexity to the catalytic system with phenomena like surface-interactions, diffusion limitations, heat transfer, and sintering that have to be taken into consideration.^{16,17} Alongside these phenomena, heterogeneous catalysts are bulk materials that are not typically well-defined unlike homogeneous molecular systems or naturally formed enzymes, but rather consist of a distribution of active sites on a support material where position, accessibility, surroundings, stability, and

composition may vary significantly within the bulk.¹⁸ For that reason, it is extremely difficult to design and synthesize heterogeneous catalysts with uniform active sites and thereby control the catalytic activity and selectivity completely.^{16,19} Consequently, heterogeneous catalysis has historically been applied for the production of bulk commodities mostly, where full control over activity and selectivity may not have been crucial or not required to obtain the desired product. However, if heterogeneous catalysis should find more usage in processes where selectivity and sensitivity are more critical, the development of new heterogeneous catalytic systems and technologies are necessary.²⁰

A type of chemical product that requires control over activity and selectivity is the production of finechemicals. Fine-chemicals is an expression used for the production of chemical compounds, which are complex in structure, highly valuable, and manufactured by involving multiple steps in more batch oriented processes operating on kilogram scale.³ In contrast, the production of bulk commodities is carried out in ton scale with an annual production that may exceed over 100 million tons. These processes often use continuous setups involving one to few reaction steps to reach the desired product.

The manufacturing of pharmaceuticals, agricultural chemicals, and life science materials are some of the most important products in the fine-chemical industry. The demand for these types of products will only continue to rise as drugs have to become more selective in their treatment and the agriculture and the life science have to accommodate an increasing human population and climate change.^{21,22} Unfortunately, the production of fine-chemicals creates a high amount of undesired waste from applying multiple reaction steps. Moreover, if homogeneous transition metal catalysts or reactants were employed in the process, possible high-energy consuming and waste producing purification processes have to be used e.g. distillation, washing, or extraction to remove the metals.⁶ Thus, it would be very attractive to apply more direct synthetic routes to reduce the amount of reaction steps and use processes with heterogeneous catalysts as it would simplify the removal of the catalytic species. Furthermore, the heterogeneous catalyst can be reused more easily increasing the sustainability and decreasing the cost. This also highlights the motivation of the dissertation; design of heterogeneous metal catalysts for organic synthesis.

1.3 Deactivation mechanisms

As pointed out already, the heterogeneous nature makes recovery and recycling of the catalyst easier. However, successful reuse of the catalyst requires that the catalytic performance is maintained with only minimal change. Unfortunately, multiple deactivation mechanisms can occur for a catalyst, which hinder its successful reuse. The most common deactivation mechanisms for heterogeneous catalysis or those observed in this dissertation will shortly be covered next.

Sintering is a classical cause of deactivation for heterogeneous catalysts where the active metal nanoparticles grow in size often by either particle migration followed by coalescence or Ostwald ripening.²³ In both cases, the activity is lowered due to the reduced surface area of the metal. Sintering can also occur for the support material where the structure, porosity, and/or composition change or decompose as a result of the catalytic conditions.^{3,24} This often causes a decrease in accessibility to the active species that will lower the activity. In this dissertation, sintering will often be evaluated by comparing fresh and used catalyst in electron microscopy as it provides visual evidence of sintering.

Metal leaching is a common deactivation mechanism for many heterogeneous catalysts especially for reactions in the liquid phase. Leaching occurs when the metal is not stabilized well enough on the support material, which makes it go partly into the reaction media before being flushed or washed out. This will decrease the amount of metal in the catalyst, reduce the catalytic activity over time, and potentially contaminate the final product(s). For this dissertation, metal leaching will be detected by induced coupled plasma (ICP) with an optical emission spectroscopy (OES) as detector and/or X-Ray fluorescence (XRF) of a filtered reaction mixture.

Pore blocking happens when the pores in the support material are blocked by chemical substances. This could be the formation of salt(s), coke, or product(s), which decrease the accessibility to the active site and thereby also lower the catalytic performance. Some catalytic systems can be regenerated by removing the species blocking the pores. For example coke in zeolites can be removed by a calcination step, which makes the system regain its activity. Possible pore blocking can be observed in physisorption experiments by comparing fresh and used catalysts.

Inhibition/poisoning occurs when the active site binds to species so strong that it hinders the catalyst ability to participate in a catalytic cycle. Inhibition is often referred to as coordination that is reversible but still strong enough to decrease the activity. Poisoning on the other hand binds a species irreversible so the catalyst cannot participate in more catalytic cycles. To evaluate whether inhibition or poisoning occur in a catalytic system is not trivial and depends on the bonded species and the system. An example of how to determine deactivation by inhibition/poisoning is presented in Section 4.4 with the α -alkylation of ketones.

Formation of inactive species covers a variety of different phenomena like the formation of inactive dimers or nanoparticles. It could also be other compositional changes like oxidation, ligand dissociation, replacement of counter ions, ligand saturation etc. Common for all of them are that the amount of catalytic active species are reduced, which diminish the catalytic activity. The way to determine if inactive species are formed rely heavily on the catalytic system similar to inhibition/poisoning. For example, the formation of nanoparticles can be elucidated from electron microscopy whereas possible metal oxidation can often be seen from XPS.

2 Introduction to nanoparticle catalysts

2.1 Nanoparticles and surface interactions

Nanoparticles of metal(s) are a very popular and appealing active phase in heterogeneous catalysis, which have found many industrial applications e.g. Fischer-Tropsch processes, catalysts in cars, and hydrogenation reactions.^{2,3} The catalytic reaction occurs on the surface of the nanoparticles when substrates are adsorbed on them. The adsorbed substrates are activated by the metal surface often by weakening a critical chemical bond, which can then undergo a chemical reaction with a lower activation energy compared to a non-catalytic pathway as mentioned previously. Classical reaction mechanism theories such as the Langmuir-Hinshelwood or the Eley-Rideal are widely used to explain surface-based reactions.³ Yet, these theories often describe active surfaces as being completely uniform with perfectly ordered active sites, however in reality the surface is highly flawed with defects, bumps, steps, edges etc. as visualized in Figure 2.1. This is actually very fortunate as most catalysis arises from these flaws and defects whereas the ordered plain surfaces are less active, if they are even active at all. As a consequence thereof, the size and shape of the nanoparticles significantly affect the active surface by the amount of defects and thereby also the catalytic performance.²⁵ Thus, designing and creating materials with more uniform metal(s) nanoparticles has been the goal for many years in the field in order to better control the active surface and to obtain highly active and selective catalysts.



Figure 2.1. Illustration of an active surface with its various flaws and defects.³

As described above, the active surface plays a critical role in surface-based catalysis and evidently the choice if metal is highly impactful. The platinum-group metals (Pd, Pt, Ir, Rh, Ru, and Os) are widely applied as active catalysts in the industry due to their high activity and selectivity in many processes like hydroformylations, coupling reactions, hydrogenations, and dehydrogenations.²⁶ Unfortunately, these metals are very scarce and costly. This highlights the appeal of using heterogeneous catalysts where recovery and reuse of the scarce metals are easier. Another way to circumvent the low abundance and high cost of platinum-group metals is to replace them with more abundant and cheaper base metals. However, the catalytic performance of base metal catalysts are in general inferior to platinum-group metal catalysts, which complicates the implementation of base metals in catalysis. Fortunately, the alloying of abundant base metals have emerged as an attractive strategy to yield materials with enhanced catalytic properties compared to the monometallic analogues and have even proven to outperform platinum-group metals.^{27–32} The principle of Sabatier on substrate binding strength is often used to

describe how an alloy can improve the catalytic properties compared to the individual metals as one metal may bind the substrate too strong, another too weak, but the mixed metal binds sufficiently for the reaction to occur. As such, the development of new base metal (alloy) catalysts with improved catalytic performance is highly desired to reduce the usage of platinum-group metals.

2.2 Support material

Metal nanoparticles used for catalysis are often deposited on a support material to increase the mechanical stability of the system, to stabilize the nanoparticles, and prevent deactivation by e.g. sintering or metal leaching. The stabilization of the metal nanoparticles can be carried out with either chemical and physical interactions.^{2,3,24,33} Chemical stabilization can be done by the incorporation of heteroatoms into the support material. These heteroatoms can bind the nanoparticles and help to stabilize them. This could be the incorporation of nitrogen, oxygen, phosphorous, or sulfur into the support material. Physical stabilization on the other hand is often established by applying porous support materials as the porosity distributes the nanoparticles over a larger area making it less likely for them to agglomerate. The nanoparticles can even be encapsulated inside the support material limiting metal leaching and sintering. Moreover, the support material can also give substrate and product selectivity by preventing larger molecules access to the active sites based on the pore size.³⁴ However, limiting the pore size or the porosity in general can induce diffusion limitations in the catalytic system, which will decrease the activity and not utilize the full potential of the catalyst. Based on these features, the support material is an important part of a catalytic system and has tremendous impact on the catalytic performance, which showcases why the development of new support materials for catalysis is highly interesting.

2.3 Carbon as support material

Carbon is a widely applied support material due its (often) low cost, high abundancy, and inert nature. Different kinds of carbon are being applied as support materials ranging from amorphous carbon to highly ordered graphene with their own advantages and disadvantages.^{35–39} For example, highly ordered graphitic carbon is electrically conductive in comparison to amorphous carbon but is more difficult and expensive to synthesize. Another widely applied feature of carbon materials is their ability to incorporate heteroatoms (e.g. N, P, and S) into their structure.^{40–42} These heteroatoms change the properties of the material, which can facilitate enhanced catalytic performance by increasing the stability of the nanoparticles as mentioned earlier. For example the incorporation of nitrogen into carbon structures, which have shown to decrease the average particle size compared to non-doped materials manifesting in enhanced catalytic performance.^{43–47} The extensive interest for carbon have also resulted in a variety of different morphologies like 1-dimensional nanotubes, 2-dimensional graphene, and 3-dimensional cubes and spheres.^{48–50} The many morphologies offer different properties where especially porosity have shown significant influence on many catalytic processes. In Figure 2.2 examples of both heteroatom doping and different existing carbon structures are presented to showcase some of the versatility that carbon materials possess. However, despite the variety of techniques to modify carbon materials, gaining access to specific carbon compositions and morphologies are not necessarily easy and can be highly demanding in term of synthetic workup and cost. Thus, new and potentially easy synthesis methods for creating carbon materials are always desirable to expand on usage of carbon as a support material.



Figure 2.2. Illustrations of heteroatom doping into a carbon structure and examples of different morphologies that carbon structures can take. Adapted from Huang *et al.* and Cheaptubes.^{51,52}

Carbonization of organic molecules such as coals and polymers is a common method to create carbonbased materials.⁵³ During a carbonization process, the organic precursor is being heated under an inert atmosphere, which decomposes the organic precursor into carbon(0). The resulting structure and composition of the carbon material depend on the organic precursor applied. For example the presence of heteroatoms during the carbonization will in most cases lead to their incorporation into the final structure and thereby create a doped material. However, if these carbon materials have to be used for catalysis, the active phase has to be incorporated into the structure afterwards, requiring at least one additional synthetic step. This could be the introduction of metal nanoparticles by an incipient wetness technique followed by hydrogenation to yield the desired active phase. However, this tedious introduction of metal nanoparticles can be avoided by using a precursor consisting of both carbon and metal(s). The mixed metal/carbon precursor acts as a reductant during the carbonization process and facilitate the formation of metallic nanoparticles while still being decomposed into carbon(0).^{54–56} As such, the carbonization of mixed metal/carbon structures have emerged as an attractive platform to synthesize nanoparticle catalysts.

2.4 Outline of the projects based on nanoparticle catalysts

Designing and synthesizing new heterogeneous catalysts are crucial in order to continue the development in the field where especially alloyed base metals are very interesting due to their enhanced catalytic properties. In this dissertation, the formation of a new alloy material was achieved by using a cobalt-based MOF, ZIF-67, as a sacrificial precursor by impregnating it with nickel prior to a carbonization process.⁵⁷ The project is presented in Chapter 3 and is the continuation of my Master's Thesis where the synthetic methodology was developed and optimized. The project was finished at the beginning of my PhD by extending the substrate scope, expanding the material characterization, elucidating the reaction pathway, and examining possible metal leaching. However, to provide the reader with a more complete story, data obtained outside the PhD period will be included in a limited extend. Only the most active catalyst, essential thoughts, and relevant characterization techniques are described briefly before a more thorough description of the hydrosilylation of ketones will be presented. The description covers filtrations tests, a scope of different ketones, recycling of the catalyst, and mechanistic tests to investigate the presence of silyl radicals. The results were published in *journal of Catalysis, Science and Technology.*⁵⁸ The increased complexity arising from using heterogeneous catalysis makes mechanistic studies nontrivial. It can make processes inefficiently designed, potentially hazardous, and limit further development if mechanistic knowledge is missing. In this dissertation, the reaction pathway for the α -alkylation of ketones with alcohols using a heterogeneous palladium catalyst was investigated and presented in Chapter 4. The project covers filtration tests, recycling of the catalyst, and a scope of different alcohols and ketones. Furthermore, the mechanism was studied thoroughly with *in-situ* IR and stoichiometric tests. The project was performed together with currently PhD student Rasmus L. Mortensen and the results were published in *Journal of Catalysis*.⁵⁹

3 Hydrosilylation of ketones using CoNi alloy nanoparticles



3.1 Introduction to metal organic frameworks

A type of mixed metal/carbon compound is MOFs as they are constructed from metal-based and organicbased building blocks that forms a porous crystalline network.⁶⁰ The metal-based building blocks, also referred to as secondary building units (SBUs), are either metal ions or a metal clusters. Whereas the organic building blocks are rigid molecules with multiple functional groups for the metal to coordinate to such as carboxylic acids, boronic acids, amines, pyridines, and imidazoles that can bridge two or more different SBUs. This facilitates the formation of either a 1-, 2-, or 3-dimensionelle network depending on the building blocks. In Figure 3.1 examples of different SBUs and organic building blocks with their corresponding MOF structures are shown. These types of materials have seen potential in various applications like catalysis, gas storage or separation, censoring, and electronics.^{61–66} Yet, MOFs' mixed carbon/metal composition makes them ideal precursors for carbon-based catalysts derived from carbonization.^{67–75} Albeit, using MOFs as a consumable precursors do not have industrial relevance currently due to the high synthesis cost, they can still provide new knowledge of carbon structures and help to develop new or improve current methodologies and catalysts.



Figure 3.1. Illustration of different SBUs and organic building blocks used to form MOFs adapted from A. Mallick, R. Banerjee *et al.*⁶⁴

Research on the formation of active catalyst derived from carbonizing MOFs is increasing rapidly in academia, but the formation of alloy nanoparticles instead of monometallic is a rather unexplored field. Few examples have been reported at the time of this study but have grown steadily over the past years due their enhanced catalytic performance.^{76–80} An interesting alloy combination is cobalt and nickel, which have shown promising catalytic properties in CO₂ dry-reforming,^{81,82} water splitting,^{83,84} and oxygen evolution reaction.⁸⁵ Moreover, the potential of Co/Ni alloy nanoparticles have also been demonstrated in silylative pinacol couplings and double bond migrations within our group at DTU.^{54,86} Despite the efforts, the usage of Co/Ni alloy materials in organic synthesis is still rare with possible unexplored applications.

3.2 Introduction to hydrosilylation of ketones

The transformation of silvl ethers from ketones is an important type of transformation in organic synthesis and in the industry as it can have multiple roles depending on the targeted application as visualized in Scheme 3.1 with a general reaction in Scheme 3.1a.^{87–94} First, the silvl group can easily be removed by acid or base treatment yielding the corresponding alcohol (Scheme 3.1b). This methodology enables the reduction of ketones to alcohols under ambient conditions (1 atm, <100 °C), which is very attractive especially in the production of fine-chemicals, where alternative high pressure processes using H_2 have potential issues related to safety and selectivity. Secondly, the silvl group does not have to be removed immediately and can therefore act as either a protecting group for the alcohol functionality (Scheme 3.1c) or a directing group for future reactions (Scheme 3.1d).



Scheme 3.1. Visualization of the hydrosilylation reaction and its versatile properties. a) General hydrosilylation of a ketone. b) Illustration of how to convert silyl ether to the corresponding alcohol by acid or base. c) How silyl ether groups can protect the alcohol functionality from reaction. d) Example of silyl ethers acting as directing groups for regioselective oxidation of C-H bond to an alcohol adapted from Hartwig *et al.*⁹⁴

Hydrosilylation of ketones can be industrial relevant in the production of e.g. (-)-polygodial, an insect antifeedant, starting from enantiopure S-(+)-carvone.⁹⁵ In the presented procedure from de Groot *et al.*, they reduce the ketone to an alcohol and then protect with a *tert*-butyldimethylsilyl ether before proceeding (Figure 3.2). Here, the hydrosilylation offers a direct route to obtain the protected alcohol, which may be more attractive to apply. As such, the development of hydrosilylation catalysts are still highly relevant and especially in the formation of fine-chemicals with its high molecular complexity.



Figure 3.2. Reaction path to synthesize (-)-polygodial from (*S*)-Carvone with the more direct path enabled by hydrosilylation shown. TBDMS is an abbreviation for *tert*-butyldimethylsilyl. Adapted from de Groot *et al*.⁹⁵

Catalysts applied for hydrosilylation of ketones have typically been homogeneous platinum-group metal catalysts with predominately Pt, Pd, Rh, or Ru as the active metal.^{96–100} However, a broad variety of more abundant transition metal catalysts have been reported over the past decades to compete with the more scarce platinum-group metals.^{101–108} Nevertheless, the examples are primarily homogeneous in nature and only limited examples of heterogeneous base metal catalysts for the hydrosilylation of ketones have been reported.^{109–111} However, these examples require organic bases such as ^tBuONa or expensive phosphine ligands like BINAP to proceed smoothly. In that perspective, hydrosilylation of ketones provided a good opportunity to test if a heterogeneous catalyst with alloyed nanoparticles between cobalt and nickel had potential in the transformation without the use of additives and if such a material could be synthesized from using MOFs as precursor.

3.3 Synthesis and characterization of CoNi alloy catalyst

In the synthesis of an alloy catalyst from a MOF, ZIF-67 was chosen as promising precursor due to its inherent content of carbon, nitrogen, and cobalt as it is built from cobalt(II)-ions and 2-methylimidazole. Moreover, the carbonization of ZIF-67 has been reported as an easy pathway to form encapsulated cobalt nanoparticles in nitrogen-doped carbon.^{71–73} Thus, only the introduction of nickel was missing to enable the formation of a CoNi alloy material. A methodology was developed, which exploited the high pore volume of ZIF-67 to introduce a solution of Ni(NO₃)₂ in MeOH into the structure by an incipient wetness technique. The added Ni(NO₃)₂ should match the cobalt content in a 1:1 ratio. Afterwards, the impregnated ZIF-67 was carbonized at 800 °C for 3 hours in argon to form metallic nanoparticles and carbon(0). The overall methodology is illustrated in Figure 3.3. The introduction of a new metal into ZIF-67 by this methodology provided multiple advantages as the amount of new metal could be modified to yield materials with different metal alloy compositions (A_xB_y) and the method was not limited to only a combination of cobalt and nickel as other metal could also be introduced. The latter had been exploited in our group at DTU where other combinations with cobalt were tested; cobalt-copper, cobalt-iron, and cobalt-platinum for different catalytic applications.^{76,112}



Figure 3.3. Illustration of the incipient wetness technique used on a ZIF-67 to form a carbon material with some inherent properties from the MOF.

The success of the method was initially examined by X-Ray diffraction (XRD) to confirm if alloyed nanoparticles had formed. The diffractogram of the carbonized material showed only one set of diffractions overlapping decently with a reported 1:1 CoNi simulation as seen in Figure 3.4a. The successful alloying was also indicated by using the principle behind Vegard's law as the formed alloy material had a 111-diffraction in between that of a monometallic cobalt and nickel nanoparticles at $2\theta = 44.34$ seen in Figure 3.4b. Monometallic cobalt or nickel have 111-diffractions in a face centered cubic (fcc) structure at $2\theta = 44.30$ and $2\theta = 44.42$, respectively. However, a linearity was expected from Vegard's law meaning that the resulting alloy material should be shifted more towards the diffraction from nickel (higher 2 θ). This indicated less nickel than the expected 1:1 ratio.



Figure 3.4. a) Diffractogram of the carbonized alloy catalyst in decent correlation with a CoNi alloy material. b) Zoomed image of the 111-diffraction with corresponding values of a 1:1 alloy material, a pure Co material, and a Pure Ni material.

Therefore, the actual metal content of the resulting material was measured by ICP-OES. The analysis revealed a ratio between cobalt and nickel of 3:2, which was more fitting with the shift in the 111-diffraction. At the same time, the total amount of metal in the sample was measured to 67% of the materials mass, which was quite high for a catalyst but could be industrially attractive as the amount of active sites per mass or volume had the potential to be very high for such a material. The high amount of metal was present as nanoparticles distributed throughout the whole sample in a broad size distribution from 10-75 nm in diameter evident from the TEM images presented in Figure 3.5.



Figure 3.5. TEM images of the carbonized material showing the distribution of alloy nanoparticles throughout the whole material adapted from Kegnæs *et al.*⁵⁸

One of the reported advantages of using ZIF-67 as a precursor is that its ordered structure and morphology can be transferred to the carbonized material. Unfortunately for this system, the presence of additional metal in the carbonization process appeared to make the original morphology of the ZIF-67 collapse as visualized in SEM images in Figure 3.6. It was speculated that the amount of carbon required to reduce the extra metal was too high to maintain the structure, which then led to a structural change. This hypothesis may also explain the reason why the metal content was very high if a significant amount of carbon was used to oxidize the metal during the carbonization process (carbonized ZIF-67 commonly have a metal content at around 20% wt).¹¹³ Following the investigation of the structure, the porosity of the carbonized material was examined by N₂-physisorption and showed a decrease in surface area (213 cm³/g) and pore volume (0.135 cm³/g) compared to the parent ZIF-67 (surface area of 1267 cm³/g and pore volume of 0.67 cm³/g) (Isotherm shown in Figure 3.7). Such a change was to be expected after the carbonization according to literature reports.^{67,71,114}



Figure 3.6. SEM images before (left) and after (right) carbonization illustrating the structural change adapted from Kegnæs *et al.*⁵⁸



Figure 3.7. Physisorption isotherms of the carbonized material adapted from Kegnæs et al.⁵⁸

The presence of heteroatoms in the carbon structure have shown beneficial features to the catalytic performance as discussed in Section 2.2 and carbonized ZIF-67 has previously been a successful precursor for forming N-doped materials. Thus, XPS analysis was conducted on the alloy material to investigate the presence of nitrogen-based species and at the same time to reveal the oxidation state of the cobalt and nickel alloyed nanoparticles. Beginning with the latter, the spectra of the two metals revealed the

presence of metallic species at 778.2 eV for Co and 852.6 eV for Ni with no profound indication of oxidation as these was expected at 779.7 and 853.7 eV for CoO/Co₃O₄ and NiO, respectively (Figure 3.8a-b).¹¹⁵ Analyzing the signals obtained from nitrogen showed the presence of pyridinic, pyrrolic, and graphitic nitrogen confirming the successful doping of nitrogen into the structure (Figure 3.8c).¹¹⁶ Carbon was analyzed as well and showed one peak lying in between the expected values of sp²- and sp³-hybridized carbon and indicated at least partial graphitization during the successful formation process (Figure 3.8d).¹¹⁵ Overall, the different characterization techniques verified the successful formation of alloyed Co/Ni nanoparticles on nitrogen-doped carbon derived from carbonization of nickel impregnated ZIF-67. The carbonized material will be abbreviated CoNi@NC from now on where NC stands for nitrogen-doped carbon.



Figure 3.8. XPS analysis of CoNi@NC with corresponding scans for a) Co2p, b) Ni2p, c) N1s, and d) C1s. Adapted from Kegnæs *et al.*⁵⁸

3.4 Catalytic assessment of CoNi alloy nanoparticles in hydrosilylation of ketones

The formed CoNi@NC was assessed in the hydrosilylation of ketones where a model reaction between cyclohexanone and Me₂PhSiH was applied. The reaction conditions were optimized and provided quantitative yields of the silyl ether with 11 mol% of catalyst with 1.2 equivalents of dimethylphenylsilane in heptane at 90 °C for 24 hours without the use of additives. The activity and product yield were obtained by nuclear magnetic resonance (NMR). Other silanes proved to be either less active and/or selective. Table 3.1 summarizes the optimization.

		CoNi@NC (11 mol% CoNi) 1.2 equiv R ₃ SiH		
	0.5 mmol	heptane (1.0 M), 90 °C, 24 h	\sim	
Entry	Conditions	Silane	Conv. ^a	Yield ^a
1	-	Me ₂ PhSiH	100%	100%
2	5.5 mol% catalyst	Me ₂ PhSiH	64%	60%
3	8.25 mol% catalys	t Me ₂ PhSiH	75%	73%
4	in air	Me ₂ PhSiH	97%	97%
5	70 °C	Me ₂ PhSiH	60%	44%
6	no catalyst	Me ₂ PhSiH	2%	0%
7	no silane	Me ₂ PhSiH	0%	0%
8	toluene as solvent	Me ₂ PhSiH	81%	81%
9	-	Et ₃ SiH	85%	50%
10	-	EtMe ₂ SiH	100%	78%
11	-	MePh ₂ SiH	51%	36%
12	-	Ph ₃ SiH	11%	0%

Table 3.1. Variations to optimized reaction conditions adapted from Kegnæs et al.⁵⁸

^a Conversion and yield quantified by ¹H-NMR using dibenzylether as standard.

The formed CoNi@NC material was magnetic, which was used to easily separate the catalyst from the reaction mixture by a magnet as illustrated in Figure 3.9. This feature made recycling of the catalyst straightforward as the reaction liquid was collected by a syringe and a new stock solution of ketone and silane was added. By this method, the catalyst was recycled 5 times, where it maintained the 100% selectivity towards the silyl ether, but a diminishing activity was observed as the conversion decreased from 100% to 60%.



Figure 3.9. Illustration of the magnetic separation and the results from the recycling experiment adapted from Kegnæs *et al.*^{54,58}

The decrease in activity was initially investigated by analyzing a filtered reaction by ICP-OES to determine if metal was leached out during the process. Fortunately, no metal was detected indicating that metal leaching was not the cause of the deactivation (Scheme 3.2). Next, the origin of the activity was assessed

by a hot filtration experiment. The experiment showed that catalytic reaction stopped completely after removal of the catalyst and demonstrated that the catalytic activity did not arise from a homogeneous specie but rather something heterogeneous that could be removed by a filter (Scheme 3.2). Yet, a diminishing activity was still observed during recycling. Thus, TEM images of the recycled catalyst were taken to visualize potential material changes. The images are shown in Figure 3.10 where it is evident that the nanoparticles have sintered, which is most likely the cause of the observed deactivation as it decreases the surface area of the active metals.







Figure 3.10. TEM images of the recovered CoNi@NC after usage adapted from Kegnæs et al.⁵⁸

The robustness of the CoNi@NC catalyst was examined by screening different ketones as substrates for the hydrosilylation reaction. The results are presented in Table 3.2, where cyclic aliphatic ketones showed good to excellent activities with very high product selectivity (entries 1-3). The presence of a bulky substituent in the *gamma*-position of cyclohexanone eliminated the activity almost completely as the hydrosilylated product was only obtained in 2% yield (entry 4). Different acyclic aliphatic ketones were tested as well, but only some activity was observed for cyclohexyl methyl ketone (entry 5) with 19% product yield, whereas 4-heptanone and 2,4-dimethyl-3-pentanone were completely inactive in the transformation (entries 6-7).



Table 3.2. Scope of different aliphatic ketones using CoNi@NC as catalyst.

^a Conversion and yield quantified by ¹H-NMR using dibenzylether as standard.

Acetophenone and derivatives thereof were tested as well and presented in Table 3.3. Acetophenone and 4-methylacetophenone showed very high activity with up to 94% conversion and moderate yields with 68% and 69%, respectively (entries 1-2). Moving the methyl group from the *para*-position to the *ortho*-position in 2-methylacetophenone significantly decreased the formation of product with a yield of 22% (entry 3). Yet, other *para*-substituted acetophenones with either fluoro, chloro, or methoxy groups were tolerated with high activity and product yields ranging from poor to good (entries 4-6). Functionalization with a methyl group on the α -carbon decreased the selectivity towards the silylated product (entry 7), however the difference between a methyl or phenyl group on the α -carbon was very small with 44% and 40% yield, respectively (entries 7-8). 4-methylbenzophenone provided full conversion with moderate product yield (entry 9). Overall, the substrate scope demonstrated tolerance for different cyclic aliphatic ketones and derivatives of acetophenone. However, precautions have to be made for sterically demanding substrates as *tert*-butyl groups and *ortho*-functionalization limited the activity significantly.



Table 3.3. Scope of different derivatives of acetophenone using CoNi@NC as catalyst.

^a Conversion and yield quantified by ¹H-NMR using dibenzylether as standard.
The observations from the substrate scope provided limited mechanistic insight and additional experiments were conducted to help investigate the reaction pathway. First, the model reaction under optimized conditions (Table 3.1 entry 1) was monitored as a function of time where an induction period of approximately four hours with no conversion was observed as visualized in Figure 3.11. The presence of an induction period when using silanes have been reported by Houk, Stoltz *et al.* in their C-H silylation of heterocycles due to the formation of silyl radicals.¹¹⁷



Figure 3.11. Time study of the hydrosilylation reaction with conversion and yield as a function of time adapted from Kegnæs *et al.*⁵⁸

The presence of radicals was investigated to help investigate the origin of the induction period and as silyl radicals were to be crucial for catalytic activity in previous studies in our group at DTU with Co/Ni alloyed materials.^{86,118} Thus, BHT or TEMPO were added as a radical scavenger or trap to prove if a similar radical pathway was present for this system. However, the reactions proceeded unaffected indicating that the formation of radicals was not critical for the transformation under these reaction conditions (Scheme 3.3). Nevertheless, the trends from the substrate scope, which showed a strong dependency on steric effects, and no formation of radicals led to the belief that substrate adsorption to the catalytic surface was critical for the catalytic activity. Such a behavior may correlate with an Ojima type mechanism.^{105,119,120} A possible Ojima type mechanism is visualized in Scheme 3.4 where both silane and ketone have to be adsorbed on the metal surface to enable the catalytic cycle. Such a mechanism would explain both the decrease in activity during recycling as the active surface area is reduced, a period without catalytic activity where adsorption occurs (the induction period), and the high influence of steric effects.



Scheme 3.3. The presence of radicals were tested with BHT and TEMPO adapted from Kegnæs et al.58



Scheme 3.4. Illustration of a possible Ojima type mechanism with Co/Ni nanoparticles as the active catalyst.

3.5 Summary

The impregnation of ZIF-67 with Ni(NO₃)₂ in MeOH provided a new and easy method to form Co/Ni alloy nanoparticles on nitrogen-doped carbon by a carbonization process. The alloyed nanoparticles had a 3:2 ratio between cobalt and nickel evident by XRD and ICP-OES. Characterization by XPS confirmed the presence of pyrrolic, pyridinic, and graphitic nitrogen-doped in the carbonized structure. A structural change was observed in the carbonized material compared to the parent ZIF-67 visual by SEM images. The alloy nanoparticles were active in the hydrosilylation of ketones where the origin of the activity was proven to be heterogeneous by a filtration experiment. Furthermore, the alloy material was easy to recover and reuse due to its magnetic properties. Quantitative yields were observed for cyclohexanone under the optimized conditions and could be extended to other cyclic aliphatic ketones with decent success. Acetophenone and derivatives thereof was tolerated ranging from poor to high activity with moderate to good product formation of the silyl ether. Acyclic aliphatic ketones gave limited to no activity and ketones with bulky substituents or functional groups in steric-sensitive position (*ortho*-position) decreased the activity significantly. The pathway for the activity showed no involvement of radicals, which led to speculations about substrate adsorption to the catalytic surface being critical to achieve activity as seen in Ojima type mechanisms.

3.6 Experimental

All chemicals used in the catalyst synthesis and in the catalytic reactions were reagent grade and utilized without further purification. Co(NO₃)₂·6H₂O, Ni(NO₃)₂·6H₂O, 2-methylimidazole, Et₃SiH, Me₂EtSiH, Ph₃SiH, Ph₂SiH, cyclopentanone, cyclo-hexanone, cycloheptanone, *tert*-butyl cyclohexanone, cyclohexyl methyl ketone, 4-heptanone, 2,4-dimethyl-3-pentanone, acetophenone, 4'-methylacetophenone, 4'-methoxyacetophenone, 4'-chloroacetophenone, 4'-fluoroacetophenone, 2'-methylacetophenone, 4'-methoxypropiophenone, 4-methyl-benzophenone and cyclopropyl 4-methoxyphenyl ketone were all purchased from Sigma Aldrich, whereas MePh₂SiH was bought from Alfa Aesar and Me₂PhSiH from Fluorochem.

Equipment

X-ray Powder diffraction (XRPD) were measured with a Cu-K α radiation source on a HUBER G760 Guinier camera. N₂-physisorption was conducted on a Micrometrics 3Flex instrument at 77 K. Samples for N₂-physisorption were degassed 24 hours before the analysis on a Micrometrics VacPrep 061 Sample Degas System at room temperature for ZIF-67 and 200 °C for the carbonized materials. TGA was performed on a Mettler Toledo TGa/DSC 1 STARe System. XPS was done with a spot size of 400 μ m with an Al alpha X-ray source with 10 scans per element. SEM images were taken on a Quanta 200 ESEM FEG microscope from FEI. TEM images were obtained from a Technai T20 G2 microscope from TEI. ICP-OES was conducted on an iCAP 7000 Plus Series from Thermo Scientific with a Teledyne CETAC ASX-560 autosampler. ¹H-NMR samples were measured on a Bruker Ascend 400 (400 Hz). All synthesized catalyst materials were stored under a protective argon atmosphere except ZIF-67, which was stored in atmospheric air.

Synthesis of ZIF-67 adapted from Lou et al.¹²¹

 $Co(NO_3)_2 \cdot 6H_2O$ (2.91 g, 10,0 mmol) was dissolved in methanol (250 mL). Similarly, 2-methylimidazole (3.28 g, 40.0 mmol) was dissolved in methanol (250 mL) as well. The two solutions were mixed by adding the 2-methylimidazole solution to the cobalt(II) nitrate solution. The resulting purple mixture was shaken for 5 min and purple precipitate was observed. The mixture was left to age for 72 h. The precipitate was isolated by centrifugation at 10000 rpm for 10 min and washed 3 times with methanol. The washed purple crystals were dried and stored in an oven at 80 °C overnight before use. 500 mg ZIF-67 was obtained; yield = 22.5% based on Co.

Catalytic tests

Inside a glovebox, the catalyst (10 mg, 11 mol%) was added to a 4 mL vial containing a stirbar. In another vial, a stock solution was made of 1 M ketone and 1.2 M silane with a total volume of 1 mL in either heptane or toluene. 0.5 mL of the stock solution was added to the vial with the catalyst and the mixture was sealed with a PTFE-lined screw cap. Outside the glovebox, the reaction mixture was placed in an aluminum-heating block at 90 °C with magnetic stirring (600 rpm) for 24 h. Next, the mixture was cooled down to room temperature and 1 mL of a 0.25 M dibenzyl ether in ethyl acetate was added as a NMR standard. Afterwards, 0.5 mL of the reaction was filtered and concentrated under vacuum. The resulting solution was analyzed by 1 H-NMR using CDCl₃ as the solvent.

Recycling experiment

The same procedure was used as described under catalytic tests until the point where the NMR standard should have been added. Instead, the mixture was taken into the glovebox where the catalyst was separated from the liquid by immobilizing the catalyst with a magnet. The liquid was collected and added to a vial with 1 mL of the 0.25 M dibenzyl ether standard. 0.5 mL of a new stock solution of ketone and silane (1 M and 1.2M, respectively) was added and sealed with PTFE-lined screw cap again and placed in an aluminum-heating block as described above. This procedure was repeated for every recycle.

Filtration test

A reaction was prepared as described in catalytic test, but was stopped after 12 h which corresponds to approximately 50% conversion. The mixture was taken into a glovebox, separated from the catalyst by a magnet, and filtered into a new 4 mL vial through a 0.22 μ m syringe filter before the vial was sealed with

a PTFE-lined screw cap. The vial was placed on an aluminum heating block at 90 °C for additional 8 hours. The mixture was analyzed as described earlier.

Leaching test

Two experiments were prepared as described earlier and stopped after for 24 h, however no NMRstandard was added to the mixture. Instead, the mixture was filtered to separate the catalyst from the liquid. The liquid was placed under vacuum to remove all volatile compounds. Afterwards, concentrated HNO₃ (65% w/w) was added to the liquid, which was subsequently diluted to form a 2% w/w HNO₃ aqueous solution and filtered again before ICP analysis. (The mixture was clear and showed no sign of precipitation prior to the last filtration.)

α -Alkylation of ketones with alcohols using Pd nanoparticles



4.1 Reaction mechanism for heterogeneous catalysis

Knowing the reaction pathway provides crucial information on how to optimize the reaction efficiently and predict tolerance for functional groups, possible deactivation mechanism etc.^{2,33} These features are even more important to understand when going from laboratory scale to industrial scale to ensure the most efficient production with the least amount of waste, energy consumption, hazardous chemicals etc. in line with the principles of green chemistry. However, elucidating the reaction pathway is not trivial and can be very difficult as very small changes in the reaction setup can facilitate a different reaction pathway, and thereby provide another reaction mechanisms for seemingly similar systems.^{54,86,122} Especially the investigation of reaction mechanisms for heterogeneous catalytic systems can be very challenging but highly attractive as they are the most applied type of catalysts in industry.^{123–126}

The complexity of heterogeneous catalysts with the combination of active sites, a support material, and a reaction media in another phase than the catalyst makes mechanistic investigations more difficult than homogeneous catalysis. Moreover, many classical characterization methods setups for solid heterogeneous catalysts like electron microscopy, XRD, XPS etc. requires conditions that are very far away from the catalytic conditions and these setups may not give a realistic picture of the actual catalyst in action. Fortunately, catalysts can be studied under reaction conditions using *in-situ* or *in-operando* setups, which can provide a more realistic picture of the actual catalysis occurring in the reaction. *In-situ* (on site) or *in-operando* (in work) studies analyze the catalysts under working condition while monitoring the activity to showcase possible trends and hopefully gain insight into the reaction pathway.¹²⁷⁻¹²⁹ However, even though these type of studies are powerful tools to investigate mechanisms, they may not be able to provide information about the whole catalytic system with the presence of two different phases. Thus, much research focuses on the part of the catalytic system that they believe provide the most useful information. The choice have to be justified and supported by other techniques and results to ensure its reliability.

A powerful tool to investigate reaction kinetics for homogeneous catalytic systems in solution is NMR as it can provide information about intermediates, molecular interactions, reaction rates, and dependencies etc. using very small quantities of compounds and can be operated at reaction temperatures commonly applied in liquid phase reactions.¹³⁰ Unfortunately, the presence of two different phases in heterogeneous catalysis makes NMR unavailable for *in-situ* studies due to poor shimming, heterogeneity in the sample, and/or diffusion/concentration differences as a result of no stirring. A more promising and powerful technique to study kinetics for heterogeneous catalytic systems is electron paramagnetic resonance (EPR). Elucidating reaction pathways by EPR have been very successful tool especially for gas phase reaction using solid catalysts. Albeit, an underlying restriction is that it requires unpaired electrons either in the presence of radicals or from transition metals/complexes limiting its usage.^{131,132} Another powerful and highly versatile technique that can be used for both gas, liquid, and solid phase compounds is IR spectroscopy as it only relies on a change in dipole moment of a molecule's rotations and vibrations. At the same time, IR spectroscopy can be conducted on solutions while there are being stirred preventing the diffusion limitations and concentration differences in the mixture. IR spectroscopy will shortly be introduced next.

IR is commonly referring to the part of the electromagnetic spectrum from 4000-400 cm⁻¹ covering excitations of vibrations and rotations within molecules.^{130,133} These excitations are specific, meaning that only the wavenumber with the exact energy can be adsorbed and excite a molecule from a ground state

to an excited state. The energy difference between the ground state and excited state(s) is very large between bonds with different bond order (single, double, triple) and bonds between different atoms (C-O, C-N, C-C), but also significant enough to separate different carbonyl functionalities (aldehyde, ketone, ester, carboxylic acid). The high versatility provides IR with good potential to elucidate kinetics of reactions especially in the α -alkylation reaction with a heterogeneous catalyst where other techniques may have their limitations.

In the setup used for this project, a vial was mounted to an IR probe by a specialized lid with a hole and an o-ring of rubber to make the setup tight and isolated from the surrounding atmosphere (Figure 4.1ab). This enabled the examination of reaction mixtures at elevated temperatures and under other atmospheres than air. After the vial was mounted, the reaction was stirred and heated as a standard reaction using a stirrer and an oil bath as seen in Figure 4.1c. IR spectra was then measured as a function of time and with appropriate references, the difference observed over time was then calculated into reaction profiles.



Figure 4.1. Pictures of the *in-situ* IR setup. a) Picture of the reaction vial fitted to the probe. b) Image of the lids and vial used. c) Picture of the overall setup with an oil bath, stirrer, probe etc.

4.2 Introduction to the α-alkylation reaction

The formation of new carbon-carbon bonds are always highly desirable in the organic synthesis and the α -alkylation reaction have been used to form key pharmaceutical intermediates.^{134–136} The α -alkylation of ketones provides a straightforward technique for forming a new C(sp³)-C(sp³) bond at the α -carbon of the carbonyl using an electrophile.^{137–139} The α -carbon is activated through a tautomerization in the presence of an acid or base forming the nucleophilic enolate that can react with an electrophile. Historically, alkyl halides have been very popular as electrophiles but they provide undesired waste in the form of halide salts providing poor atom efficiency, which is undesired based on the principles of green chemistry. Fortunately, a promising new approach that utilizes alcohols as a "masked" electrophile have gained significant scientific attention as a more green and sustainable transformation yielding only water as

byproduct. The methodology relies on increasing the electrophilicity of alcohols through a dehydrogenation step, yielding the more electrophilic aldehyde/ketone that can react with the nucleophilic enolate. The pathway have been known as a hydrogen-borrowing, hydrogen-transfer, or auto-transfer mechanism.

The pathway that have been observed and demonstrated for many catalytic systems between ketones and primary alcohols is illustrated in Figure 4.2 with an internal hydrogen-transfer facilitated by a metal catalyst ([M]). Initially, the alcohol is oxidized through a dehydrogenation step as mentioned previously and the hydrogen is stored within the catalytic system. The resulting aldehyde can attack the nucleophilic ketone/enolate and form a α , β -unsaturated ketone by a base-catalyzed aldol condensation. The catalytic cycle is finished by a hydrogenation of the C-C double bond using the released hydrogen from the dehydrogenation step yielding the alkylated product and the active metal catalyst. The terminology arise from the internal release and use of hydrogen.



Figure 4.2. Schematic illustration of a hydrogen-borrowing pathway between an alcohol and a ketone adapted from Kegnæs *et al.*⁵⁹

The requirement of a catalyst is evident according to the reaction pathway to facilitate the dehydrogenation and hydrogenation step. Platinum group metals like Ir, Pd, and Ru are the most active metals for hydrogen-borrowing reactions despite numerous reports of catalytic systems utilization base metal catalysts.^{140–144} In the aim of this project, a more thorough investigation of heterogeneous palladium catalysts will be presented next.

In 2005 Cho published an α -alkylation between a ketone and primary alcohol using commercially available Pd/C as catalyst.¹⁴⁵ In his work, the reaction conditions were optimized to 5 mol% Pd at 100 °C for 40 h with 1-decene as additive to react acetophenone and 1-butanol in 75% yield. The presence of 1-decene was crucial to achieve good activity and selectivity in the work. The requirement of additives was also demonstrated by Uozumi *et al.* where 7 equivalents of water boosted the yield from 59% to 83% between 1-octanol and 2-octanone with their Pd nanoparticles in a self-assembled polymeric matrix.¹⁴⁶ Hori and coworkers showcased the effect of having Pd nanoparticles on different support materials where one of the most active catalysts with full selectivity towards the α -alkylated product between acetophenone and benzyl alcohol was a carbon material.¹⁴⁷ The versatility of α -alkylation transformation was demonstrated by Park *et al.* where the presence of oxygen or an inert atmosphere facilitates either the α , β -unsaturated ketone or the alkylated ketone as the final product, respectively.¹⁴⁸ Ying and coworkers published their

one-pot synthesis of polysubstituted quinolines using a catalyst with both Pd and Ag nanoparticles, where the Pd was active for the initial α -alkylation whereas the silver facilitated the Friedländer annulation yielding the desired quinolines.¹⁴⁹ The use of palladium catalysts for α -alkylation reaction is both common, versatile, and successful as described above. Yet to give a more comprehensive overview, the reaction conditions and results from the reaction between acetophenone and benzyl alcohol are presented in Table 4.1 as this reaction has been reported by them all and is an ideal model reaction.

Table 4.1. Conditions and yields for different reports of heterogeneous Pd-catalyzed α -alkylation between acetophenone and benzyl alcohol.



Despite numerous reports, the mechanistic understanding of heterogeneous Pd-catalyzed α -alkylation are only speculative as no thorough investigation have been performed and in general only sparse kinetic studies have been reported for heterogeneous catalytic systems using the hydrogen-transfer methodology.^{150–152} As such, the potential of heterogeneous Pd catalyst may still be unexplored, especially as fairly simple commercially available catalyst shows promising catalytic performance.

4.3 Catalytic performance of the α-alkylation between ketones and alcohols

Initial studies using commercially available Pd/C provided promising catalytic activity for the α -alkylation reaction between acetophenone and benzyl alcohol. The reaction conditions were optimized to provide quantitative NMR yields under mild conditions (80 °C, 6 h, 1 mol% Pd) in a 0.25 M solution of acetophenone in toluene with a small excess of benzyl alcohol (Table 4.2, entry 1). Alterations to the optimized conditions are shown in Table 4.2. The origin of the activity was assessed by carrying out the reaction without catalyst and without palladium (with activated carbon) where both experiments demonstrated the requirement of palladium as only 0% or 3% product yield were observed, respectively (entries 2-3). Replacing the catalyst from a 5 wt% to a 10 wt% Pd/C did not provide any difference with 100% conversion and yield (entry 4). Conducting the catalytic reaction in air only showed minimal product formation with 7% yield showcasing the need of an inert atmosphere (entry 5). The influence of base was demonstrated as replacing K₃PO₄ with other bases had significant effect by either decreasing or completely suppressing the activity (entries 6-9). Varying the amount of base from 1.5 equivalents to either 1.0 or 2.0 equivalents did not yield any difference (entries 10-11). The potential of elucidating the reaction pathway with *in-situ* IR would require a different reaction setup than used for the optimization process, where possible changes in concentration and headspace volume may affect the catalytic performance.

Therefore, these alterations were tested as well and demonstrated promising results with no significant change in product yield (entries 12-17).

O Me	OH	1 mol% Pd/C (5 v 1.5 equiv K ₃ PO ₄	vt%) C	
		toluene (0.25 M),	80 °C,	
0.125 mmol	1.1 equiv	6 h, Ar, headspac	ce 3.5 mL 💙	~
Entry	Conditions		Conv. ^a	Yield ^a
1	-		100%	100%
2	no catalyst		6%	0%
3	activated ca	rbon	46% ^b	3% ^b
4	10 wt% Pd/0	C	100%	100%
5	in air		32%	7%
6	K ₂ CO ₃		0%	0%
7	Li ₂ CO ₃		0%	0%
8	Cs_2CO_3		66%	86%
9	Et ₃ N		0%	0%
10	1.0 equiv K ₃	PO ₄	100%	100%
11	2.0 equiv K ₃	PO ₄	100%	100%
12	headspace	3.0 mL	100%	100%
13	headspace 2	2.5 mL	99%	99%
14	headspace 2	2.0 mL	97%	97%
15	0.125 M		100%	100%
16	0.50 M		100%	100%
17	1.0 M		100%	100%

Table 4.2. Variations to reaction conditions and their effect adapted from Kegnæs et al.⁵⁹

^a Conversion and yield quantified by ¹H-NMR using dibenzylether as standard. ^b Reaction time was 24 h.

The heterogeneous nature of the catalyst was verified by a hot filtration experiment and by analyzing a filtered reaction mixture by ICP-OES for potential metal leaching similarly to the previous project. The experiments are showcased in Scheme 4.1, where both tests indicated no leaching of either inactive or active palladium species.



Scheme 4.1. Illustration of the procedure and results of the hot filtration experiment and leaching test by ICP and adapted from Kegnæs *et al.*⁵⁹

The versatility and chemical tolerance of the optimized conditions were tested by screening different alcohols and ketones. Functionalizing benzyl alcohol in the *para*-position with either electron donating (Me, MeO) or withdrawing groups (F, CF₃) were tolerated completely providing quantitative yield in all cases (Table 4.3, entries 2-5). A secondary benzylic alcohol was on the other hand completely inactive in the transformation with 0% conversion (entry 6). Aliphatic alcohols gave good yields at slightly elevated temperatures (100 °C) with 72% and 73% yield for 1-heptanol and 1-propanol, respectively (entries 7-8). Ketones showed a similar tendency providing quantitative yields for different *para*-substituted acetophenones with either electron donating (Me, MeO) or withdrawing groups (F, CF₃) (Table 4.4, entries 2-5). More sterically hindered acetophenone derivatives bearing a phenyl on the α -carbon provided only 52% yield (entry 6). This demonstrated some limitation to the system as functional groups on the α -carbon decreased the activity significantly. Yet, the steric hindered *ortho*-position was tolerated completely with 100% yield using 2-methylacetophenone (entry 7). Aliphatic ketones gave quantitative yields of the least steric hindered product when applying cyclohexyl methyl ketone and 4-phenylbutan-2-one as substrates (entries 8-9).

	O Ma	ОН	1 mol% Pd/C (5 wt%) 1.5 equiv K ₃ PO ₄	C C	
	Me	R	toluene (0.25 M), 80 °C, 24 h Ar headspace 3.5 r	ml	~ R
	0.125 mmol 1.	2 equiv			
Entry	Alcohol		Product	Conv. ^a	Yield ^a
1	ОН	^		100%	100%
	Н		Н		
2	ОН		0	100%	100%
3	Me		Me O	100%	100%
5			OMe	100 /0	100 /0
4	MeO' ~ OH	^		100%	100%
	F		F		
5	ОН		0	98%	98%
	F ₃ C		CF3		
6	OH		O Me	0%	0%
	F		F		
7 ^b	Me	ОН	O Me	72%	72%
			0		
8 ^b	Me		Me	73%	73%

Table 4.3. Scope of different alcohols in the α -alkylation reaction.

 $^{\rm a}$ Conversion and yield quantified by $^{\rm 1}{\rm H}\text{-}{\rm NMR}$ using dibenzylether as standard. $^{\rm b}$ Reaction temperature was 100 °C

	0	OH	1 mol% Pd/C (5 wt%) 1.5 equiv K ₃ PO ₄		
	R ¹ R ²		toluene (0.25 M), 80 °C, 24 h, Ar, headspace 3.5 mL	R^2	
	0.125 mmol	1.2 equiv			
Entr	y Ketone	e	Product	Conv. ^a	Yield ^a
1	H	O ∭ Me	H	100%	100%
2	Me	Me	Me	100%	100%
3	MeO	Me	MeO	100%	100%
4	F	O Me	F	100%	100%
5	F ₃ C	Me	F ₃ C	100%	100%
6	H	Ph	H Ph	67%	52%
7	Me	Ме	O Me	100%	100%
8		Ме		100%	100%
9		O Me		100%	100%

Table 4.4. Scope of different ketones in the $\alpha\text{-alkylation}$ reaction.

^a Conversion and yield quantified by ¹H-NMR using dibenzylether as standard.

With the knowledge that the origin of the activity was heterogeneous, palladium did not leach, and the overall catalytic setup had a high tolerance for different alcohols and ketones, a recycle experiment was carried out to utilize one of the advantages of heterogeneous catalysis over its homogeneous counterpart. A standard reaction between benzyl alcohol and acetophenone were conducted where the catalyst was recovered after the reaction and reused. Four recycles were done and the results are illustrated in Figure 4.3. The selectivity towards the α -alkylation reaction remained unchanged at 100%, but a clear loss in activity between the third and fourth recycle occurred.



Figure 4.3. Illustration of the recycling properties of the Pd/C catalyst with conversion and selectivity over five consecutive reactions adapted from Kegnæs *et al.*⁵⁹

The cause of the deactivation was investigated by comparing fresh catalyst with recycled catalyst in TEM and by XPS analysis. The TEM images showed that the nanoparticles had not agglomerated or changed significantly in size, which seemingly ruled out sintering as a potential deactivation mechanism (Figure 4.4a-b). According to the XPS analysis, the carbon support did not change whereas in the spectra for palladium, there was a clear difference between the fresh and recycled catalyst (Figure 4.4c-d). The fresh catalyst had signals corresponding to two different palladium species at the $3d_{5/2}$ transition with metallic Pd and PdO at 335.4 eV and 336.8 eV, respectively. The same trend was at the $3d_{3/2}$ transition with Pd at approximately 340 eV and PdO at 342 eV. For the recycled catalyst, the signals from PdO was barely visible, meaning that metallic palladium was the most abundant palladium specie present. However, if having partial presence of PdO, which seemingly was the only difference between the fresh and recycled catalyst, was the cause of the observed deactivation, is still unclear.



Figure 4.4. a) TEM image of unused Pd/C catalyst. b) TEM image of recycled Pd/C that have been used for five consecutive reactions. XPS analysis of the fresh Pd/C catalyst and the recycled Pd/C catalyst. c) Pd3d analysis and d) C1s analysis. Adapted from *Kegnæs* et al.⁵⁹

4.4 Elucidation of reaction mechanism

The hydrogen-borrowing pathway has been reported as a type of mechanism occurring for α -alkylation reactions under similar reaction conditions as those used for this project. Thus, to elucidate if a similar pathway occurred for this heterogeneous system, the hydrogen-transfer mechanism was divided into 3 parts; A dehydrogenation step, an aldol condensation step, and a hydrogenation step. Each individual part of the hydrogen transfer pathway were validated by stoichiometric test as seen by Scheme 4.2. The dehydrogenation step was tested by exposing benzyl alcohol to the reaction conditions in the absence of acetophenone. Approximately 30% of the alcohol was dehydrogenated into the aldehyde confirming that the dehydrogenation step could occur. The presence of base was not important for this transformation as it proceeded with or without it. Similarly, mixing benzaldehyde and acetophenone together yielded the α , β -unsaturated ketone with or without the palladium catalyst demonstrating that the aldol condensation step did not require palladium as catalyst. The last part was tested by exposing the α,β -unsaturated ketone, chalcone, to the hydrogen source of the reaction, benzyl alcohol, which also proved to be possible as chalcone was completely hydrogenated providing the saturated ketone. A cross-over experiment with a CF₃-labelled benzyl alcohol and unlabeled benzaldehyde yielded scrambling of CF₃-labelled and unlabeled products, intermediates (aldehydes), and reagents (alcohols) showcasing both the strong possibility of a hydrogen-transfer pathway but also the reversibility in the dehydrogenation step. These four experiments gave a strong indication that a hydrogen transfer pathway occurred for this heterogeneous catalytic palladium system as well.



Conversion and yield quantified by ¹H-NMR using dibenzylether as standard.

^a Values for yield and conversion is based on the initial amount of benzylic alcohol.

Scheme 4.2. Stoichiometric tests to verify individual steps of a possible hydrogen-borrowing pathway adapted from Kegnæs *et al.*⁵⁹

In-situ IR experiments had the potential to obtain further evidence for a hydrogen-borrowing pathway by providing reaction rates and profiles. As stated previously, the IR experiment required a different reaction setup, which was believed not to change the reaction pathway based on experiments from Table 4.2. Thus, a 1.25 mmol experiment between acetophenone and benzyl alcohol was carried out with the reaction profile is shown in Figure 4.5. The appearance of the profile was both chemically reasonable and matched NMR samples taken after 20 min and 180 min. The consumption of acetophenone (blue) fitted very well with the formation of the alkylated product (purple) and with the two intermediates (red = benzaldehyde and green = chalcone) had a low concentration throughout the whole reaction. These results provided viable results for further kinetic studies and investigation of the reaction mechanism.



Figure 4.5. Reaction profile of a standard experiment between acetophenone and benzyl alcohol showing the concentration profiles of acetophenone, benzaldehyde, chalcone, and alkylated product adapted from Kegnæs *et al.*⁵⁹

A time adjusted experiment was done by comparing the reaction profile under standard conditions with one conducted with the same ratio between acetophenone and benzyl alcohol but at a lower concentration. Time adjusting the two experiments and comparing the rates provided evidence of catalyst poisoning and/or product inhibition. The resulting graph is shown in Figure 4.6 where the high similarity in curves, and thereby rates, suggested that neither catalysts poisoning nor product inhibition occurred during the reaction.



Figure 4.6. A time adjusted experiment demonstrating the overlap between the two experiments adapted from Kegnæs *et al.*⁵⁹

The catalyst loading was changed in a range from 0.5 mol% to 2.0 mol% palladium to determine the influence of the catalyst on the reaction rate (Figure 4.7). Surprisingly, the rate did not change as the reaction profiles were overlapping nicely, leading to a zero order dependency for the catalyst and demonstrated that the Pd/C did not take part in the rate-limiting step. This was further supported by decreasing the Pd loading to 0.25 mol%, which showed similar activity after 3 hours in a standard 0.125 mol% experiment. The same trend was seen for the base as changing the amount to either 1.3 or 1.7 equivalents did not yield any difference in rate leading to a zero order dependency as well.



Figure 4.7. Reaction profiles varying catalyst loading (left) or base (right) adapted from Kegnæs et al.⁵⁹

The total order of the reaction was determined to be a first order with a linear dependency on a one-axe logarithm plot shown in Figure 4.8a. A zero order dependency will yield a linear curvature plotting concentration as a function of time and a second order dependency is linear by applying reciprocal concentrations ($[C]^{-1}$). To elucidate the reaction rate further, a variable time normalization method analysis was applied to identify the order of the individual components.¹⁵³ The method uses graphical expression to analyze kinetics by taking advantage of simple overlays, linearity etc. This method was used in Figure 4.8b-d where an overlap between two experiments with different concentrations of acetophenone occurred when the concentration of acetophenone had a power of one in the normalized time scale (Σ [Acetophenone]¹ Δ t) leading to a first order rate dependency in acetophenone concentration. Applying other values etc. 0.5 or 1.5 did not give same overlap demonstrating the simplicity and power of the method.



Figure 4.8. Rate order determination by graphical methods. a) The overall order of the reaction. b) First order dependency of acetophenone, c) 0.5 order dependency of acetophenone, and d) 1.5 order dependency of acetophenone. Adapted from Kegnæs *et al.*⁵⁹

These observations suggested that the rate-limiting step was the aldol condensation as the catalyst had a zero order dependency and acetophenone had a first order dependency. This also correlated with the high influence observed by changing base in Table 4.2 (entries 6-9) as the aldol condensation is base-catalyzed. Yet, a second order dependency would be expected if the aldol condensation was the rate limiting step, albeit a first order was measured. This suggested that the limiting step may be the deprotonation of acetophenone or the presence of a pseudo-first order due to a steady state behavior of benzaldehyde.

The results from the stoichiometric tests and *in-situ* IR have led to the mechanistic proposal seen in Scheme 4.3, which follows a similar hydrogen-borrowing pathway seen for many homogeneous catalysts. The cycle begins with a reversible dehydrogenation step of the alcohol to an aldehyde followed by the rate-limiting base catalyzed aldol condensation. The pathway finishes by hydrogenation of the α , β -unsaturated ketone yielding the alkylated product. The role of palladium is in the dehydrogenation and hydrogenation step.



Scheme 4.3. Proposed reaction mechanism based on the results from stoichiometric tests and *in-situ* IR adapted from Kegnæs *et al.*⁵⁹

4.5 Summary

It was demonstrated that commercially available Pd/C was an excellent catalyst for α -alkylation of ketones with alcohol as a "masked" electrophile under mild conditions without the need of additives. A high tolerance for different functional groups was demonstrated by a series of different alcohols and ketones. The activity was heterogeneous of nature and the catalyst did not leach metal during the reaction. The catalyst was reused up to four consecutive times without any significant loss of performance, however, further usage decreased the activity but it remained 100% selective towards the α -alkylation transformation. The reaction pathway was elucidated by both stoichiometric experiments and *in-situ* IR where a hydrogen-borrowing mechanism matched the obtained results and trends. The rate-limiting step was determined to be the base-catalyzed aldol condensation.

4.6 Experimental

Chemicals

All chemicals were reagent grade and used as received without further purification. Pd/C 5 wt.% was purchased from Sigma-Aldrich (catalog number 75992). K₃PO₄ was purchased from Sigma-Aldrich (anhydrous, reagent grade, \geq 98%, catalog number RDD019). Both Pd/C and K₃PO₄ were stored and used under a protective argon atmosphere. Benzyl alcohol, 4'-methylbenzyl alcohol, 4'-methoxybenzyl alcohol, 4'-fluorobenzyl alcohol, 4'-trifluoromethylbenzyl alcohol, acetophenone, 4'-methylacetophenone, 4'-methylacetophenone, 2'-methylacetophenone, benzaldehyde, *trans*-chalcone, Pd/C 10 wt.%, and activated carbon were purchased from Sigma Aldrich. 1-heptanol was purchased from Fluka and cyclohexyl methyl ketone was purchased from Alfa Aesar.

Equipment

XPS was done with a spot size of 400 μ m with an Al alpha X-ray source with 10 scans per element. TEM images were obtained from a Technai T20 G2 microscope from TEI. ¹H NMR was measured on a Bruker

Ascend 400 (400 Hz). The React-IR instrument used was a Mettler Toledo model ic10. ICP-OES was conducted on an iCAP 7000 Plus Series from Thermo Scientific with a Teledyne CETAC ASX-560 autosampler.

General procedure for optimization and substrate scope investigation

In an argon-filled glovebox, a stock solution of ketone and alcohol was prepared with concentrations of 0.25 M of the ketone and either 0.275M or 0.30 M of the alcohol in toluene. Then, to a 4 mL vial was added Pd/C 5 wt.% (2.7 mg, 0.00125 mmol Pd), K_3PO_4 (40 mg, 0.1875 mmol), a stirbar, and 0.50 mL of the stock solution. The vial was sealed with a PTFE-lined screw cap. Outside the glovebox the vial was placed in a pre-heated aluminum block and stirred (1000 rpm) for either 6 or 24 h at 80 °C. After the specified time, the mixture was cooled down to room temperature and 0.50 mL of a 0.125 M solution of dibenzyl ether in diethyl ether was added. The mixture was shaken vigorously before 0.20 mL was filtered off and briefly concentrated in vacuo to remove diethyl ether. The residue was diluted with CDCl₃ and analyzed by ¹H NMR.

General procedure for In-situ IR measurements (React-IR)

In an argon-filled glovebox, a reaction tube for the React-IR instrument was charged with Pd/C 5 wt.% (26.6 mg, 0.0125 mmol Pd), K_3PO_4 (398 mg, 1.875 mmol), acetophenone (150.2 mg, 1.25 mmol), and benzyl alcohol (162.2 mg, 1.5 mmol). The tube was sealed with a PTFE-lined cap. Outside the glovebox, the tube was mounted on the React-IR-probe under nitrogen atmosphere and sealed with a PTFE-lined cap with a hole for the probe. Then, the reaction tube was placed in a pre-heated oil bath and the reaction stirred (700 rpm) at 80 °C. The experiment was monitored for 3 hours. Afterwards, 0.50 mL of reaction mixture was filtered through a 0.22 μ m syringe filter, diluted with CDCl₃, and analyzed by ¹H NMR.

The same ratio experiment: The reaction was set-up according to the general procedure, but with different reagent quantities: Pd/C 5 wt.% (26.6 mg, 0.0125 mmol Pd), K₃PO₄ (398 mg, 1.875 mmol), acetophenone (75.1 mg, 0.625 mmol), and benzyl alcohol (94.6 mg, 0.875 mmol).

Filtration experiment

A reaction was set up as described in the general procedure. After 1 h, the reaction vial was quickly brought into a glovebox and filtered through a 0.22 μ m syringe filter into a new 4 mL vial, which contained K₃PO₄ (40 mg corresponding; 1.5 equiv) and a stirbar. Then, the vial was sealed with a PTFE-lined screw cap. The vial was removed from the glove box and placed in a pre-heated aluminum block where the reaction was stirred (1000 rpm) for 5 hours 80 °C.

Recycling procedure

A reaction was set up as described in the general procedure. After the 6 hours of heating, the reaction was allowed to cool to room temperature, and the liquid phase removed by syringe. An aliquot (0.2 mL) of the liquid phase was filtered through a syringe filter (0.22 μ m), diluted with CDCl₃, and analyzed by ¹H NMR. The solid phase was extracted with toluene (5 x 1 mL), then dried under vacuum for 30 minutes to remove any remaining toluene. The dried catalyst material was stored in a glovebox freezer until the next day. Still in the glovebox, the next cycle was started by addition of K₃PO₄ (40 mg, 0.1875 mmol) and 0.50 mL of a new stock solution of acetophenone (0.25 M) and benzyl alcohol (0.30 M) in toluene. The vial was

sealed with a PTFE-lined screw cap. Outside the glovebox the vial was placed in a pre-heated aluminum block and stirred (1000 rpm) for 6 hours. The procedure was repeated for every recycle.

Leaching test

A reaction was set up as described in the general procedure. After 6 hours, the reaction was allowed to cool to room temperature, filtered, and the organic phase was removed under vacuum. The remaining residues were dissolved in 10 mL 65 wt.% HNO₃ and diluted 32.5 times to yield a 2 wt.% HNO₃ solution suitable for ICP analysis.

5 Catalysis with porous organic polymers

5.1 Heterogeneous single atomic catalyst

Classical heterogeneous catalysts consisting of metal nanoparticles on a support material have been addressed in the past projects. However, these systems can be considered flawed and inefficiently designed especially for highly selective reactions as the metal nanoparticles will have different facets and defects that may provide a variety of catalytic properties in terms of activity and selectivity. Moreover, only the surface of the nanoparticles are catalytically active. This results in an inefficient usage of the metal, which is especially undesired for scarce platinum-group metals as stated earlier. Fortunately, both flaws can be circumvented by decreasing the size of the "nanoparticle" down to a single atom as such a catalytic design will not have multiple facets and will utilize the metal most efficiently.

Heterogeneous single atomic metal catalysts (SAMCs) have been pursued by scientists as the optimal design of a catalyst and many examples of SAMCs have been reported using a variety of methods ranging from single atomic copper in zeolites to palladium atoms supported in a liquid of gallium.^{28,154–158} Still, SAMCs need to be stabilized to prevent deactivation. Therefore, many researchers have taken inspiration from the most well established use of SAMCs, molecular homogeneous catalysis. In homogeneous catalysis, organometallic complexes are a highly utilized type of catalyst constructed from a metal surrounded by coordinating ligands. These systems have been studied for more than a century and can now be modified and fine-tuned by the choice of ligand and metal to obtain specific catalytic properties for a variety of processes.^{33,159,160} As such, many heterogeneous SAMCs are developed to have ligand-metal interactions similar to homogeneous catalysis to utilize already existing knowledge with some of the more recent examples of SAMCs being MOFs, COFs, and POPs.^{66,161–163}

MOFs, COFs, and POPs are all made from building blocks giving them some sort of ordered and systematic structure as mentioned for MOFs previously.^{162–164} The building blocks can be designed to have specific properties such as metal coordination similar to ligands used in homogeneous catalysis. These ligands can then become an active catalyst in the presence of a metal to create molecular heterogeneous catalysts. The catalysts have the potential to mimic activity and selectivity from homogeneous catalysis while being heterogeneous in nature for easier recovery and reuse. The concept is illustrated in Figure 5.1 with different building blocks and two potential ordered structures built from some of these building blocks (A and **B**). The two structures are different as **A** is not constructed from any building blocks capable of coordinating to metals or additional metals in the case of MOFs. In contrast, structure B can bind to metal atoms and can thereby create heterogeneous SAMCs as visualized with structure C. This concept has been exploited to yield many promising catalytic systems, but the crystalline nature of MOFs and COFs are a double-edged sword for these systems. On one hand, the crystallinity provides a systematic order, easier theoretical simulation, and enables the use X-Rays for characterization. On the other hand, it complicates the synthesis, may limit the incorporation of some functional groups, and makes the system more fragile to structural changes.^{165,166} Whereas POPs are stable amorphous materials that are easier to synthesize and are able to accommodate a large variety of functional groups, albeit they are harder to characterize as X-Ray techniques cannot be used. Nevertheless, the amorphous structure of POPs and the advantages thereof were targeted as being very promising for creating heterogeneous SAMCs.



Figure 5.1. Schematic illustration of how MOFs, COFs, or POPs can be used to form heterogeneous SAMC.

5.2 Introduction to porous organic polymers

POPs are constructed from organic building blocks by irreversible covalent bonds in contrast to both MOFs and COFs. The building blocks can be connected by a variety of methods with their own benefits and disadvantages. As an example, POPs synthesized from palladium catalyzed Suzuki- and Sonogashira cross-coupling reactions have a systematic order to the material as a halogenated unit (X) reacts with a boronic acid/ester or alkyne unit (Y) yielding an XYXYXY repetition in the structure. Other polymerization techniques only rely on a single functionality providing a more random composition e.g. radical polymerization by vinyl groups or alkyne trimerization facilitated by a cobalt catalyst. Different polymerization techniques are presented in Scheme 5.1 with the resulting polymer repetition and requirements for the synthesis. Besides the composition, the polymerization technique will also affect the properties of the final POP and those important for catalysis, will be discussed next.



Scheme 5.1. Different polymerization techniques for synthesizing POPs with their respective resulting building block repetition and synthetic requirements.

The covalent irreversible bonds in POPs make them more physically and chemically stable compared to MOFs and COFs. However, some of the polymerization techniques will yield functional groups that can decrease the chemical stability of the POP. This is exemplified by polymerizing with the Sonogashira cross-coupling technique as it will yield alkyne groups that can be reactive towards certain transformations compared to polymerization by e.g. Suzuki cross-coupling.¹⁶⁷ Another important parameter in heterogeneous catalysis is to make the active sites more accessibility and is classically facilitated by making the material porous as discussed in Section 2.2. However, POPs can achieve accessibility to the active sites by either porosity or by swelling. Both properties have been exploited in this dissertation and will be addressed individually.

5.3 Porosity in porous organic polymers

Porosity arises from the use of rigid building blocks that after polymerization results in voids, channels, and pores in the material. The porosity can be controlled by the size and geometry of the building blocks as seen in the report by Li *et al.* where BINAP was polymerized with different building blocks, which altered the porosity of the material and manifested in different catalytic activities as well.¹⁶⁸ Other groups have reported a similar change in porosity when changing the ligand.^{169–171} In general, POPs are capable of obtaining very high surface areas and pore volumes, which have made them great materials for gas related applications such as catalytic reactions involving gases. An example is given in Figure 5.2 with a catechol-based POP that in the in presence of different first-row transition metal was able to semihydrogenate alkynes with molecular H_2 .¹⁷² This example also illustrate the potential issue of having alkyne functionality in the POP resulting from the use of Sonogashira couplings as the polymerization technique. Other reports

of POP-based catalysts have shown promising results in other reaction involving gases such as hydrogenations and hydroformylations.^{168,169,173–179}



Figure 5.2. Example of a catechol-based POP active in alkyne semihydrogenation. Adapted from Ngyuen et al.¹⁷²

5.4 Swelling properties for porous organic polymers

Swelling is a well-known property in polymer science, where solvent-polymer interactions can compete with polymer-polymer interactions and thereby let solvent mix into the polymer.¹⁸⁰ This increases the volume of the polymer as the space between polymer chains increases and the chains also become more flexible. The swelling of a coil-shaped polymer is visualized in Figure 5.3a where the polymer is initially swelled by an appropriate solvent, which increases its volume and flexibility, before being deswelled back to the original coil shape by another solvent. This is very similar to solvation of molecules, but the crosslinking effect of the polymers and their high molecular weight make it difficult for them to go into solution - instead they swell. Swelling properties are primarily a solvent phenomenon applied in liquid phase, however, swelling induced by gas can also occur.¹⁸¹ The swelling property is often described as a drawback giving a loss in material integrity as the polymer changes properties when swelled e.g. it can go from being a hard surface to a soft material undesired for some applications.¹⁸² At the same time, the polymer may not be able to regain its properties after being swelled if the packing of the polymer is important for its attributes like crystalline polymers.¹⁸⁰ However, swelling has shown to be an advantageous property in catalysis as it has been reported that swollen polymers can create a quasi-homogeneous environment. This has been showcased by Xiao et al. with their PS-based POP with 1,2-bis(diphenylphosphino)ethane (dppe) ligands as they compared the ³¹P cross-polarized magic angle spinning (CP/MAS) NMR spectra of a dried and swollen POP and noticed the appearance of a fairly sharp signal matching the chemical shift of the dppe in solution showcased in Figure 5.4.¹⁷⁵



Figure 5.3. Schematic illustration of swelling on a coil shaped polymer where the introduction of a swelling solvent makes the polymer expand in size. The polymer regains its original shape by the introduction of a non-swelling solvent.



Figure 5.4. ³¹P CP/MAS NMR adapted from the work of Xiao *et al.* on their dppe-POP.¹⁷⁵ The red curve (a) shows the spectrum of their dried POP and the black curve (b) of a swollen POP. The blue curve (c) is an example of a "non-porous" POP swollen by toluene.

POPs' ability to swell has been used as a potent property by Sawamura and coworkers for their POP-based catalysts. In their work, they synthesized a 1,2-bis(diphenylphosphino)benzene (dppBz) containing POP that showed activity in various types of reactions ranging from coupling reactions, hydroboration, hydrogenation, and dehydrogenation reactions with different metals as illustrated in Scheme 5.2.^{183–186} They created their POP by polymerizing styrene, divinylbenzene (DVB), and the vinylated dppBz together using Azobisisobutyronitrile (AIBN) as radical initiator by an emulsion methodology. This yielded small polymer beads capable of swelling in solvents like THF, dioxane, benzene, and toluene, whereas solvents like water, methanol, and hexane did not make the POP swell. Furthermore, they demonstrated that their POP could prevent some deactivation mechanisms often observed in homogeneous catalysis such as the formation of inactive dimers due to the anchoring of the dppBz ligand to the polymer backbone. Thus, the formation of POP-based catalytic systems are not just capable of mimicking homogeneous catalysis, but can potentially be superior.

Work by Sawamura et al.



Scheme 5.2. Work by Sawamura and coworkers with a DPPBz-^tBuPS-POP.^{183–186}

5.5 Outline of the projects based on porous organic polymers as catalyst.

POPs have emerged as an attractive platform to create heterogenized ligands capable of mimicking the activity and selectivity from homogeneous catalysis. In Chapter 6, the synthesis of PP-based POPs with either bpy or phenanthroline (Phen) in the backbone was carried out. The POPs were mixed with IrCl₃ to create a catalytic system *in-situ* that was assessed in the hydrogenation of CO₂ to FA. The reversible reaction, dehydrogenation of FA, was tested as well to evaluate if the catalytic system could use FA to both store and release hydrogen. The project was done in collaboration with the group of Ryan Wang from UCL, my fellow PhD colleague, David B. Christensen, and now PhD student Rasmus L. Mortensen. A manuscript for a publication has been submitted.¹⁸⁷

The recent development of POPs as heterogeneous ligands for catalysis has shown great potential. Yet, only few reports of asymmetric catalysis have been done and none on the challenging $C(sp^3)$ -H functionalization. In Chapter 7, the potential of POPs was examined by synthesizing a chiral POP with swelling properties, which was tested in the asymmetric β -arylation of 3-arylpropanamides. The work included a scope of different 3-arylpropanamides and aryl halides and characterization of the POP before and after catalytic reaction to showcase potential material changes. A manuscript of the work has been submitted.¹⁸⁸

The borylation of arenes is a widely used transformation to access key building blocks in organic synthesis. However, limited POP-based systems have shown to be active in this reaction. Therefore, two PS-based POPs were synthesized with bpy incorporated into the backbone and presented in Chapter 8. The POPs catalytic performance were assessed in the borylation of arenes by forming an Ir/POP catalytic system *insitu*. The project attempted to elucidate the reaction pathway with different experiments. A manuscript is in progress.¹⁸⁹

6 Formation of formic acid by a polyphenylene-based catalyst



6.1 Formic acid as a hydrogen source

Man-made climate changes are one of the major concerns of the 21st century. The emission of greenhouse gases such as CO₂ has negatively contributed to the climate causing an undesired increase in the average global temperature. Efforts to decrease this development have been made by forming international aims through the United Nations e.g. Paris Agreement from 2016.¹⁹⁰ To help reach the goals, new and sustainable technologies are necessary to adapt our modern society to a more renewable one and decrease man-made climate changes.

Hydrogen (H₂) has the potential to become a renewable and sustainable energy source that can diminish the use of fossil fuels and help to reach our climate goals. H₂ has a high gravimetric energy density, which far exceeds currently used energy sources such as natural gas, gasoline, and diesel visualized in Figure 6.1 highlighted with red circles. However, H₂ is an explosive gas that is difficult to store and transport in a safe and sustainable way due to requirement of pressurizing the gas into a liquid, which has limited its implementation.¹⁹¹ Scientists have tried to overcome this obstacle by finding new ways to store and release hydrogen, where liquid organic hydrogen carriers (LOHCs) have emerged as a very promising solution.^{192–194} A promising LOHC is formic acid (FA) with its high volumetric capacity of H₂ (52g/L) that selectively can be released by dehydrogenation under mild conditions.^{195–198} At the same time, FA can be formed from hydrogenating CO₂ and thereby utilizing the greenhouse gas as a valuable chemical providing a neutral carbon balance in contrast to many other fuels used today.^{199–202} An illustration of how H₂ can be stored and transported using FA as a LOHC is presented in Scheme 6.1.



Figure 6.1. Graph showing the gravimetric energy as a function of volumetric energy.²⁰³



Scheme 6.1. Illustration of a cycle for storing and transporting H₂ using FA.

6.2 Formation of formic acid by CO₂ hydrogenation

Unfortunately, hydrogenation of CO₂ to FA is a challenging reaction that is thermodynamically unfavorable due to the entropy change of going from two molecules to one as seen in Figure 6.2.^{199,204} The unfavorable entropy of the process can be circumvented by doing the reaction in aqueous solution resulting in favorable thermodynamics ($\Delta G^{\circ} < 0$). However, the process is still sluggish and most reported examples utilize the presence of bases to trap the FA as formate in order to drive the reaction. Therefore, most reported research is carried out under aqueous alkaline conditions.

$CO_2(g) + H_2(g)$		HCOOH (I)	∆G° _(298K) = 32.9 kJ/mol
CO ₂ (aq) + H ₂ (aq)	catalyst	HCOOH (aq)	∆G° _(298K) = -4.0 kJ/mol
CO ₂ (aq) + H ₂ (aq)	catalyst	HCOOH (aq)	base HCOO ⁻ (aq)

Figure 6.2. Illustration of the thermodynamics of the hydrogenation of CO₂ under different conditions.¹⁹⁹

The hydrogenation of CO₂ to formate have received tremendous attention over the past decade where predominately homogeneous catalysts utilizing Ir, Rh, or Ru are among the most successful ones.^{205–207} These catalysts can achieve impressive conversion, but they often lose activity over time and cannot be recycled. Consequently, classical heterogeneous catalysts using nanoparticles as the active phase have been studied as alternatives due to their better stability, recovery, and recycling properties. Unfortunately, these catalyst have very poor activity compared to their homogeneous counterparts.¹⁹⁹ Lately, POPs have emerged in the field as a promising type of catalyst that can achieve both high activity with the possibility of recovery and reuse due to the heterogeneous polymer backbone.^{167,208–211} Two powerful demonstrations of POPs were reported by Yoon *et al.* with a Ir/Phen-based POP yielding turnover-numbers (TON) up to 14,400 and a POP with Ir/N-heterocyclic carbene complex that achieved a TON value of 24,300.^{167,211} A more comprehensive overview is given in Table 6.1 with reaction conditions and catalytic performance of different POP-based catalysts for hydrogenation of CO₂ to FA. The table highlights

the extensive use of Et₃N as base to trap the FA as the formate in an aqueous solution as mentioned previously.

Table 6.1. Reaction conditions and TON values of different POP-based catalytic systems for CO₂ hydrogenation to formate.

metal_POP

$H_2 CO_2 \xrightarrow{\text{time, temp., pressure,}} HCO_2^-$ base, solvent								
report	metal (loading μM)	time (h)	temp. (°C)	pressure (MPa)	base	solvent	TON ^a	TOF ^b
Yoon <i>et al.</i>	lr (50)	2	120	8	1 M Et ₃ N	H ₂ O	14,400	7,200 h ⁻¹
Yoon <i>et al.</i>	lr (12)	15	120	8	1 M Et ₃ N	H ₂ O	24300	1.620 h ⁻¹
Hicks <i>et al.</i>	lr (0.185)	1	120	4	1 M Et ₃ N	H ₂ O	310	310 h ⁻¹
Liu <i>et al.</i>	Ru (48)	24	40	12	Et ₃ N	Et ₃ N	2254	94 h ⁻¹
Huang <i>et al.</i>	lr (0.13)	24	120	6	1 M Et ₃ N	H ₂ O	6784	283 h ⁻¹

^a TON values taken from original papers or calculated based on the following equation: n(formate)/n(Ir).

^b TOF values calculated by TON/time.

Albeit, If FA has to be used as a renewable hydrogen carrier, it must be implemented in a system capable of both storing (hydrogenation of CO₂) and releasing H₂ (dehydrogenation of FA), which should ideally be done with the same catalyst. However, catalysts that are active in both reactions are rare with only a few reported examples.^{212,213} Yet, the reports from Yoon *et al.* mentioned earlier for the hydrogenation step combined with the work from Palkovits *et al.*²¹⁴ on the dehydrogenation step using bpy-based POP catalyst, showcase the potential of POPs as catalysts for both reactions. The two POP-based systems are presented in Scheme 6.2.



Scheme 6.2. Illustration of the POPs made from Yoon *et al.*¹⁶⁷ and Palkovits *et al.*²¹⁴ and their respective reported reaction.

6.3 Polyphenylene-based porous organic polymers

According to the promising results of POP-based catalytic systems, it was believed that a POP with high porosity containing nitrogen-based ligands in the presence of iridium would be active for both storing and releasing hydrogen using FA as a LOHC. A previous project attempted to use polymers with swelling properties for this transformation, but was unsuccessful.²¹⁵ The reaction conditions for CO₂ hydrogenation

can be fairly harsh with temperatures above 100 °C in aqueous alkaline conditions with high pressures as seen in Table 6.1. Thus, the targeted POP should have high thermal and chemical stability to increase the potential of successful recovery and recycle of the system. Moreover, it has been reported that the change of ligand and ligand concentration in the POP can effect both the porosity and catalytic performance as mentioned in Section 5.3. As such, the synthesis of the POP should be straightforward with the possibility to readily alter building block(s) for easier fine-tuning of the catalytic system. Based on these criteria, the formation of PP-based materials from Suzuki cross-coupling appeared to be a good choice as it is built from aromatic building blocks creating good potential for high stability.^{216,217} This approach made it easy to do compositional changes to the resulting POP as many building blocks were commercially available with either boronic acid or halide functionality. Furthermore, a PP-based catalyst was made by Schüth *et al.* in collaboration with the group of Søren Kegnæs with excellent results previously.²¹⁸ The development of similar PP materials have continued in the field with examples incorporated with different functional groups to stabilize and improve catalytic performance.^{219–223} Yet, the potential of PP have not been explored in the hydrogenation of CO₂ to FA.

The syntheses of the POPs were done in collaboration with the group of Dr. Ryan Wang from UCL in London. In the syntheses, 1,2,4,5-tetrabromobenzene, 1,4-phenylenediboronic acid, and a brominated Nbased ligand (bpy or Phen) were coupled through a palladium catalyzed Suzuki cross-coupling. The resulting POPs had Pd nanoparticles entangled into the structure due to the decomposition of the palladium catalyst. This was exploited previously as an excellent palladium catalyst, but undesired for this project.²¹⁸ Therefore, the POPs were exposed to a solution with H₂O₂ followed by a solution with Na₂EDTA·H₂O to first oxidize the Pd and thereafter wash it out as a soluble EDTA-complex. A schematic illustration of the syntheses is presented in Scheme 6.3. The polymerization methodology and the structure of the building blocks allowed for the easy change of POP composition by altering the ratio between the brominated building blocks (brominated ligand and 1,2,4,5-tetrabromobenzene). This property was used to synthesize 5 different POPs; one with Phen as ligand (Phen-PP-POP), one without any ligands (PP-POP), and three with bpy as the ligand but with different ligand concentration (bpy-PP-POP, 2xbpy-PP-POP, and 4xbpy-PP-POP). The numbers state the increase from the parent POP (bpy-PP-POP) with 2xbpy-PP-POP having twice as much bpy building block in the synthesis and four times as much in the case of 4xbpy-PP-POP. The amounts of building block added for each POP during the polymerization are shown in Table 6.2.



Scheme 6.3. Illustration of the syntheses of the POPs. Adapted from Kegnæs et al. 187

РОР	1,2,4,5- tetrabromobenzene	1,4-phenylene- diboronic acid	Ligand: 4,4'dibromo-2,2'bipyridine or 3,8-dibromo-1,10-phenanthroline
bpy-PP-POP	3.34 mmol	7.78 mmol	1.09 mmol
2xbpy-PP-POP	2.80 mmol	7.78 mmol	2.19 mmol
4xbpy-PP-POP	1.70 mmol	7.78 mmol	4.36 mmol
Phen-PP-POP	3.34 mmol	7.78 mmol	1.09 mmol
PP-POP	3.88 mmol	7.78 mmol	-

Table 6.2. Listed amounts of building blocks used for the different synthesized POPs. Adapted from Kegnæs et al.¹⁸⁷

The thermal stability of the synthesized POPs were examined by TGA where no loss of mass was observed for the material in air up to 400 °C as illustrated in Figure 6.3a. The Phen-PP-POP showed slightly higher stability by not losing any mass up to 500 °C. The high thermal stabilities matched well with the formation of the desired PP structures.^{218,224} The choice of rigid building blocks for the POPs should enable the formation of pores in the structure, which were examined by N₂-physisorption experiments with the corresponding isotherms shown in Figure 6.3b. In the figure, the PP-POP showed good porosity whereas all the POPs incorporated with N-containing ligands did not show any significant adsorption. However, it has been reported that the quadrupole moment of N₂ can interact with the adsorbent (the material adsorbing) in particular for materials containing nitrogen and hinder the adsorption of N_2 . At the same time, it has been demonstrated that some micropores may not be accessible with N_2 as adsorbate (specie being adsorbed) at -196 °C.²²⁵ Thus, complementary CO₂-adsorption experiments were carried out as the guadrupole moment of CO_2 does not have the same effect and the technique is commonly done at higher temperatures, which should make the micropores more accessible.²²⁶ The corresponding CO₂ isotherms are shown in Figure 6.3c, where adsorption could be observed for all the POPs with a clear trend that as the density of bpy-sites in the backbone increased the adsorption of CO₂ decreased. The isotherms also showed that the Phen-PP-POP did not adsorb CO₂ to the same extent as bpy-PP-POP in agreement with similar other reports of changing ligand as mentioned previously. Nevertheless, all materials showed some extent of adsorption, which may be an important property for a reaction involving CO₂ but it also highlighted the importance of choosing the right adsorbate when examining porosity. This was further

illustrated in Figure 6.3d with the corresponding surface areas between using the two different adsorbates.



Figure 6.3. a) TGA of the synthesized POPs. b) N₂-physisorption, c) CO₂-physisorption and d) corresponding surface areas from both techniques. Adapted from Kegnæs *et al.*¹⁸⁷

Electron microscopy was carried out on bpy-PS-POP to get a better structural understanding of the material. The resulting images showed no crystalline areas or presence of metal nanoparticles as seen in Figure 6.4a-b. Complementary analysis with XRD did not show any crystallinity in the diffractogram either as seen in Figure 6.4c. These observations matched with the formation of an amorphous PP material without any presence of metallic nanoparticles from the polymerization.



Figure 6.4. a) TEM image, b) SEM image, and c) XRD diffractogram of bpy-PP-POP. Adapted from Kegnæs et al.¹⁸⁷
The composition of the synthesized POPs were investigated by CHN-analysis with the corresponding results presented in Table 6.3. It was evident from these values, that the expected 1, 2, 4 ratio from the synthesis of the bpy-based POPs did not match the actual nitrogen content as a 1, 1.5, 2.5 ratio was measured instead. Nevertheless, the nitrogen content still increased from bpy-PP-POP up to 4xbpy-PP-POP as intended and would still demonstrate the effect of increasing the ligand concentration in the POP. As for the Phen-PP-POP, it had the lowest accumulated mass from C, H, and N of all the POPs, which indicated that the polymerization had not completed resulting in many unreacted bromo- and/or boronic acid groups.

POP	C (mass %)	H (mass %)	N (mass %)	Accumulated mass from C, H, and N (%)	N ratio
bpy-PP-POP	75.2%	4.3%	3.3%	82.8%	1.0
2xbpy-PP-POP	72.2%	4.1%	4.9%	81.2%	1.5
4xbpy-PP-POP	78.8%	4.3%	8.2%	91.3%	2.5
Phen-PP-POP	53.0%	3.2%	3.8%	60.0%	1.2
PP-POP	79.2%	4.4%	0.5%	84.1%	0.1

|--|

The nitrogen contents indicated the successful incorporation of either bpy or Phen ligands into the structures of the POPs, and XPS was carried out to examine it further. N1s scans of the bpy-PP-POP, 2x-bpy-PP-POP, and 4xbpy-PP-POP all showed a peak overlapping nicely with pyridinic nitrogen showcased in Figure 6.5a.¹¹⁶ The binding energy of Phen-PP-POP deviated more than expected even when having a Phen moiety rather than a bpy, whereas the PP-POP did not give any signal as expected for nitrogen. The C1s scans showed one signal for each POP with a binding energy in good agreement with C-C bonded carbons (Figure 6.5b).¹¹⁵ The presence of oxidized carbon species from the H₂O₂ treatment seemed unlikely as such species would be expected at values above 286 eV highlighting the chemical stability of the PP backbone. However, the 4xbpy-PP-POP was fronting a bit in both spectra, which may be due to a less homogeneous structure in the polymer.¹¹⁵ Unfortunately, the binding energies from Phen-PP-POP and PP-POP seemed to be shifted compared to the other POPs, which were believed to be caused by a drift from the instrument rather than structural differences as the samples were measured on another session. This would also explain the shift in binding energy for the Phen-PP-POP compared to the bpy-based POPs.



Figure 6.5. XPS spectra of the synthesized POPs with a) N1s scan and b) C1s scan. Adapted from Kegnæs et al.¹⁸⁷

6.4 Catalytic assessment for the hydrogenation of CO₂

The synthesized POPs were assessed in the hydrogenation of CO_2 to formate where the active catalyst was formed in-situ. The reactions were carried out by mixing the POP, iridium precursor, and a 1 M solution of Et₃N (aq) into a 70 mL stainless steel autoclave with a Teflon lining. The autoclave was flushed three times with nitrogen to remove air, before being filled with 28 bar of CO₂ and 28 bar of H₂ and heated to the specified temperature. The results of varying the POP and the iridium concentration are presented in Table 6.4 where the formation of formate was quantified by NMR using Et₃N as standard. First, the bpy-PP-POP, Phen-PP-POP, and PP-POP were assessed with a 1000 μ M concentration of iridium (entries 1-3). The two POPs containing ligands were both active in the process whereas the PP-POP did not show any activity verifying the importance of having ligands present during the reaction. The performance of the POPs was further examined by decreasing the iridium concentration to 100 μ M (entries 4-5), where the bpy-based POP had superior activity over Phen-PP-POP. The concentration of iridium could be further decreased down to 10 µM for bpy-PP-POP, which provided an impressive TON of 20041 (entry 6). The TON value is one of the highest for POP-based catalysts, albeit a more modest TOF value of 835 h^{-1} is obtained. The 2xbpy-PP-POP and 4xbpy-PP-POP were tested under the same conditions, but they both showed inferior activity (entries 7-8). Lastly, the amount of bpy-PP-POP added to the reaction was doubled, but did not improve the catalytic performance (entry 9). These results showed that the bpy-PP-POP provided the highest activity of all the synthesized POPs and was chosen for further studies.

Table 6.4. Results of the CO₂ hydrogenation with different POPs and varying the iridium concentration. Adapted from Kegnæs *et al.*¹⁸⁷

	$CO_2 + H_2$	IrCl ₃ •xH ₂ O, POP 56 bar (1:1 CO ₂ :H ₂)	HCO ²⁻	
002 • 112		1 M Et ₃ N (aq) (5mL), 24 h, 140 °C	11002	
Entry	POP	[IrCl ₃ •xH ₂ O](conc.)	Yield ^a	TON ^b
1	boy-PP-POP	1000 µM	32%	38
2	Phen-PP-POP	1000 μM	34%	36
3	PP-POP	1000 μM	>1%	-
4	bpy-PP-POP	100 μM	42%	4676
5	Phen-PP-POP	100 μM	12%	1336
6	bpy-PP-POP	10 μM	18%	20041
7	2xbpy-PP-POP	10 μM	5%	5567
8	4xbpy-PP-POP	10 μM	5%	5567
9	bpy-PP-POP ^c	10 μM	16%	17814

^aYield quantified by ¹H-NMR using D₂O as solvent and Et₃N as a standard. ^bTON calculated by the following equation: the n(formate)/n(Ir) where n(formate) is given by yield*n(Et₃N) and the total amount of iridium is estimated based on a iridium content of 52% for the IrCl₃• xH₂O salt. ^cTwice the normal amount of POP.

The reaction conditions were evaluated further for the *in-situ* made IrCl₃/bpy-PP-POP system by increasing the reaction time to 48 hours, but it did not increase the yield (Table 6.5, entry 1). Changing iridium source to either [IrCp*Cl]₂ or [Ir(cod)MeO]₂ did not improve the TON (entries 2-3). Lowering the reaction temperature to 120 °C decreased the activity tremendously providing only 2% yield (entry 4). A control experiment with commercially available iridium nanoparticles on carbon (Ir/C) was tested and showed very poor activity indicating that the observed activity did not arise from the formation of nanoparticles

(entry 5). An experiment was carried out where the solid bpy-PP-POP was replaced with the nonpolymerized ligand, 2,2'-bipyridine, creating a homogeneous catalytic setup (entry 6). Under these conditions, the amount of formate formed was neglectable with a yield <1% indicating that incorporation of bpy into a polymer backbone was essential to achieve catalytic activity. This was further illustrated by synthesizing K[IrbpyCl₄], which was used as a catalyst but also provided poor activity (entry 7). If 2,2'bipyridine was added to an experiment with bpy-PP-POP, the yield was suppressed significantly from 18% down to 6% showcasing that excess amount of homogeneous bpy inhibited the catalysis (entry 8). According to these observations, it was clear that the incorporation of bpy into a polymer backbone did more than providing a heterogeneous structure as the same activity cannot be created from homogeneous systems. It has been reported, that incorporating ligands into POPs can prevent the formation of inactive saturated or dimer complexes due to the rigid structure of the polymer backbone. A similar behavior could explain the observed low activity when using homogeneous setups (entries 6-7) or when both bpy-PP-POP and homogeneous bpy were added to the same reaction (entry 8). This hypothesis is illustrated in Scheme 6.4 by comparing the potential active specie arising from a homogeneous complex and from a POP-based catalyst.

Table 6.5. Optimization of reaction conditions and investigation of the catalytic active specie. K[IrbpyCl₄] was synthesized from reported literature.²²⁷ Adapted from Kegnæs *et al.*¹⁸⁷

	CO ₂ + H ₂	[Ir], ligand 56 bar (1:1 CO ₂ :H ₂) 1 M Et ₃ N (aq) (5mL), time, temp	HCO ₂ -			
Entry	Ligand	[Ir] (conc.)	time (h)	temp. (°C)	Yield ^a	TON ^b
1 2	bpy-PP-POP bpy-PP-POP	IrCl ₃ •xH ₂ O (10 μM) [IrCp*Cl] ₂ (10 μM)	48 24	140 140	15% 12%	16701 13360
3	bpy-PP-POP	[lr(cod)MeO] ₂ (10 μM)	24	140	10%	11134
4 5 ^c	bpy-PP-POP -	IrCl ₃ •xH ₂ O (10 μM) Ir/C (100 μM)	24 24	120 140	2% 3%	2227 3340
6	2,2'-bipyridine	IrCl ₃ •xH ₂ O (10 μM)	24	140	<1%	-
7 0 ^d		K[lrbpyCl ₄] (10 μM)	24	140	2%	2227
84	bpy-PP-POP + 2,2'-bipyridine	IrCl ₃ •xH ₂ O (10 μM)	24	140	6%	6080

^aYield quantified by ¹H-NMR using D₂O as solvent and Et₃N as a standard. ^bTON calculated by the following equation: the n(formate)/n(Ir) where n(formate) is given by yield*n(Et₃N) and the total amount of iridium is estimated based on a iridium content of 52% for the IrCl₃• xH₂O salt. ^cCommercially available Ir/C. ^dThe amount of added 2,2'-bipyridine is 1 equivalent of the added iridium.



Scheme 6.4. Potential deactivation pathways for homogeneous systems which can be prevented by the rigid structure of the POP. Adapted from Kegnæs *et al.*¹⁸⁷

The inherent heterogeneous nature of the POP made it possible to recover the catalyst by centrifugation. The recovered solid was used as a catalyst in an experiment under the same conditions as used in Table 6.4 entry 6 (10 μ M IrCl₃, 140 °C, 24 h). Here, the catalyst still showed to be active in the formation of formate, but the yield was lower than that of a fresh catalyst with 12% yield compared to 18% before (Table 6.6, entry 1). However, the activity could be reestablished if fresh amount of IrCl₃·xH₂O was added to the recovered catalyst (entry 2), which highlighted the robustness of the POP itself. Control experiments were carried out to determine if the observed activity came from contaminants or could be done without a catalyst. First, an experiment without iridium and POP was completely inactive showing that the activity did not arise from a background reaction (entry 3). Conducting the reaction without the presence of POP did not show any activity at all (entry 4), whereas a reaction without iridium surprisingly showed formation of formate arising from the POP itself (entry 5). This activity could potentially originate from remaining palladium from the polymerization despite it was not visual in the XRD diffractogram or TEM images.

	CO. + H.	[Ir], liga 56 bar	nd (1:1 CO₂:H₂)			
		→ HCO ₂ 1 M Et ₃ N (aq) (5mL), 24 h, 140 °C				
Entry	y Ligand		[lr] (conc.)	Yield ^a	TON ^b	
1	bpy-PP-POP (recover	ed)	-	12%	13361	
2	bpy-PP-POP (recover	ed)	IrCl ₃ •xH ₂ O (10 μM)	17%	18928	
3	-		-	<1%	-	
4	-		IrCl ₃ •xH ₂ O (10 μM)	<1%	-	
5	bpy-PP-POP		-	6%	6680	

Table 6.6. Results for recycling the IrCl₃/bpy-PP-POP system and control experiments. Adapted from Kegnæs et al.¹⁸⁷

^aYield quantified by ¹H-NMR using D₂O as solvent and Et₃N as a standard. ^bTON calculated by the following equation: the n(formate)/n(Ir) where n(formate) is given by yield*n(Et₃N) and the total amount of iridium is estimated based on a iridium content of 52% for the IrCl₃• xH₂O salt.

A possible deactivation mechanism for the loss in activity during reuse was assessed by analyzing a filtered reaction mixture for leached metal by XRF. The analysis revealed an average iridium intensity of 0.232 counts/s that correlated to an iridium concentration of 1 μ M according to a calibration curve made from IrCl₃·xH₂O. The result indicated a loss of approximately 10% of the initial amount of iridium and was likely a cause of deactivation. However, to ensure that the observed activity did not arise from a homogeneous specie, a filtration experiment was done where a reaction was stopped after 2 hours. Afterwards, the mixture was filtered, and a small portion was analyzed by NMR whereas the majority of the liquid was put into another stainless steel autoclave with Teflon lining again and reheated to 140 °C for 22 h in a H₂/CO₂ (1:1) atmosphere at 56 bar pressure. Next, the reaction was stopped, analyzed by NMR, and compared with the sample after 2 hours. The results are presented in Scheme 6.5 where it clearly demonstrated that the activity stopped when the solid was removed from the mixture. This behavior correlated nicely with other experiments where homogeneous complexes (Table 6.5, entries 6-7) or just the iridium precursor itself were used as a catalyst (Table 6.6, entry 4) as these experiments did not provide any product yield.

	1) IrCl ₃ •xH ₂ O (10 μM), 111 mg bpy-PP-POP, 1 M Et ₃ N (aq) (5mL), 2 h, 140 °C		
CO ₂ + H ₂	2) Filtration	HCC	0 ₂
	3) Applying H_2 and CO_2	2 h:	1.4% yield
	pressure, 140 °C, 22 h	24 h:	2.3% yield

Scheme 6.5. Illustration of the different steps and results for the filtration experiment conducted to assess the nature of the observed catalytic activity. Adapted from Kegnæs *et al.*¹⁸⁷

To understand the deactivation more thoroughly, the recovered $IrCl_3/bpy-PP-POP$ material was investigated in a STEM microscope and the resulting images are presented in Figure 6.6. The images showed the presence of iridium nanoparticles with a particle size between 4-10 nm in diameter. Nanoparticles of iridium had shown to be inactive in the formation of formate from CO_2 and H_2 according to the results from Ir/C (Table 6.5, entry 5) and was likely another deactivation mechanism besides metal leaching.



Figure 6.6. STEM images of the recovered IrCl₃ /bpy-PP-POP catalyst. Adapted from Kegnæs et al.¹⁸⁷

6.5 Testing formic acid in the selective dehydrogenation

The $IrCl_3/bpy$ -PP-POP system was tested in the dehydrogenation of FA to finish the cycle required for enabling FA as a LOHC and utilize H_2 as a renewable energy source. This time, the catalytic $IrCl_3/bpy$ -PP-POP system was made prior to the catalytic test by soaking the bpy-PP-POP in a solution of $IrCl_3 \cdot xH_2O$ in

 $CH_3CN:H_2O$ (3:1) overnight, collect the resulting POP on a filter, wash it extensively, and dry it before being tested in a flow-bed reactor. In the test setup, a saturated gas flow of FA was passed over the reactor in air and the level of hydrogen was measured as a function of temperature. The result for the IrCl₃/bpy-PP-POP is shown in Figure 6.7, where the dehydrogenation occurred at temperatures above 160 °C showcasing that this system was active in both the formation and dehydrogenation of FA, albeit, the conditions were not as mild as state-of-the-art reports.^{228–230}



Figure 6.7. The measured amount of H₂ as a function of temperature for the IrCl₃/bpy-PP-POP system. Adapted from Kegnæs *et al.*¹⁸⁷

6.6 Summary

Different novel PP materials were synthesized bearing Phen or bpy ligands. The POPs showed high thermal stability up to 400 °C in air. The incorporation of N-based ligands in the polymer backbone made N₂adsorption unreliable as these POPs did not show any inherent porosity. However, changing the adsorbant to CO₂ clearly showed their porous nature with bpy-PP-POP being the one capable of adsorbing the most CO₂ of the POPs with N-based ligands in their backbone. CHN-analyses demonstrated that amount of incorporated nitrogen followed the trend of bpy-PP-POP < 2xbpy-PP-POP < 4xbpy-PP-POP, however the ratio was 1:1.5:2.5 rather than 1:2:4. XPS confirmed the successful incorporation of the ligands and with no indication of undesired reactions from the *post*-polymerization treatments. The POPs were assessed in the challenging hydrogenation of CO₂ to formate where the active catalyst was formed *in-situ* by mixing with IrCl₃. The bpy-PP-POP was the most promising material capable of providing a TON of >20,000 with 10 µM Ir, 140 °C, 56 bar CO₂/H₂ (1:1) after 24 h which is one of the highest TON values for POP-based systems. The active specie was shown to be heterogeneous in nature and the incorporation of the ligand into a polymer backbone seemed to prevent the formation of inactive species. The catalyst could be recovered and maintain most of its activity during recycling. The same system was also shown to be active in the dehydrogenation of FA enabling the catalyst to be used in both transformation required to implement FA as a LOHC and utilization of hydrogen as a renewable energy source.

6.7 Experimental

Chemicals

All chemicals were reagent grade and used as received without further purification. 1,4phenylenediboronic acid, 1,2,4,5-tetrabromobenzene, Pd(PPh₃)₄, Na₂EDTA·2H₂O were purchased from Sigma Aldrich. Et₃N was obtained from Merck. 5,5'-dibromo-2,2'-bipyridine and 3,8-dibromo-1,10phenanthroline was bought from Fluorochem. Commercially available Ir/C was bought from VWR (Product number: 38330.06 - Iridium on activated carbon 1% wetted with ca. 50% water, powder, reduced). Formic acid was purchased from Fischer Chemicals and the $IrCl_3 \cdot xH_2O$ is from Pressure Chemicals.

Equipment

TEM images were obtained using a Technai T20 G2 microscope from TEI. STEM images are from a FEI Titan 80-300ST with an accelerating voltage of 300 kV. SEM images were taken on a Quanta 200 ESEM FEG microscope from FEI. Samples were deposited on 300 mesh Cu grids with no prior treatment. N₂ and CO₂-physisorption were conducted on a Micrometrics 3Flex instrument at 77 K or 273 K, respectively. Samples for N₂ and CO₂-physisorption were degassed 24 hours before the analysis on a Micrometrics VacPrep 061 Sample Degas System at room temperature. TGA was performed on a Mettler Toledo TGa/DSC 1 STARe System. X-ray Powder diffraction (XRPD) were measured with a Cu-K α radiation source on a HUBER G760 Guinier camera. XPS was done with a spot size of 400 μ m with an Al alpha X-ray source with 10 scans per element. XRF analysis was conducted on a PANalytical Epsilon3 system. ¹H NMR was measured on a Bruker Ascend 400 (400 Hz).

Synthesis of polyphenylene POPs adapted from Schüth et al.²¹⁸

In a standard procedure using bpy-PP-POP as an example, 4,4'-dibromo-2,2'-bipyridine (0.34 g, 1.09 mmol), 1,2,4,5-tetrabromobenzene (1.32 g, 3.34 mmol), 1,4-phenylenediboronic acid (1.29 g, 7.78 mmol), Pd(PPh₃)₄ (0.30 g, 0.24 mmol) were weighted off in a round-bottom flask and a stir bar was added. The setup was connected to a reflux condenser and made inert by 3 vacuum/N₂ cycles with Schlenk techniques before adding degassed DMF (120 mL) and an aqueous solution of degassed 2M K₂CO₃ (15 mL). The reaction is heated to 150 °C for 24 h while refluxing. The mixture is cooled down and transferred to a glass beaker with 600 mL water. The resulting solids are collected by a glass funnel and washed with 3x H₂O and 3x MeOH before being dried in a vacuum oven.

To remove Pd^0 the solid is treated with H_2O_2 followed by EDTA. First, the collected solids are placed in a round-bottom flask connected to a reflux condenser and a stir bar. A solution of EtOH (100 mL), 32 wt.% HCl (50 mL), H_2O (50 mL), and 30 wt.% H_2O_2 (10 mL) is added and the slurry is stirred at room temperature overnight. The next day, the mixture is heated to 60 °C for 4 h before the solids are collected on a glass funnel, washed with 3x H_2O and 3x MeOH, and dried in a vacuum oven.

Next, the resulting solid is transferred to a round-bottom flask connected to a condenser and with a stir bar. A solution of EtOH (150 mL), H_2O (75 mL), 30 wt.% $NH_3(5 mL)$ and $Na_2EDTA\cdot 2H_2O$ (7.50 g, 0.02 mol) is added and the resulting slurry is stirred at 70 °C for 24 h. The solids are collected on a glass funnel, washed with 3x H_2O and 3x MeOH, and dried in a vacuum oven yielding a yellow fine powder (1.3 g).

Standard catalytic reaction setup

A standard reaction was started by adding POP (44.4-222 mg), stock solution of $IrCl_3 \cdot xH_2O$ (100-1000 µL, 0.0005 M), and an aqueous solution of Et₃N (4-4.9 mL, 1 M) to a 70 mL stainless steel autoclave with a Teflon lining. The autoclave was flushed three times with nitrogen to remove air, before being filled with 28 bar of CO₂ and 28 bar of H₂. The autoclave was mounted on a magnetic stirrer with a heating mantel and the reaction was heated to 140 °C over 1 hour and left to run for an additional 24 hours. The autoclave was cooled down in ice and 0.5 mL of the reaction mixture was filtered through a 0.22 µm syringe filter, combined with of D₂O (0.2 mL) and analyzed by NMR. The yield was calculated based on the ratio between Et₃N and formate.

Filtration experiment

A standard reaction was started by adding bpy-PP-POP (111 mg), stock solution of $IrCl_3 \cdot xH_2O$ (100 µL, 0.0005 M), and an aqueous solution of Et₃N (4.9 mL, 1 M) to a 70 mL stainless steel autoclave with a Teflon lining. The autoclave was flushed three times with nitrogen to remove air, before being filled with 28 bar of CO₂ and 28 bar of H₂. The autoclave was mounted on a magnetic stirrer with a heating mantel and the reaction was heated to 140 °C over 1 hour and left to run for an additional 2 hours. The autoclave was cooled down by ice and the reaction mixture was filtered through a 0.22 µm syringe filter to remove the POP from the mixture. The resulting solution was added to the 70 mL stainless steel autoclave with a new Teflon lining, which was flushed three times with nitrogen to remove air, before being filled with 28 bar of CO₂ and 28 bar of H₂ again. The autoclave was mounted on a magnetic stirrer with a heating mantel and the reaction was heated to 140 °C over 1 hour and left for an additional 2.2 µm syringe filter to remove the POP from the mixture. The resulting solution was added to the 70 mL stainless steel autoclave with a new Teflon lining, which was flushed three times with nitrogen to remove air, before being filled with 28 bar of CO₂ and 28 bar of H₂ again. The autoclave was mounted on a magnetic stirrer with a heating mantel and the reaction was heated to 140 °C over 1 hour and left for an additional 22 hours. After the specified time, the autoclave was cooled down by ice and 0.5 mL of the resulting mixture was filtered through a 0.22 µm syringe filter, combined with D₂O (0.2 mL) and analyzed by NMR. The yield was calculated based on the ratio between Et₃N and formate.

Laboratory procedure for leaching test

A standard reaction was started by adding bpy-PP-POP (111 mg), stock solution of $IrCl_3 xH_2O$ (100 µL, 0.0005 M), and an aqueous solution of Et_3N (4.9 mL, 1 M) to a 70 mL stainless steel autoclave with a Teflon lining. The autoclave was added to a 70 mL stainless steel autoclave with a Teflon lining, which was flushed three times with nitrogen to remove air, before being filled with 28 bar of CO_2 and 28 bar of H_2 . The autoclave was mounted on a magnetic stirrer with a heating mantel and the reaction was heated to 140 °C over 1 hour and left to run for an additional 24 hours. The autoclave was cooled down in ice and 0.5 mL of the resulting mixture was filtered through a 0.22 µm syringe filter, and the resulting liquid was analyzed by XRF and quantified against a calibration curve made of known Ir concentrations.

Impregnation of bpy-PP-POP with IrCl₃·xH₂O to form Ir-bpy-PP-POP

 $IrCl_3 \cdot xH_2O$ (7.88 mg, 0.0225 mmol) was weighed into a 4 mL vial with a stir bar and a 3:1 CH₃CN:H₂O mixture (2 mL) was added to yield an orange/brown solution. bpy-PP-POP (50 mg, 0.0075 mmol bpy) was added and the mixture was stirred overnight at room temperature. The solid was collected by a glass funnel and washed with H₂O, CH₃CN, and Et₂O before being dried in a vacuum oven.

Selective dehydrogenation of formic acid

Ir-bpy-PP-POP (30 mg) was mixed with fractionated quartz (270 mg, 355-700 nm) to prevent plugging up the reactor. The powder was transferred to a quartz reactor tube heated by an aluminum block. A flow of N₂ (50 ml/min) was bubbled through a flask of formic acid (100 mL, 98-100 wt.%). The formic acid was heated to 40 °C to saturate the flow before the gas was passed over two condensers kept at 20 °C to remove excess formic acid. This guarantee the same degree of saturation of the gas flow. The saturated gas was passed through the reactor containing the catalyst and quartz, followed by a cold trap to capture unreacted formic acid before reaching the detector. The detector was a Rosemount Binos 100 IR gas analyzer, which measures the percentage of CO and CO₂ in the product flow. Hydrogen yield was based on the amount of CO₂ measured as they were produced in equal amounts from the reaction. The detector was calibrated using pure nitrogen and a gas mixture of 1% CO, 20% O₂, and 79% nitrogen. The CO₂ signal was calibrated by adding 200 mg of a gold on silicalite-1 catalyst in the reactor and passing the 1% CO mixture through. The Au catalyst easily converted the 1% CO to 1% CO₂ for the calibration. The flow was checked before and after each experiment using a flowmeter to ensure no leaks or blockage were present.

7 Asymmetric C(sp²)-H functionalization by chiral porous organic polymer



7.1 Introduction to chiral porous organic polymers

The use of heterogeneous catalysts for production of fine-chemicals and especially optical pure compounds remains a challenge due to heterogeneous catalysts' limited selectivity. As such, the usage of homogeneous catalysts are still favored despite tremendous efforts in the field attempting to develop highly selective heterogeneous catalysts.^{16,20} However, as POPs can recreate the catalytic performance of homogeneous catalysis while being heterogeneous, they are ideal candidates for forming new and highly selective heterogeneous catalysts. Yet, their potential in asymmetric catalysis has only been studied in a limited extent and will be briefly covered next.

The formation of POPs that can induce enantioselectivity have been accomplished by different methodologies. Gagné *et al.* have introduced chirality by polymerizing their Pt-dppe-POP with an enantiopure BINOL moiety bound to their platinum center as visualized in Scheme 7.1.²³¹ After the polymerization, the BINOL is removed but its presence during the polymerization will leave a binding pocket with enantiomeric recognition. Another approach is to introduce enantiopure ligands into the polymer backbone. This method is by far the most common as POPs with well-known chiral ligands such as salen,¹⁶⁹ BINAP,²³² and phosphoramidites²³³ have all been synthesized. These POPs can in the presence of a metal induce enantioselectivity and thereby lead to enantioenriched products. However, these POP-based systems have predominately been applied for alkylations, hydroformylations, and hydrogenations while other types of catalysis are still unexplored.



Scheme 7.1. Schematic illustration of the methodology from Gagné *et al.* and a more common approach exemplified with BINAP or salen-based ligand on how to introduce chirality to POPs.^{163,169,232} Adapted from Kegnæs *et al.*¹⁶³

If enantioselective POP catalysts should be used for other types of transformation, it was believed that POPs with swelling properties had high potential for doing asymmetric catalysis with the formation of a quasi-homogeneous environment as discussed in Section 5.4. The resulting POP can potentially create enantioenriched products while being easy to recover and reuse. To test this concept, the asymmetric $C(sp^3)$ -H functionalization was targeted as an interesting type of reaction possessing both high complexity and difficulty while being industrial relevant.

7.2 Introduction to C(sp³)-H functionalization

 $C(sp^3)$ –H functionalization is a highly sought out type of reaction in both academia and industry as it can give access to highly valuable chemicals more directly without the need of e.g. pre-halogenation, silylation, or borylation.^{234–237} This provides more economical and sustainable processes in agreement with the principles of green chemistry. However, $C(sp^3)$ –H functionalization is a challenging reaction with high complexity due to the inert nature of the $C(sp^3)$ -H bond and the high abundance of these bonds in many substrates and emphasizes the requirement of high regioselectivity.^{238,239}

Over the past decades, organometallic palladium-catalysts have shown promising performance in C(sp³)-H functionalization using an auxiliary directed strategy with pyridine and quinoline as directing groups.^{240–}²⁴⁵ The use of directing groups induces molecular interactions that can stabilize one transition state over competing ones and thereby provide both high regioselectivity and activity to the reaction. Fortunately, the auxiliary strategy does not limit the potential of doing asymmetric catalysis if enantiopure ligands are chelating to the active palladium center.^{246–248} The auxiliary strategy have been utilized to synthesize different natural products up to gram scale showcasing the versatility and industrial attraction for this kind of transformation.^{246,249} The synthetic strategy by Chen *et al.* and Reisman *et al.* in the formation of Celogentin C and (+)-rumphellaone, respectively, are given in Scheme 7.2 where they both use aminoquinoline as directing groups.



Scheme 7.2. Synthetic overview of the synthesis of Celogentin C and (+)-rumphellaone A applying a palladium catalyzed C(sp³)-H strategy.^{246,249}

The β -carbon functionalization of propanamides have been targeted as an attractive model system by many researches with possible applications exemplified by the work of Chen *et al.* in their synthesis of Celogentin C. Daugulis *et al.* pioneered the process using an auxiliary technique to provide excellent activity and selectivity.^{249–252} However, the asymmetric β -carbon functionalization of 3-arylpropanamides remains a challenge with the most successful systems utilizing Pd in the presence of chiral BINOL-based phosphoric acid or phosphoramidites.^{247,248} The two best performing ligands from the reports are presented in Scheme 7.3 with their highest respective obtained ee. Yet, the success of these reports have not been transferred to heterogeneous systems where recovery and recyclability of the catalytic species are easier especially when applying expensive enantiopure ligands such as phosphoramidites. The only example of C(sp³)-functionalization using a POP catalyst was reported by Jones *et al.*, albeit their POP was not chiral and consequently did not lead to enantioenriched products.²⁵³ As such, the incorporation of chiral phosphoramidite ligands into PS-POPs have the potential to give materials with catalytic properties similar to the homogeneous catalysts but with better potential for recovery and reuse.



Scheme 7.3. Illustration of the asymmetric β -carbon arylation of 3-propanamides using either phosphoric acids or phosphoramidites as ligands.^{247,248}

7.3 Synthesis and polymerization of chiral porous organic polymers

In order to create PS-POPs with phosphoramidite ligands, it was necessary to introduce vinyl functionality to the ligands. Therefore, two different vinylated phosphoramidites were synthesized from (*R*)-BINOL by the synthetic procedure visualized in Scheme 7.4. In the first step of the synthesis, (*R*)-BINOL was brominated selectively in the 4,4' position with high yield forming compound **1**. Afterwards, vinylation of **1** proceeded smoothly through a palladium catalyzed Suzuki cross coupling reaction using potassium vinyltrifluoroborate to form **2**. Phosphoramidite **3** was then synthesized by treating **2** with phosphor trichloride in the presence of *N*-methyl-2-pyrrolidone (NMP) followed by addition of morpholine. Ligand **4** was synthesized from substrate **2** by the addition of P(NMe₂)₃.



Scheme 7.4. Illustration of the synthesis pathway for the phosphoramidite ligands with vinyl functionality. Adapted from Kegnæs *et al.*¹⁸⁸

After the synthesis of the vinylated phosphoramidites, the free radical polymerization of the building blocks could occur to form the desired POPs containing phosphoramidite ligands. Unfortunately, it was believed that the P-N bond in the phosphoramidites would easily hydrolyze when exposed to an aqueous environment at elevated temperature making polymerization by the emulsions methodology developed by Sawamura *et al.* unwise for this project. Fortunately, reports of free radical polymerization techniques not evolving emulsions are also present in literature where the polymerization takes place under non-aqueous conditions.^{232,233} Inspired by these reports, the POP were polymerized by mixing phosphoramidite **3** or **4** with 50 equivalents of styrene and 1.06 equivalents of divinylbenzene in THF before adding the radical initiator, AIBN. The mixture was stirred vigorously overnight under refluxing conditions to yield a fine white powder. The reaction scheme for the polymerization is shown in Scheme 7.5.



Scheme 7.5. Synthetic procedure for forming PS-based POPs with phosphoramidite ligands. Adapted from Kegnæs *et al.*¹⁸⁸

The two different POPs were tested in the β -carbon arylation of 3-phenylpropanamide where the active catalyst was made *in-situ* by mixing 7.5 mol% Pd₂dba₃ with 20 mol% POP followed by 0.1 mmol 3-phenylpropanamide, 4 equivalents of iodoanisole, 2 equivalents of Cs₂CO₃, and 0.6 mL *m*-xylene. The resulting mixture was stirred at 100 °C for 72 hours with the corresponding results of the two POPs presented in Table 7.1. The morpholine derived phosphoramidite showed superior catalytic performance with 70% yield and 86% ee and was studied further as the most promising chiral POP catalyst. The absolute configuration of the product was determined based on the report from Duan *et al.*²⁴⁸

Table 7.1. Catalytic performance of the two POPs in the C(sp³)–H functionalization. Adapted from Kegnæs et al.¹⁸⁸



^aConversion and yield determined by ¹H-NMR using an internal standard. ^bEnantiomeric excess determined by chiral HPLC.

Next, the effect of ligand density in the POP was investigated by synthesizing a series of POPs with different phosphoramidite to styrene ratio (1:50, 1:25, 1:15, 1:5). The catalytic performance of these POPs are presented in Table 7.2. The results clearly indicated that the catalytic activity decreased when the concentration of ligand sites in the POP increased with the 1:50 being the most active. Similar tendency was observed in the previous project (Section 6) and have also been reported by Jones *et al.* in their catalytic POP system with a very similar reaction.²⁵³ Furthermore, the change in ratio between ligand and styrene resulted in visual differences in the POPs as well, where the highly concentrated polymer appeared more colored and agglomerated likely due to the crosslinking effect of the ligand (Figure 7.1). The POP with the 1:50 ratio between morpholine derived phosphoramidite and styrene will be studied further and abbreviated (*R*)-Pamidite-POP from now on.

Table 7.2. The influence on the catalytic performance of the POP by altering the ratio between ligand and styrene. Adapted from Kegnæs *et al.*¹⁸⁸

O Ph 0.1 mmol	IHAQ +	OMe 4 equiv	Pd ₂ (dba) ₃ 15 mol% (<i>R</i>)-POP 2 equiv C <i>m</i> -xylene 100 °C, 7	Pd (20 mol%) s ₂ CO _{3,} (0.167M) 2 h P	OMe o h	NHAQ
Entry	Ligan	d:Styrer	ne ratio	Conv. ^a	Yield ^a	
1	1:50			70%	70%	
2	1:25			30%	27%	
3	1:15			29%	23%	
4	1:5			20%	16%	

^aConversion and yield determined by ¹H-NMR using an internal standard.



Figure 7.1. Picture of the synthesized POPs with various ligand to styrene ratio. From left to right the ratio increases starting from 1:5 up to 1:50. Adapted from Kegnæs *et al.*¹⁸⁸

7.4 Characterization of (R)-Pamidite-POP

The synthesized (*R*)-Pamidite-POP was characterized to investigate its properties and confirm the successful formation of a swellable POP with phosphoramidite ligands incorporated into its structure. First, the thermal stability was examined by TGA where (*R*)-Pamidite-POP showed no loss of mass when heated in air up to over 300°C (Figure 7.2a). This is both in good agreement with previous reported PS-based POPs and hopefully indicate that the POP does not decompose during the catalytic conditions. ^{183,232} When the POP was analyzed by N₂-physisorption, it did not show any inherent porosity with a pore volume of 0.049 cm³/g and surface area of 24 m²/g and highlight the importance of swelling properties as the driving force to access the active sites compared to classical heterogeneous catalysis (Figure 7.2b).³⁴ SEM was performed to visualize the POP and showcased that the synthesized POP had a morphology of spherical particles in a broad size distribution from 100 nm up to 3 µm (Figure 7.2c and d). These particles were in general smaller than those reported by Sawamura *et al.* with their emulsion methodology, but that was not surprisingly considering the difference in polymerization technique.



Figure 7.2. Characterization of (*R*)-Pamidite-POP. a) TGA with a heating ramp of 10 °C/min up to 500 °C in air, b) N₂-physisorption isotherm, c) and d) SEM images showing the morphology and particle size of the synthesized POP. Adapted from Kegnæs *et al.*¹⁸⁸

The (*R*)-Pamidite-POP was designed to have swelling properties to make the active sites accessible. Therefore, the POP was exposed to six different solvents to examine its swelling properties. An image of the POP exposed to the solvents is presented in Figure 7.3a. The POP swelled in *m*-xylene, toluene, benzene, dioxane, and THF evident by the resulting clear solutions. The swelling properties of (*R*)-Pamidite-POP were further illustrated by exposing the POP to d₈-toluene and doing a standard liquid ³¹P-NMR. In the resulting spectrum, the phosphoramidite moiety at δ 144 ppm was both clearly visible and fairly sharp indicating the formation of a quasi-homogeneous environment similar to the report from Xiao *et al.* mentioned earlier (Figure 7.3b).¹⁷⁵ In contrast, the POP did not swell in hexane with the appearance of the POP in the bottom of the vial and was therefore an excellent solvent to recovery the POP from the reaction mixture.



Figure 7.3. (a) Picture showing the appearance of (*R*)-Pamidite-POP in a range of solvents. (b) Liquid phase ³¹P NMR of (*R*)-Pamidite-POP in d₈-toluene. Adapted from Kegnæs *et al.*¹⁸⁸

The amorphous structure of (*R*)-Pamidite-POP made it more difficult to obtain structural information as many X-Ray relying techniques could not be applied. Fortunately, the material could be examined by solid-state NMR, which provided structural information about both the ligand and polymer backbone. First, the presence of the phosphoramidite specie in the POP was assessed by a ³¹CP/MAS NMR experiment and with the resulting spectrum shown in Figure 7.4. The spectrum showed the presence of the phosphoramidite specie with a characteristic chemical shift at δ 143, which was very consistent with the chemical shift from building block **3** and of that obtained in Figure 7.3b. However, another small signal was also present at δ 9-10 ppm, which corresponded to a P^V-specie indicating partial oxidation of the phosphoramidite.²⁴⁷ Yet, the majority of the incorporated phosphor species were the targeted phosphoramidite (approximately 86%) with a ligand density of 0.11 mmol/g based on NMR quantification using NH₄H₂PO₄ as standard. Secondly, analysis by ¹³C–¹H CP/MAS NMR demonstrated the formation of a PS-POP with signals in agreement with reported literature.^{183,233} Another distinguished peak at 67 ppm was observed too that correlated with the morpholine and demonstrated the successful incorporation of the ligand into the POP.



Figure 7.4. (Left) ³¹P CP/MAS NMR of the (*R*)-Pamidite-POP at a spinning frequency of 15 kHz where the spinning side bands are indicated. (Right) ¹³C–¹H CP/MAS NMR of the POP at a spinning frequency of 15 kHz showing the PS polymer and a signal from the ligand at 67 ppm. Adapted from Kegnæs *et al.*¹⁸⁸

7.5 Catalytic performance in the asymmetric C(sp³)-H functionalization

After the successful incorporation of the phosphoramidite ligand in the (R)-Pamidite-POP, the reaction conditions of the C(sp³)–H functionalization of 3-arylpropanamides were evaluated. Table 7.3 represents the route to the optimized reaction conditions initially inspired from Chen et al., which the previous test were conducted under.²⁴⁷ The active catalyst was again formed *in*-situ by exposing the (*R*)-Pamidite-POP to Pd₂(dba)₃·CHCl₃ in *m*-xylene with excess amount of 4-iodoanisole, cesium carbonate as base, and gave the desired β -carbon arylated product in 66% yield after 48 hours at 100 °C with an ee of 61% (entry 1). Applying *p*-xylene as solvent instead decreased both the activity and ee (entry 2). Changing the palladium source from $Pd_2(dba)_3$ ·CHCl₃ to $Pd(dba)_2$ lowered the activity significantly to 46% conversion (entry 3). Whereas the use of $Pd_2(dba)_3$ as palladium source yielded the best catalytic performance with good conversion, high yield, and an ee of 69% (entry 4). A lower activity was observed when decreasing the excess of iodoanisole from 4 to 3 equivalents (entry 5). Increasing the palladium loading to 15 mol% provided a significant boost in ee up to 87% (entry 6) and by increasing the reaction to 72 h the activity was improved without any loss of selectivity (entry 7). Attempts to increase the performance further were carried out by introducing more POP (entry 8) or by utilization silver(I)carbonate as an promoter (entries 9-10), but were not successful.^{241,254–256} Conducting the reaction in absence of POP provided good activity, but a racemic mixture of the product was formed whereas a commercially available palladium nanoparticle catalyst proceeded with high conversion but with no formation of the desired product (entries 11-12).

Table 7.3. Optimization table of the catalytic conditions for the $C(sp^3)$ –H functionalization utilization a heterogeneous POP. Adapted from Kegnæs *et al.*¹⁸⁸



^aThe loading is based on the amount of palladium added.

^bConversion and yield determined by ¹H-NMR using internal standard.

^cEnantiomeric excess determined by chiral HPLC.

The versatility of the catalytic system using(R)-Pamidite-POP was assessed by changing both the aryl iodide and the 3-arylpropanamide as seen in Table 7.4. Replacing the 4-iodoanisole (entry 1) with 4iodotoluene decreased the yield and enantiomeric excess slightly from 70% to 51% and 86% to 78%, respectively (entry 2). Using less electron-rich aryl iodides such as 1-fluoro-4-iodobenzene (entry 3) or 1bromo-4-iodobenzene (entry 4) were unfruitful with either very low or no activity. These results are in line with previous reports of homogeneous systems where electron-rich aryl iodides performs better than electron-poor.^{247,248} Different 3-arylpropanamides were tested as well by introducing either a methoxy (entry 5), methyl (entry 6) or fluoro (entry 7) group in the meta position of the phenyl group. All substrates were tolerated with high ee ranging from 68% to 86%, however the more electron donating groups provided higher yields with 62% for methoxy and 70% for methyl than the fluoro functionalized 3arylpropanamide as it only gave a yield of 45%. Moving the fluoro functionality from meta to para-positon gave a small decrease in activity and ee (entry 8). The presence of methyl groups in both meta-positions provided 70% yield and 86% ee similar to the other meta-functionalized substrates with electron donating groups (entry 9). These results showcased that the system was capable of reacting with different types of aryl iodides and 3-arylpropanamides, but the highest results were obtained with electron rich aryl iodides and electron donating groups in the *meta*-position for the 3-arylpropanamide.

Table 7.4. Assessment of the robustness of the catalytic system was carried out by changing aryl iodides and 3-phenylpropanamides. Adapted from Kegnæs *et al.*¹⁸⁸



^aConversion and yield determined by ¹H-NMR using an internal standard. ^bEnantiomeric excess determined by chiral HPLC.

One of the benefits of using a heterogeneous catalyst is the easier recovery and recyclability of the catalyst. To test if (*R*)-Pamidite-POP could be recovered and reused successfully, a reaction was started as presented in Table 7.3 entry 7. The POP catalyst was then readily recovered from the reaction mixture by extracting the organic residues with hexane as the POP deswelled and solidified in the bottom of the vial. An illustration of the methodology used to recover the POP is illustrated in Scheme 7.6. Thereafter, the recovered solid was dried and reused as a source of both Pd and ligand in the initial recycle attempt (Table 7.5 entries 1-4). Unfortunately, it was clear from the initial recycling experiment that both the catalytic activity and the enantioselectivity were significantly reduced between each new cycle. In an attempt to maintain higher activity and ee, a new reaction was started where a fresh amount of Pd₂dba₃ was added to every new cycle (entries 5-8). An increased activity was observed between the first and second catalytic reaction (entries 5-6) with a small decrease in ee. Further recycles under same conditions yielded full

conversion of the starting material with decreasing selectivity for the desired product and ee for each new reaction. Unfortunately, the recycling of the (*R*)-Pamidite-POP were not ideal as the catalyst could not maintain its catalytic performance over consecutive reactions. Still, the catalysts was easily recovered and show the potential of POP-based catalytic systems for future applications.



Scheme 7.6. Illustration of how to catalyst is recovered from the reaction mixture.

Table 7.5. Results obtained from using the recovered POP with or without the addition of fresh palladium. Adapted from Kegnæs *et al.*¹⁸⁸

Ph	0 0.1 mm	NHAQ ol	I OMe 4 equiv	Pd ₂ (dba) ₃ 15 mol% Pd (<i>R</i>)-Pamidite-F 2 equiv Cs ₂ CC <i>m</i> -xylene (0.16 100 °C, 72 h	POP (20 m D ₃ 67 M),	ol%) Ph	
	Entry	Recycle	es Mo	difications	Conv. ^a	Yield ^a	ee ^b
	1	0	-		70%	70%	86%
	2	1	-		32%	32%	73%
	3	2	-		15%	10%	65%
	4	3	-		0%	0%	-
	5	0	-		70%	70%	86%
	6	1	Ad	d. of fresh Pd	100%	99%	74%
	7	2	Ad	d. of fresh Pd	100%	91%	62%
	8	3	Ad	d. of fresh Pd	100%	73%	54%

^aConversion and yield determined by ¹H-NMR using an internal standard. ^bEnantiomeric excess determined by chiral HPLC.

The reused catalyst was characterized to investigate possible deactivation mechanisms and explain the reason behind the POP's diminishing activity and selectivity. First, the catalyst was examined by XRD, where the diffractogram showed the presence of both palladium nanoparticles and cesium iodide with diffractions at $2\theta = 40$ and 28, 39, 49, respectively (Figure 7.5). The presence of nanoparticles indicated that the palladium precursor had decomposed during either the reaction or recovery of the catalyst. As the test reaction from Table 7.3 entry 12 showed that palladium nanoparticles were still active as they

convert the substrate but not into the desired product, it was definitely a deactivation mechanism even with the addition of fresh Pd_2dba_3 .



Figure 7.5. XRD diffractogram of the used (*R*)-Pamidite-POP with corresponding diffractions from CsI and Pd nanoparticles in a fcc crystal structure. Adapted from Kegnæs *et al.*¹⁸⁸

The presence of both cesium iodide and palladium nanoparticles were further verified by electron microscopy with the appearance of both small and large particles (Figure 7.6). The biggest particles (20-250nm) in the images were cesium iodide according to energy dispersive X-Ray (EDX) analysis whereas the palladium was distributed throughout the whole sample as smaller nanoparticles with a diameter of 2-4 nm (Figure 7.8). Fortunately, the same analysis also showed the presence of phosphorous in the POP, which may indicate that the ligands sites was still present.







Figure 7.8. EDX analysis of the used (*R*)-Pamidite-POP showing the presence of Cs, I, Pd, and P throughout the whole sample. Adapted from Kegnæs *et al.*¹⁸⁸

Another potential reason behind the lowering in catalytic performance during reuse may arise from metal leaching (at least for the first attempt). Thus, the extracted hexane-phase was examined where it revealed minimal leaching of palladium (0.63 mM Pd or 2.5% of the original palladium concentration) in XRF and complementary ICP analysis showed a Pd concentration barely above the blank (0.21 μ M Pd <0.001% of the original palladium concentration). As such, metal leaching was not a major contributor to the observed loss in activity.

The EDX analysis indicated that phosphorus was still present for the recovered solid and to investigate the form of this phosphorus, ³¹P CP/MAS NMR was carried out with the resulting spectrum in Figure 7.9. The spectrum showed that the formed phosphoramidite moiety had disappeared completely with the signal at 9-10 ppm being the one predominately found now. The newly formed phosphor specie at 10 ppm ariso from an oxidized phosphoramidite as mentioned previously and according to the work from Chen *et al.*, the oxidation of the phosphoramidite takes place during the catalytic conditions and similar behavior for this POP-based system was not unlikely.²⁴⁷ Corresponding ¹³C–¹H CP/MAS NMR was also carried out and still showed the presence of the PS backbone and some sharp signals from hexane trapped inside the POP at δ 30.7, 21.7 and 13.2 ppm and showcased the stability of the PS backbone.



Figure 7.9. (Left) ³¹P CP/MAS NMR of the used (*R*)-Pamidite-POP at a spinning frequency of 8 kHz where the spinning side bands are indicated. (Right) ¹³C–¹H CP/MAS NMR of the used POP at a spinning frequency of 8 kHz showing the PS polymer and the presence of hexane at δ 30.67, 21.73 and 13.24 ppm. Adapted from Kegnæs *et al.*¹⁸⁸

With the *post*-characterization of the used (*R*)-Pamidite-POP in hand, different deactivation mechanisms was postulated and they have been illustrated in Scheme 7.7. Mechanism **A** is caused by the formation of Pd nanoparticles, which convert the substrate but do not form the desired product leading to poor product yield. In path **B**, the presence of excess amount of Pd₂dba₃ will lead to competing non-enantioselective formation of the product, which increases the activity, but decreases the ee. Deactivation mechanisms **C** originates from Pd leaching, which was shown to be minimal by XRF and ICP, but will lead to a decrease in overall activity. The last proposed deactivation mechanisms is path **D**, where the ligand is oxidized from a P(III) to a P(V) specie. Based on the report from Duan *et al.*²⁴⁸ the resulting P(V) specie is still a good ligand for the β -functionalization of 3-arylpropanamides, albeit with lower ee. The different deactivation pathways was assigned to the two different recycle attempts where the first attempt supposedly was influenced by path **A** and **D** as the formation of nanoparticles of palladium was evident from XRD and STEM images, whereas the oxidation of the phosphoramidite was observed by ³¹P CP/MAS NMR. Similar to the first recycling attempt, the second was also affected by oxidation of the phosphoramidite (**D**), however the high activity accommodated with a loss in ee fitted very well with path **B** where excess Pd₂dba₃ catalyzed a non-entioselective reaction.

Deactivation mechanisms





7.6 Summary

In this project, the first reported POP active in the asymmetric $C(sp^3)$ –H functionalization was synthesized. The (*R*)-Pamidite-POP was constructed from a PS backbone with phosphoramidite acting as a chiral ligand. The POP had swelling properties that enable a quasi-homogeneous environment at the ligand sites. The successful incorporation of the ligand into a PS backbone was confirmed by solid-NMR. The ratio between ligand and styrene played an important role in the catalytic performance of the polymer. The reaction conditions were optimized and resulted in adequate activity and high selectivity towards the desired $C(sp^3)$ –H functionalization with up to 86% ee. The substrate scope demonstrated that the activity and enantioselectivity were very influenced by the electronic effects of the aryl iodides with the electron rich substrates performing the best similar to other published reports. Screening of different 3-arylpropanamides showed that electron donating groups provided the highest yields whereas the ee was less affected by different functional groups. Attempts to recover and recycle the POP were not completely successful as diminishing product yield and ee were observed for each consecutive reaction. Investigation of the used catalyst revealed that the diminishing catalytic performance likely arise from an oxidation of the phosphoramidite and formation of metal nanoparticles.

7.7 Experimental

Chemicals

All chemicals were reagent grade and used as received without further purification. 4-iodotoluene was acquired from Fluka Chemie Ag and the remaining chemicals were from Sigma Aldrich: (*R*)-1,1'-Bi-2-naphthol, bromine, tetrakis(triphenylphosphine)palladium(0), 5 wt.% Pd/C (catalog number 75992), potassium vinyltrifluoroborate, K_2CO_3 , PCl₃, P(NMe₂)₃, morpholine, *N*-methyl-2-pyrrolidone, Et₃N, dibenzylether, Pd(dba)₂, Pd₂(dba)₃, Pd₂(dba)₃·CHCl₃, Cs₂CO₃, *m*-xylene, *p*-xylene, 4-iodoanisole, 4-iodotoluene, 4-fluoro-1-iodobenzene, styrene, divinylbenzene, AIBN, thionylchloride, 3-(3-methylphenyl)-1-propionic acid, 3-(3-fluorophenyl)-1-propionic

acid, 3-(4-fluorophenyl)-1-propionic acid, 3-(3,5-dimethylphenyl)-1-propionic acid, 3-phenylpropionyl chloride, and 8-aminoquinoline.

Equipment

Anhydrous solvents were dried/purified using the solvent purification system Puresolv MD-7. TEM images were obtained from a Technai T20 G2 microscope from TEI. STEM images are from a FEI Titan 80-300ST with 300 kV voltage. SEM images were taken on a Quanta 200 ESEM FEG microscope from FEI. Samples were deposited on 300 mesh Cu grids with no prior treatment. N₂-physisorption was conducted on a Micrometrics 3Flex instrument at 77 K. Samples for N₂-physisorption were degassed 24 hours before the analysis on a Micrometrics VacPrep 061 Sample Degas System at room temperature. TGA was performed on a Mettler Toledo TGa/DSC 1 STARe System. XRF analysis was conducted on a PANalytical Epsilon3 system. X-ray Powder diffraction was measured with a Cu-Ka radiation source on a HUBER G760 Guinier camera. The enantiomeric excess was determined by HPLC with a chiral stationary phase. ¹H-NMR, ¹³C-NMR, and ³¹P-NMR were measured on a Bruker Ascend 400 (400 Hz) with chemical shifts in ppm reported relative to the solvent peak. The peak patterns are indicated as follows: s, singlet; d, doublet; t, triplet; m, multiplet; dd, doublet of doublets; ddd, doublet of doublets of doublets; dt, doublet of triplets. ³¹P MAS NMR spectra were recorded with a Bruker AVANCE III HD spectrometer operating at a 14.1 T magnetic field with a 4 mm o.d. CP/MAS BBFO probe. A ³¹P-¹H CP/MAS spectrum was acquired using a ramped contact pulse of 3 ms, an interscan delay of 3 seconds and 392 transient scans. In addition, a simple blochdecay experiment was acquired with an interscan delay of 90 seconds and 1024 transient scans allowing for a quantitative analysis of the present phosphor sites. High-power SPINAL-64 ¹H decoupling was employed for all experiments. Spectra were acquired with spinning frequencies between 8 and 15 kHz in order to identify the isotropic chemical shifts. These are reported relative to $NH_4H_2PO_4$ (0.81 ppm).



(R)-6,6'-Dibromo-2,2'-dihydroxy-1,1'-dinaphthyl (1) adapted from Izumi et al.²⁵⁷

(*R*)-BINOL (5 g, 17.5 mmol) was dissolved in anhydrous CH_3CN (90 mL) with a magnetic stir bar and kept at 0 °C. Br₂ (8.38 g, 2.7 mL, 52.4 mmol) was added dropwise to the solution and left to stir for 3 hours. The mixture was quenched with Na_2SO_3 , and the organic phase was extracted 3 times with CH_2Cl_2 . The combined organic phase was washed with brine, dried over $MgSO_4$, and the solvent removed yielding a white powder (6.70 g, 86% yield).

¹**H-NMR (400 MHz, CDCl₃,)** δ 8.05 (d, *J* = 2.0 Hz, 2H), 7.90 (d, *J* = 8.9 Hz, 2H), 7.44-7.34 (m, 4H), 6.96 (d, *J* = 8.9 Hz, 2H), 5.05 (s, 2H).

¹³C-NMR (101 MHz, CDCl₃) δ 153.0, 131.9, 130.9, 130.7, 130.6, 130.4, 125.9, 119.0, 118.0, 110.6.



(R)-6,6'-Divinyl-2,2'-dihydroxy-1,1'-dinaphthyl (2) adapted from Jia et al.²⁵⁸

(*R*)-6,6'-Dibromo-2,2'-dihydroxy-1,1'-dinaphthyl (1) (888 mg, 2.00 mmol), potassium vinyltrifluoroborate (964 mg, 7.20 mmol), and Pd(PPh₃)₄ (231 mg, 0.20 mmol) were weighed off in a round-bottom flask and a stir bar was added. The setup was connected to a reflux condenser and made inert by 3 vacuum/N₂ cycles with Schlenk techniques. Degassed THF (60 mL) and degassed 1M K₂CO₃ (12 mL) were added and the mixture was kept at refluxing conditions at 75 °C for 24 h. Next, the reaction was cooled down to room temperature, water (30 mL) was added, and the organic residues were extracted with heptane. The combined organic phase was dried over MgSO₄, concentrated, and purified by silica gel chromatography (9:1 heptane:ethyal acetate (EtOAc)) affording the product as a white solid (490 mg, 72% yield).

¹**H-NMR (400 MHz, CDCl₃,)** δ 7.92 (d, *J* = 8.9 Hz, 2H), 7.81 (d, *J* = 1.7 Hz, 2H), 7.46 (dd, *J* = 8.7, 1.8 Hz, 2H), 7.34 (d, *J* = 8.9 Hz, 2H), 7.11 (d, *J* = 8.7 Hz, 2H), 6.85 (dd, *J* = 17.6 Hz, 10.9 Hz, 2H), 5.79 (d, *J* = 17.6 Hz, 2H), 5.29 (d, *J* = 10.9 Hz, 2H) 5.10 (s, 2H).

¹³**C-NMR (101 MHz, CDCl₃)** δ 152.8, 136.5, 133.5, 133.0, 131.6, 129.5, 126.7, 124.9, 124.5, 118.1, 113.9, 110.9.



O,O'-(R)-(6,6'-Divinyl-1,1'-Dinaphthyl-2,2'-diyl)-N-(1-morpholinyl)phosphoramidite (3)

Inside an argon filled glovebox, (*R*)-6,6'-divinyl-2,2'-dihydroxy-1,1'-dinaphthyl (**2**) (200 mg, 0.60 mmol) was mixed with one drop of NMP (*N*-methyl-2-pyrrolidone), PCl₃ (2 mL), and a magnetic stir bar in a round-bottom flask. The flask was sealed with a rubber septum. Outside the glovebox, the mixture was heated to 60 °C for 1 hour. The excess amount of PCl₃ was removed under vacuum before anhydrous THF (2 mL) was added to the mixture. A solution of morpholine (520 μ L, 6.00 mmol) in anhydrous THF (2 mL) was added slowly to the mixture at 0 °C. After stirring overnight at room temperature, the mixture was quenched with water (6 mL) followed by extraction with EtOAc (3x 10 mL). The organic phase was combined, dried over MgSO₄, and concentrated before purified by silica gel chromatography (8:2 heptane:EtOAc) yielding the product as a white powder (146 mg, 53% yield).

¹**H-NMR (400 MHz, d₆-DMSO)** δ 8.10 (m, 2H), 8.03 (d, *J* = 6.2 Hz, 2H), 7.64-7.56 (m, 4H), 7.16 (dd, *J* = 20.1, 8.9 Hz, 2H), 6.89 (m, 2H), 5.92 (dd, *J* = 17.6, 3.9, 2H), 5.35 (dd, *J* = 11.0, 3.5 Hz, 2H), 3.44 (t, *J* = 4.7 Hz, 4H) 2.99 (m, 2H), 2.85 (m, 2H).

¹³**C-NMR (101 MHz, d₆-DMSO)** δ 149.3, 149.2, 148.9, 136.2, 133.9, 133.7, 131.6, 131.6, 131.4, 131.2, 130.8, 130.6, 126.9, 126.3, 126.2, 123.8, 123.2, 123.1, 122.4, 122.2, 121.7, 121.7, 115.0, 114.9, 66.9, 66.8, 44.1, 43.9.

³¹P-NMR (162 MHz, d₆-DMSO) δ 144.



O,O'-(R)-6,6'-Divinyl-1,1'-dinathyl-2,2'-diyl)-N,N-dimethylphosphoramidite (4)

(*R*)-6,6'-Divinyl-2,2'-dihydroxy-1,1'-dinaphthyl (**2**) (200 mg, 0.60 mmol) was weighed off in a round-bottom flask before a stir bar was added. The setup was connected to a condenser and made inert by 3 vacuum/N₂ cycles with Schlenk techniques before adding anhydrous toluene (3 mL). PMe₃ (98.0 mg, 108 μ L, 0.60 mmol) was slowly added to the solution and the mixture was left to stir at refluxing conditions at 120 °C for 2 h. The mixture was cooled down to room temperature before being purified by silica gel chromatography (9:1 heptane:EtOAc) yielding the product as a white powder (86 mg, 35% yield).

¹**H-NMR (400 MHz, d₆-DMSO)** δ 8.10 (dd, J = 19.2, 8.8 Hz, 2H), 8.03 (dd, J = 7.5, 1.7 Hz, 2H), 7.58 (d, J = 8.7, 2H), 7.48 (d, J = 8.8 Hz, 2H), 7.16 (dd, J = 17.8, 8.9 Hz, 2H), 6.89 (ddd, J = 17.7, 11.0, 2.9, 2H), 5.93 (dd, J = 17.6, 4.3, 2H), 5.35 (dd, J = 11.0, 3.7 Hz, 2H), 2.48 (d, J = 9.8 Hz, 6H).

¹³C-NMR (101 MHz, d₆-DMSO) δ 149.7, 149.7, 149.0, 136.3, 136.2, 133.8, 133.6, 131.6, 131.4, 131.1, 130.8, 130.7, 130.6, 126.9, 126.9, 126.3, 126.2, 123.8, 123.2, 123.2, 122.4, 122.3, 121.8, 121.8, 115.0, 114.9, 35.5, 35.3.

³¹P-NMR (162 MHz, d₆-DMSO) δ 148.

Synthesis of (R)-P-amidite-POP

In a round-bottom flask connected to a condenser, phosphoramidite (**3**: 800 mg, 1.76 mmol or **4**: 723 mg, 1.76 mmol) and AIBN (1.35 g, 8.25 mmol) were weighed off and a stir bar was added. The setup made inert by 3 vacuum/N₂ cycles with Schlenk techniques before divinylbenzene (0.24 g, 0.27 mL, 1.87 mmol), styrene (9.09 g, 10.0 mL, 88.0 mmol), and THF (30 mL) were added and the resulting mixture was left to stir at refluxing conditions at 85 °C overnight. The POP was precipitated out by adding the reaction mixture to a stirring solution of CH₃OH. The POP was collected on a glass sintered funnel, washed with $5x CH_3OH$, and dried under vacuum affording a white solid (7.46 g).



3-Phenyl-N-(quinolin-8-yl)propionamide adapted from Chen et al.²⁴⁷

In a round-bottom flask, 8-aminoquinoline (432 mg, 3.00 mmol) was dissolved in anhydrous CH_2CI_2 (20 mL) and a stir bar was added. The setup was made inert by 3 vacuum/N₂ cycles with Schlenk techniques. 3-Phenylpropionyl chloride (504 mg, 444 μ L, 3.00 mmol) and Et₃N (830 μ L, 6.00 mmol) were added dropwise at 0 °C. The reaction was kept at 40 °C overnight. Water (30 mL) was added to the reaction and the organic phase was extracted with 3x EtOAc. The combined organic phase was dried over MgSO₄, concentrated, and purified by silica gel chromatography (90:10 heptane:EtOAc) yielding a white powder (679 mg, 82% yield). NMR of the isolated product was in accordance with previous reports.²⁴⁷

¹**H-NMR (400 MHz, CDCl₃)** δ 9.82 (s, 1H), 8.83-8.76 (m, 2H), 8.17 (dd, J = 8.3, 1.6 Hz, 1H), 7.58-7.48 (m, 2H), 7.46 (dd, J = 8.3, 4.2 Hz, 1H), 7.30 (d, J = 4.4 Hz, 4H), 7.21 (m, 1H), 3.15 (dd, J = 9.0, 6.7 Hz, 2H) 2.90 (dd, J = 9.0, 6.8 Hz, 2H).

General Procedure for Remaining substrates (not optimized)

3-Aryl-1-propionic acid (3.00 mmol) was weighed off in a round-bottom flask and a stir bar was added. The setup was made inert by 3 vacuum/N₂ cycles with Schlenk techniques. Anhydrous CH₂Cl₂ (10 mL) was added to dissolve the solid before SOCl₂ (322 mg, 197 μ L, 2.70 mmol) was slowly added to the solution and the mixture was kept at 45 °C overnight while stirring. Next, the CH₂Cl₂ was removed under vacuum and fresh anhydrous CH₂Cl₂ (10 mL) was added. In another round-bottom flask, 8-aminoquinoline (388.8 mg, 2.7 mmol) was dissolved in anhydrous CH₂Cl₂ (10 mL) and a stir bar was added. The setup was made inert by 3 vacuum/N₂ cycles with Schlenk techniques. The acid chloride solution was slowly added to the solution of 8-aminoquinoline at 0 °C followed by Et₃N (830 μ L, 6.00 mmol) before the reaction was heated and kept to 40 °C overnight. Next, water (30 mL) was added to the reaction and the organic phase was extracted with 3x EtOAc. The combined organic phase was washed with 1M HCl (aq) and brine before being dried over MgSO₄, concentrated, and purified by silica gel chromatography (90:10 heptane:EtOAc). All starting materials are known compounds with NMR in accordance with previously reports.²⁴⁷



3-(3-Methylphenyl)-N-(quinolin-8-yl)propionamide

The compound was prepared according to the general procedure and was isolated as a pale yellow solid (282 mg, 39% yield).

¹**H-NMR (400 MHz, CDCl₃)** δ 9.81 (s, 1H), 8.82-8.77 (m, 2H), 8.17 (dd, J = 8.3, 1.6 Hz, 1H), 7.59-7.48 (m, 2H), 7.45 (dd, J = 8.2, 4.2 Hz, 1H), 7.19 (t, J = 7.5 Hz, 1H), 7.14-7.08 (m, 2H), 7.02 (d, J = 7.5 Hz, 1H), 3.11 (dd, J = 9.2, 6.6 Hz, 2H) 2.89 (dd, J = 9.1, 6.7 Hz, 2H), 2.32 (s, 3H).



3-(3-Methoxyphenyl)-N-(quinolin-8-yl)propionamide

The compound was prepared according to the general procedure and was isolated as a yellow oil (124 mg, 15% yield).

¹**H-NMR (400 MHz, CDCl₃)** δ 9.80 (s, 1H), 8.84-8-72 (m, 2H), 8.16 (dd, *J* = 8.2, 1.6 Hz, 1H), 7.58-7.48 (m, 2H), 7.45 (dd, *J* = 8.3, 4.2 Hz, 1H), 7.21 (t, *J* = 7.8 Hz, 1H), 6.89 (d, *J* = 7.7 Hz, 1H), 6.85 (t, *J* = 2.1 Hz, 1H), 6.75 (dd, *J* = 8.2, 2.6 Hz, 1H), 3.78 (s, 3H), 3.13 (dd, *J* = 9.1, 6.7 Hz, 2H), 2.89 (dd, *J* = 9.0, 6.7 Hz, 2H).



3-(3-Fluorophenyl)-N-(quinolin-8-yl)propionamide

The compound was prepared according to the general procedure from 3-(3-methylphenyl)-*N*-(quinolin-8-yl)propionamide and was isolated as a pale brown solid (459 mg, 62% yield).

¹**H-NMR (400 MHz, CDCl₃)** δ 9.82 (s, 1H), 8.87-8.63 (m, 2H), 8.18 (dd, J = 8.3, 1.7 Hz, 1H), 7.59-7.49 (m, 2H), 7.46 (dd, J = 8.3, 4.2 Hz, 1H), 7.28-7.21 (m, 1H), 7.08 (d, J = 7.6 Hz, 1H), 7.01 (dt, J = 9.9, 2.1 Hz, 1H), 6.93-6.85 (m, 1H), 3.15 (dd, J = 8.7, 6.8 Hz, 2H) 2.90 (dd, J = 8.7, 6.8 Hz, 2H).



3-(4-Fluorophenyl)-N-(quinolin-8-yl)propionamide

The compound was prepared according to the general procedure from 3-(3-methylphenyl)-*N*-(quinolin-8-yl)propionamide and was isolated as a pale yellow solid (350 mg, 48% yield).

¹**H-NMR (400 MHz, CDCl₃)** δ 9.78 (s, 1H), 8.84-8.67 (m, 2H), 8.17 (dd, J = 8.3, 1.6 Hz, 1H), 7.58-7.48 (m, 2H), 7.45 (dd, J = 8.3, 4.2 Hz, 1H), 7.29-7.21 (m, 2H), 7.02-6.93 (m, 2H), 3.12 (t, J = 7.7 Hz, 2H) 2.87 (dd, J = 8.5, 6.9 Hz, 2H).



3-(3,5-Dimethylphenyl)-N-(quinolin-8-yl)propionamide

The compound was prepared according to the general procedure from 3-(3-methylphenyl)-*N*-(quinolin-8-yl)propionamide and was isolated as a yellow oil (454 mg, 62% yield).

¹**H-NMR (400 MHz, CDCl₃)** δ 9.80 (s, 1H), 8.83-8.76 (m, 2H), 8.16 (dd, *J* = 8.2, 1.6 Hz, 1H), 7.59-7.48 (m, 2H), 7.45 (dd, *J* = 8.3, 4.2 Hz, 1H), 6.92 (s, 2H), 6.84 (s, 1H), 3.08 (dd, *J* = 9.3, 6.6 Hz, 2H) 2.87 (dd, *J* = 9.3, 6.6 Hz, 2H), 2.28 (s, 6H).

Standard Catalytic Reaction

In a standard catalytic experiment, Pd source (0.010-0.015 mmol Pd), 3-phenyl-*N*-(quinolin-8-yl)propionamide (0.10 mmol), aryliodide (0.30-0.40 mmol), Cs_2CO_3 (65.2 mg, 0.20 mmol), and POP (0.02-0.03 mmol ligand) were mixed with a stir bar in a 4 mL vial inside an argon filled glovebox. Solvent (0.6 mL) was added to the mixture and the vial was sealed with a PTFE-lined screw cap. Outside the glovebox, the vial was put into an aluminum heating block at 100 °C for the specified time at 1000 rpm. After the specified time, the reaction mixture was cooled down to rt. before a stock solution of dibenzylether in EtOAc was added as a NMR standard – 0.5 mL of a 0.05 M stock solution. The mixture was filtered through a 0.22 μ m syringe filter and concentrated on vacuum before analysis by NMR for assessing conversion and yield. The enantiomeric excess was quantified by HPLC after purification of crude mixture by silica gel chromatography (85:15 heptane:EtOAc).



3-Phenyl-3-(4-methoxyphenyl)-N-(quinolin-8-yl)propionamide

The compound was prepared according to the procedure above (standard catalytic reaction) using, Pd_2dba_3 (6.9 mg, 0.0075 mmol), 3-phenyl-*N*-(quinolin-8-yl)propionamide (27.6 mg, 0.10 mmol), 4-iodoanisole (93.6 mg, 0.40 mmol), Cs_2CO_3 (65.2 mg, 0.20 mmol), and (*R*)-P-amidite-POP (187 mg, 0.02 mmol) applying *m*-xylene as solvent. The reaction time was 72 h at 100 °C. The enantiomeric excess was determined by a Chiralcel-OD-H column with hexane/*i*-PrOH = 80:20, flow rate 0.9 mL/min, retention times = 22.3 min for major isomer and 26.9 min for minor isomer.



3-Phenyl-3-(4-methylphenyl)-*N*-(quinolin-8-yl)propionamide

The compound was prepared according to the procedure above (standard catalytic reaction) using, Pd_2dba_3 (6.9 mg, 0.0075 mmol), 3-phenyl-*N*-(quinolin-8-yl)propionamide (27.6 mg, 0.10 mmol), 4-iodotoluene (87.2 mg, 0.40 mmol), Cs_2CO_3 (65.2 mg, 0.20 mmol), and (*R*)-P-amidite-POP (187 mg, 0.02 mmol) applying *m*-xylene as solvent. The reaction time was 72 h at 100 °C. The enantiomeric excess was determined by a Chiralpack-AD column with hexane/i-PrOH = 85:15, retention times = 15.0 min for minor isomer and 18.5 min for major isomer.



3-Phenyl-3-(4-fluorophenyl)-N-(quinolin-8-yl)propionamide

The compound was prepared according to the procedure above (standard catalytic reaction) using, Pd_2dba_3 (6.9 mg, 0.0075 mmol), 3-phenyl-*N*-(quinolin-8-yl)propionamide (27.6 mg, 0.10 mmol), 4-fluoro-1-iodobenzene (88.8 mg, 0.40 mmol), Cs_2CO_3 (65.2 mg, 0.20 mmol), and (*R*)-P-amidite-POP (187 mg, 0.02 mmol) applying *m*-xylene as solvent. The reaction time was 72 h at 100 °C. The enantiomeric excess was determined by a Chiralcel-OD-H column with hexane/*i*-PrOH = 80:20, retention times = 20.1 min for major isomer and 29.9 min for minor isomer.



3-(3-Methoxyphenyl)-3-(4-methoxyphenyl)-N-(quinolin-8-yl)propionamide

The compound was prepared according to the procedure above (standard catalytic reaction) using, Pd_2dba_3 (6.9 mg, 0.0075 mmol), 3-(3-methoxyphenyl)-*N*-(quinolin-8-yl)propionamide (30.6 mg, 0.10

mmol), 4-iodoanisole (93.6 mg, 0.40 mmol), Cs_2CO_3 (65.2 mg, 0.20 mmol), and (*R*)-P-amidite-POP (187 mg, 0.02 mmol) applying *m*-xylene as solvent. The reaction time was 72 h at 100 °C. The enantiomeric excess was determined by a Chiralcel-OD-H column with hexane/*i*-PrOH = 80:20, retention times = 27.6 min for major isomer and 35.1 min for minor isomer.



3-(3-Methylphenyl)-3-(4-methoxyphenyl)-N-(quinolin-8-yl)propionamide

The compound was prepared according to the procedure above (standard catalytic reaction) using, Pd₂dba₃ (6.9 mg, 0.0075 mmol), 3-(3-methylphenyl)-*N*-(quinolin-8-yl)propionamide (29.0 mg, 0.10 mmol), 4-iodoanisole (93.6 mg, 0.40 mmol), Cs₂CO₃ (65.2 mg, 0.20 mmol), and (*R*)-P-amidite-POP (187 mg, 0.02 mmol) applying *m*-xylene as solvent. The reaction time was 72 h at 100 °C. The enantiomeric excess was determined by a Chiralcel-OD-H column with hexane/*i*-PrOH = 85:15, retention times = 25.9 min for major isomer and 31.8 min for minor isomer.



3-(3-Fluorophenyl)-3-(4-methoxyphenyl)-N-(quinolin-8-yl)propionamide

The compound was prepared according to the procedure above (standard catalytic reaction) using, Pd₂dba₃ (6.9 mg, 0.0075 mmol), 3-(3-fluorophenyl)-*N*-(quinolin-8-yl)propionamide (29.4 mg, 0.10 mmol), 4-iodoanisole (93.6 mg, 0.40 mmol), Cs₂CO₃ (65.2 mg, 0.20 mmol), and (*R*)-P-amidite-POP (187 mg, 0.02 mmol) applying *m*-xylene as solvent. The reaction time was 72 h at 100 °C. The enantiomeric excess was determined by a Chiralpack AD column with hexane/*i*-PrOH = 85:15, retention times = 25.1 min for minor isomer and 35.5 min for major isomer.



3-(4-Fluorophenyl)-3-(4-methoxyphenyl)-N-(quinolin-8-yl)propionamide

The compound was prepared according to the procedure above (standard catalytic reaction) using, Pd_2dba_3 (6.9 mg, 0.0075 mmol), 3-(4-fluorophenyl)-*N*-(quinolin-8-yl)propionamide (29.4 mg, 0.10 mmol), 4-iodoanisole (93.6 mg, 0.40 mmol), Cs_2CO_3 (65.2 mg, 0.20 mmol), and (*R*)-P-amidite-POP (187 mg, 0.02 mmol) applying *m*-xylene as solvent. The reaction time was 72 h at 100 °C. The enantiomeric excess was determined by a Chiralpack AD column with hexane/*i*-PrOH = 80:20, retention times = 27.0 min for minor isomer and 32.3 min for major isomer.



3-(3,5-Dimethylphenyl)-3-(4-methoxyphenyl)-N-(quinolin-8-yl)propionamide

The compound was prepared according to the procedure above (standard catalytic reaction) using, Pd_2dba_3 (6.9 mg, 0.0075 mmol), 3-(3,5-dimethylphenyl)-*N*-(quinolin-8-yl)propionamide (30.4 mg, 0.10 mmol), 4-iodoanisole (93.6 mg, 0.40 mmol), Cs_2CO_3 (65.2 mg, 0.20 mmol), and (*R*)-P-amidite-POP (187 mg, 0.02 mmol) applying *m*-xylene as solvent. The reaction time was 72 h at 100 °C. The enantiomeric excess was determined by a Chiralcel-OD-H column with hexane/*i*-PrOH = 85:15, retention times = 22.9 min for major isomer and 27.2 min for minor isomer.

Recycling Experiment

An experiment was started as described for 3-phenyl-3-(4-methoxyphenyl)-*N*-(quinolin-8-yl)propionamide with $Pd_2(dba)_3$ (6.9 mg, 0.0075 mmol), 3-phenyl-*N*-(quinolin-8-yl)propionamide (27.6 mg, 0.10 mmol), 4-iodoanisole (93.6 mg, 0.40 mmol), Cs_2CO_3 (65.2 mg, 0.20 mmol), and (*R*)-P-amidite-POP (187 mg, 0.02 mmol) were mixed with a stir bar in a 4 mL vial inside an argon filled glovebox. *m*-Xylene (0.6 mL) was added to the mixture and the vial was sealed with a PTFE-lined screw cap. Outside the glovebox, the vial was put into an aluminum heating block at 100 °C for 72 h at 1000 rpm. After the specified time, the reaction mixture was cooled down to rt. before a stock solution of dibenzylether in EtOAc was added as a NMR standard – 0.5 mL of a 0.05 M stock solution. The organic residues were extracted from the solids with hexane 3 times and the combined organic phase was concentrated and analyzed by NMR. The crude mixture was purified by silica gel chromatography (85:15 heptane:EtOAc)

before the enantiomeric excess was quantified by HPLC on a Chiralcel-OD-H column with hexane/*i*-PrOH = 80:20, flow rate 0.9 mL/min, 22.3 min for major isomer and 26.9 min for minor isomer. The remaining solids from the extraction with hexane were dried before being taken into a glovebox and reused as the source of P-amidite-POP and with either adding or not adding a fresh amount of $Pd_2(dba)_3$. Thereafter, the procedure was repeated as described in the beginning with the addition of 3-phenyl-*N*-(quinolin-8-yl)propionamide (27.6 mg, 0.10 mmol), 4-iodoanisole (93.6 mg, 0.40 mmol), and Cs_2CO_3 (65.2 mg, 0.20 mmol) and *m*-xylene (0.6 mL).

Leaching Test

An experiment was started as described for 3-phenyl-3-(4-methoxyphenyl)-*N*-(quinolin-8-yl)propionamide with $Pd_2(dba)_3$ (6.9 mg, 0.0075 mmol), 3-phenyl-*N*-(quinolin-8-yl)propionamide (27.6 mg, 0.10 mmol), 4-iodoanisole (93.6 mg, 0.40 mmol), Cs_2CO_3 (65.2 mg, 0.20 mmol), and (*R*)-P-amidite-POP (187 mg, 0.02 mmol) were mixed with a stir bar in a 4 mL vial inside an argon filled glovebox. *m*-Xylene (0.6 mL) was added to the mixture and the vial was sealed with a PTFE-lined screw cap. Outside the glovebox, the vial was put into an aluminum heating block at 100 °C for 72 h at 1000 rpm. After the specified time, the reaction mixture was cooled down to room temperature and the organic residues were extracted from the solids with hexane 3 times. The solvent was removed from the combined organic phase and the resulting mixture was dissolved 2% HNO₃ for ICP-OES, EtOAc for analysis XRF, or CDCl₃ for NMR.
8 Direct C(sp²)-H borylation of arenes with porous organic polymers



8.1 Introduction to C(sp²)-H borylation of arenes

Organoboron compounds have played an important role in the development of organic synthesis as a versatile building block frequently used to access a variety of other functional groups.^{259–262} Important transformation involving C-C, C-O, C-N, C-X bond formation can readily be accessed through organoboron compounds with Suzuki cross-couplings, Chan-Lam couplings etc. Moreover, the use of organoboronic compounds have also found pharmaceutical applications for example with the anti-cancer drug, Bortezomib.²⁶² As such, the benign formation of organoboron compounds is highly attractive. However, the general method to access boron functionality goes through halides either directly or by an organometallic intermediate using lithium or magnesium resulting in high amount of waste (Scheme 8.1 path a and b). A more attractive alternative is the direct C-H borylation as it generate less waste and reduces the need of prehalogenation (path c) in line with the principles of green chemistry.²⁶³



Scheme 8.1. Different methodologies to form organoboron compounds. path a) Through an organometallic intermediate using stoichiometric metal, path b) a metal-catalyzed process, and path c) the direct metal-catalyzed C-H borylation.

For the borylation of arenes, iridium catalysts using bpy-type ligands have shown very promising results. Hartwig and Miyaura *et al.*²⁶⁴ reported one of the first examples of an Ir/bpy-based catalytic systems in 2002, which was capable of borylating twice per pinacolborane (H₂pin₂) with up to 95% yield using 3 mol% iridium ([Ir(cod)Cl]₂) under fairly mild conditions compared to alternative ligand systems at the time.^{265,266} In their study, they tested other ligands like Phen, PPh₃ and dppe, but they were either completely inactive (PPh₃ and dppe) or had inferior activity compared to bpy (Phen). They also tried to replace iridium with other metals like rhenium, as the first example of direct C-H borylation was conducted with a rhenium complex, but these metals were either completely inactive or only provided sluggish results.²⁶⁷ Thus, the combination of iridium and bpy was proven to be the most promising and have led to the formation of many derivatives of similar systems.^{264,268–272}

For borylation of arenes using $[Ir^{I}(cod)Cl]_{2}$ and bpy as the active catalyst, it has been reported that the active catalyst is not the formed $Ir^{I}(cod)(bpy)Cl$ but rather an $Ir^{III}(bpy)(pin)_{3}$ -complex.²⁵⁹ This Ir^{III} -complex can undergo C-H activation by oxidative addition of the arene followed by reductive elimination forming the borylated arene. The catalytic active complex is then regenerated by reacting with $B_{2}pin_{2}$ or HBpin to

release either HBpin or H₂, respectively. The mechanism is visualized in Scheme 8.2. As a consequence of this pathway, complex **4** in Scheme 8.2 must be reactive towards both B_2pin_2 and HBpin to utilize both boron in the reaction. If not, B_2pin_2 can only borylate once per molecule, which will decrease the atom economy significantly and lead to undesired byproducts in the form of HBpin.²⁷³



Scheme 8.2. Established mechanism for the borylation of arenes using an Ir/bpy catalytic system with corresponding oxidation states of iridium. COD is an abbreviation of 1,5-cyclooctadiene. Adapted from Li *et al.*²⁵⁹

When Ir/bpy systems are used on functionalized arenes, borylation can occur either *ortho, meta,* or *para* to the functional group yielding different products. The selectivity will to a high degree follow steric effects as the *para and meta* positions are favored over the more sterically hindered *ortho* position.^{260,264–266,274} The product distribution often follows a statistic distribution of 1:2 between *para* and *meta* with deviations based on the functional groups. Over the past decades catalytic Ir/bpy-based systems have been developed that are capable of borylating selectively in either the *ortho-, meta-* or *para*-position exclusively.^{275–280} These strategies rely on chemical charges, chelating effects, and other kinds of chemical interaction to favor a certain geometry of the transition state to activate the C-H bond similar to the auxiliary strategy seen in Section 7.2 for the asymmetric C(sp³)-H arylation. Yet, these examples require either specific functional groups on the aryl or expensive catalytic systems, which remove some of the benefits of direct C-H borylation.

Most of the reported examples of active catalysts are homogeneous, but as mentioned throughout the dissertation, the use of heterogeneous catalysts is beneficial over homogeneous catalysis and evidently attractive in the direct C-H borylation of arenes as well. Reports of heterogeneous systems capable of borylating arenes are present using grafted silica,^{268–271,273,281} MOFs,^{282,283} COFs,^{284,285} and POPs²⁸⁶ as catalyst. Still, the reports of only one POP-based system highlights the unexplored potential for these

systems in the direct borylation of arenes. A schematic illustration of the POP-based catalytic systems is shown in Figure 8.1.



Figure 8.1. Schematic presentation of the POP-based catalytic system from Nakano et al.²⁸⁶

It was attractive to test the potential of a swellable PS-POP incorporated with bpy as catalysts similar to the previous project. Sawamura *et al.* have already shown that swollen PS POPs are active in C(sp²)-H alkene borylation, but no reports of borylation of arenes exist for PS-based POPs.¹⁸⁴ On the contrary, Inagaki *et al.* have reported that a PS-based catalyst was completely inactive in their study.²⁷⁰ Despite this, the incorporation of bpy into a PS-based POP have good potential to create an active heterogeneous catalyst in the presence of iridium especially as more constrained bpy-ligands have demonstrated to be superior in the transformation.²⁸⁷ Furthermore, the POP-based system can potentially induce regioselectivity due to the steric hindrance of the polymer backbone. The idea is visualized in Scheme 8.3 where the potential of steric hindrance may favor borylation in the *para*-position rather than *meta*.



Scheme 8.3. Illustration of borylation *para* and *meta* to a mono-functionalized arene and how the POP may induce regioselectivity through steric hindrance.

8.2 Synthesis and polymerization of bpy-based porous organic polymers

With the promising reports from Ir/bpy-based systems for the borylation of arenes, two different PSbased POPs with bpy ligands were synthesized. To gain access to these POPs, vinylated 2,2'-bipyridine was readily made from 4,4'-dibromo-2,2'-bipyridine by a Suzuki cross-coupling similar to the previous project (Section 7.3).²⁸⁸ The synthetic procedure is seen in Scheme 8.4. Next, the emulsion polymerization methodology developed by Sawamura *et al.* was applied as it was believed that the 4,4'-divinyl-2,2'- bipyridine would not be sensitive towards the conditions in contrast to the phosphoramidites. Two POPs were synthesized using either styrene or 4-*tert*-butylstyrene to give different steric hindrance at the bpy site. They are abbreviated bpy-PS-POP if styrene was applied and bpy-^tBuPS-POP if 4-*tert*-butylstyrene was used instead. The emulsion methodology yielded small polymer beads with similar swelling properties as the previous PS-POPs as they swelled in THF, benzene, toluene, and dioxane and deswelled in hexane (see Figure 8.2 for an image of the two synthesized POPs). It was assumed that all bpy had been incorporated into the POP during the polymerization, which then provided a ligand density of 0.00054 mmol bpy/mg POP.



Scheme 8.4. Illustration of how to form bpy-PS-POP and bpy-^tBuPS-POP. a) Synthesis path to get access to vinylated 2,2'-bipyridine and b) how the resulting bpy-based POPs are synthesized via an emulsion methodology. Adapted from Kegnæs *et al.*¹⁸⁹



Figure 8.2. Image of the two synthesized bpy-POPs with bpy-PS-POP to the left and bpy-^tBuPS-POP to the right. Adapted from Kegnæs *et al.*¹⁸⁹

8.3 Catalytic assessment in the borylation of arenes

The synthesized POPs were initially evaluated in the borylation of benzene where the active catalytic specie was formed *in-situ* by mixing the bpy-POP with [Ir(cod)Cl]₂. To ensure consistent results, premixing of the POP and iridium source were necessary before adding the boron precursor, which have also been demonstrated by Smith *et al.* to influence the reaction.²⁸⁷ Initial results of the Ir/POP-system showed excellent performance when benzene was used in excess as solvent and B₂pin₂ was used as boron source. Under these conditions, the system was able to borylate twice per B₂pin₂ providing yields exceeding 100% based on the amount of boron reagent added (this way of presenting yields will be continued so all values

are based on the amount of $B_2 pin_2$ added). With 0.5 mol% [Ir(cod)Cl]₂ (1 mol% Ir), 5% bpy-PS-POP at 60 °C for 6 h using benzene as solvent (1 mL) with 0.1 mmol B₂pin₂ as limiting reagent, the system provided quantitative yields of borylated benzene (200%) for both POPs (Table 8.1 entries 1-2). Decreasing the reaction time down to 4 h still gave 200% yield for bpy-PS-POP, but bpy-^tBuPS-POP did not reach completion with 178% yield (entries 3-4). Next, the concentration of B₂pin₂ was increased to 0.2 M instead of 0.1 M, which lowered the yield to either 180% or 172% for bpy-PS-POP and bpy-^tBuPS-POP, respectively (entries 5-6). Changing the iridium source to [Ir(cod)MeO]₂ decreased the yield slightly for both POPs (entries 7-8) in line with other reports under similar conditions.²⁸⁷ Surprisingly, decreasing the amount of ligand (POP) to 2.5 mol% resulted in a significant drop in product yield and upon decreasing to 1.5 mol% bpy, no catalytic activity was observed (entries 9-10). This illustrated a strong dependency on ligand concentration in the reaction. A test reaction without POP gave no formation of product (entry 11). Replacing benzene with toluene provided only sluggish product formation initially with 65% yield, but by prolonging the reaction to 24 hours resulted in quantitative yield of the borylated products (entries 12-13). The bpy-^tBuPS-POP was also active using toluene as arene, but did not reach the same yield as bpy-PS-POP. The borylated products had a statistic distribution between being meta or para functionalized with a 2:1 ratio with no indication of incorporation of the boronic ester ortho to the methyl group when toluene was used as substrate.

Table 8.1. Optimization of the reaction condition for borylation of arenes with POPs. Adapted from Kegnæs et al. 189

	B ₂ pin ₂	0.5 mol% [lr(cod)Cl] ₂ 5 mol% bpy-PS-POP → 6 h, 60°C	Bpin 2
solvent (0.1M) 0.1 mm	ol	
Entry ^a	Modification		Yield ^b
1	_		200%
2	bpy- ^t BuPS-F	198%	
3	4 h	200%	
4	4 h, bpy- ^t BuPS-POP		178%
5	0.2 M		180%
6	0.2 M, bpy- ^t BuPS-POP		172%
7	[Ir(cod)MeO] ₂		189%
8	[Ir(cod)MeO] ₂ bpy- ^t BuPS-POP		183%
9	2.5 mol% bpy-PP-POP		121%
10	1.5 mol% bpy-PP-POP		0%
11	no POP	0%	
12 ^c	toluene 65%		
13 ^c	toluene, 24 h 200%		
14 ^c	toluene, 24 h, bpy- ^t BuPS-POP 174%		

^a Iridium and POP are premixed for 5 min in the solvent before the addition of $B_2 pin_2$.

^b Yields are quantified by NMR using 1,3,5-trimethoxybenzene as standard.

^c Regioselectivity = *para:meta:ortho* 1:2:0.

Next, the robustness of the systems were examined by scaling up the reaction from 0.1 mmol to 2.0 mmol B_2pin_2 using either bpy-PS-POP and bpy-^tBuPS-POP under similar condition as presented in Table 8.1 entries 13-14 (toluene, 0.5 mol% [Ir(cod)Cl]₂, 5 mol% bpy-POP for 24 h at 60 °C). The results are presented in Scheme 8.5 where using the bpy-PS-POP reached 165% isolated yield of the products. However, the

more sterically hindered bpy-^tBuPS-POP only managed 94% isolated yield under the same conditions. Nevertheless, the results demonstrated that the processes were scalable, albeit with a small drop in yield for bpy-PS-POP and a significant drop for bpy-^tBuPS-POP.



Scheme 8.5. Illustration of the scaled up borylation of toluene using either bpy-PS-POP or bpy-^tBuPS-POP with corresponding isolated yields and product distribution. Adapted from Kegnæs *et al.*¹⁸⁹

Different arenes and heterocycles were tested next to see if the success with benzene and toluene could be transferred to other aryls. The results are presented in Table 8.2 where each aryl have been tested with both POPs. The use of anisole as substrate proceeded nicely providing either 192% yield or 165% depending on the POP (entries 1-2). The product distribution favored meta over para with no reaction taking place at the ortho position. Fluorobenzene on the other hand gave a mixture of both ortho, meta, and para functionalized products in an excellent yield for bpy-PS-POP and lower yield for the bpy-^tBuPS-POP (entries 3-4). The use of chlorobenzene provided good yields for both POPs with a product distribution favoring the meta functionalized product as well (entries 5-6) whereas iodobenzene proceeded in more moderate yields for both POPs (entries 7-8). m-Xylene provided very limited yield under normal conditions, but a raise in temperature from 60 °C to 100 °C provided an increase in the yield from 18% to 100% for the bpy-PS-POP system and 16% to 48% for the bpy-^tBuPS-POP system (entries 9-10). Non-coordinating heterocycles such as 1-methylpyrrole and benzofuran were tested too, but even at 100 °C the yield was very limited or the reaction did not proceed at all as no borylated products were observed (entries 11-14). Attempts to use trifluorotoluene were unfruitful as the POPs did not swell in this polar solvent and demonstrated one of the limitations of using swollen POPs as part of the active catalyst. Nevertheless, the results combined with the previous trends clearly indicated that the introduction of tert-butyl in bpy-^tBuPS-POP hindered the activity with overall lower yields than for the bpy-PS-POP. Moreover, the regioselectivity was not effected by incorporating the bpy ligand into a polymer backbone as even the very sterically hindered ortho-position was borylated for fluorobenzene. Not even the introduction of the more bulky tert-butyl groups into the polymer provided any significant change in regioselectivity as the trends from the product distribution seemed to follow the substrate rather than the POP with the only exception being fluorobenzene that had less functionalization in meta and *ortho* position for bpy-^tBuPS-POP compared to bpy-PS-POP.

Table 8.2. Results of using different arenes and heterocycles with bpy-PS-POP and bpy-^tBuPS-POP. Adapted from Kegnæs *et al.*¹⁸⁹

	Ar	$B_2 pin_2$	0.5 mol% [lr(coo 5 mol% POP 24 h, 60°C		n
	solvent (0.	1M) 0.1 mmol			
Entry ^a	POP	Substrate	Product	Yield ^b	Product distribution para:meta:ortho
1 2	bpy-PS-POP bpy- ^t BuPS-POP	OMe	OMe	192% 165%	1:3.6:0 1:3.5:0
3 4	bpy-PS-POP bpy- ^t BuPS-POP	F	F	183% 106%	1:2.7:1.8 1:1.4:1.2
5 6	bpy-PS-POP bpy- ^t BuPS-POP			196% 172%	1:2.2:0 1:2.2:0
7 8	bpy-PS-POP bpy- ^t BuPS-POP	В	pin	122% 76%	1:1.4:0 1:1.5:0
9 10	bpy-PS-POP bpy- ^t BuPS-POP	Me Me Me	Me Bpin	18% (100% 16% (48%)') ^c
11 12	bpy-PS-POP bpy- ^t BuPS-POP	Me N	Me N	0% (9%) ^c 0% (9%) ^c	
13 14	bpy-PS-POP bpy- ^t BuPS-POP(Bpin O Bpin	0% (0%) ^c 0% (0%) ^c	

^a The iridium and POP are premixed for 5 min in the solvent before the addition of B₂pin₂.

^b Yields are quantified by NMR using 1,3,5-trimethoxybenzene as standard.

^c Yields for reaction at 100 °C shown in parantheses.

It has already been demonstrated that the Ir/POP-based catalysts are capable of borylating twice per B_2pin_2 , which is a very nice feature in term of economics and sustainability. As a result thereof, it was expected that H_2 was released from the reaction. Thus, the headspace volume was analyzed by gas chromatography (GC), which confirmed the presence of gaseous H_2 as illustrated in Figure 8.3a. The POP may potentially work as a hydrogen acceptor in the reaction and push the reaction towards completion by removing hydrogen. Therefore, the POPs were recovered after reaction and analyzed by XPS to investigate any potential structural changes (Figure 8.3b). The signals obtained from the C1s transitions did not show any change between the recovered and fresh POPs. Albeit, if the released H_2 could reduce

the double bonds in the POP and with the presence of more than 2.1 mmol double bonds coming from the POP, it was unlikely that such changes could be detected by XPS as a maximum of 0.05 mmol H_2 was released per reaction. Yet, when doing the reaction without a POP acting as a potential hydrogen acceptor, the reaction proceeded nicely with homogeneous 2,2'-bipyridine (Figure 8.3c). As such, the POP was not necessary for the reaction to occur if homogeneous bpy was present and with the presence of H_2 in the headspace volume strongly indicated that the POP did not act as a hydrogen acceptor.



Figure 8.3. a) Test to determine if H_2 is released by analyzing the head space volume with GC-FID. b) XPS spectra of the C1s signal for the two different POPs before and after (used) a catalytic reaction. c) A homogeneous setup to examine if the POP backbone is required as a H_2 acceptor for the catalytic activity to occur. Adapted from Kegnæs *et al.*¹⁸⁹

The release of H₂ matched well with the pathway from Scheme 8.2 and suggests that a similar mechanism occurred for these POP-based systems. To further assess if that was the case, experiments using HBpin as the boron source were done as it should also proceed if the catalytic active Ir^{III}-complex was formed from the pre-catalyst (going from complex **1** to **2** in Scheme 8.2). Two different experiments were performed where either some or all of the B₂pin₂ was replaced with HBpin. The results from these test are shown in Scheme 8.6 and demonstrated that HBpin could be used as a borylation reagent as well, but did not reach completion for bpy-^tBuPS-POP compared to Table 8.1 entry 2. A similar tendency have been reported for other [Ir(cod)Cl]₂/bpy catalytic systems where B₂pin₂ reacts more smoothly than HBpin.²⁸⁷



Scheme 8.6. Reaction conditions and results of replacing B₂pin₂ with HBpin partially or completely as the borylation reagent. Yields are relative to using 0.10 mmol B₂pin₂. Adapted from Kegnæs *et al.*¹⁸⁹

Next, competition studies were done between different functionalized arenes and benzene to investigate the electronic influence on the rate. The corresponding product distributions are presented in Table 8.3. These results showcased that electron rich arenes such as toluene and anisole reacted slower than benzene for both POPs (entries 1-4). Whereas less electron rich arenes such as fluorobenzene and chlorobenzene reacted faster than benzene (entries 5-8). However, the more electron deficient arenes did not reach completion with overall lower combined yields similar to Table 8.2. The influence on the reaction rate are in line with previous reports of homogeneous Ir-catalyzed systems and fits well with oxidative addition (going from specie **2** to **3** in Scheme 8.2) being selectivity determining.^{264,266,287}

1 : solvent	$ \begin{array}{c} R \\ B_2 pin_2 \\ 1 \\ (0.1M) \\ 0.1 mmol \end{array} $	nol% [Ir(cod nol% POP h, 60°C	\rightarrow \square	R H ₂ Bpin 2
Entry	^a POP	R	Combined	yield ^b Ratio (1:2)
1	bpy-PS-POP	CH ₃	200%	1:0.3
2	bpy- ^t BuPS-POP	CH_3	182%	1:0.3
3	bpy-PS-POP	OMe	200%	1:0.4
4	bpy- ^t BuPS-POP	OMe	173%	1:0.4
5	bpy-PS-POP	F	175%	1:3.0
6	bpy- ^t BuPS-POP	F	129%	1:4.2
7	bpy-PS-POP	CI	199%	1:2.6
8	bpy- ^t BuPS-POP	CI	83%	1:2.5

Table 8.3. Competitive studies between benzene and different arenes. Adapted from Kegnæs et al.¹⁸⁹

^a The iridium precursor and POP are premixed for 5 min in the solvent before the addition of $B_2 pin_2$. ^b Yields are quantified by NMR using 1,3,5-trimethoxybenzene as standard.

To further assess the pathway of the reaction, a time study was made by stopping reactions after specific times with benzene as substrate. The yields from these results were plotted against the reaction time and showed a sigmoidal curve with the appearance of an induction period (Figure 8.4 orange color). An induction period is common when applying B_2pin_2 as boron-source and $[Ir(cod)Cl]_2$ as precatalyst.²⁸⁷ In order to assess if the C-H bond played a central role in the kinetics, three experiments using d₆-benzene were made and stopped after 1.5, 2, and 2.5 hours, respectively (Figure 8.4 blue color). These two sets of data points were used to calculate the initial rates of the reaction and demonstrate if there was a difference in rate between using benzene or deuterated benzene. A linear approximation between 1.5-2 hours was made for the orange data points, whereas the three experiments from using deuterated benzene provided good linearity up to similar activity as when using normal benzene (57% yield for orange and 40% for blue). Thus, two trend lines were made and by comparing their slopes, a kinetic isotope effect (KIE) of 3.7 was obtained. This was consisting with a primary KIE effect and implied that the C-H bond was central in the rate-determining step. Furthermore, the two trend lines crossed the y-axis in almost the same value, which marked the time of the induction period (1.39 h for benzene and 1.35 h for d₆-benzene).

This observation demonstrated that the induction period was not affected by the C-H bond in agreement with the mechanism from Scheme 8.2 going from the pre-catalyst (1) to the active catalyst (2).



Figure 8.4. Time study with initial rates as trend lines. The orange data points are from using benzene and the blue data points are when d₆-benzene was applied instead. Adapted from Kegnæs *et al.*¹⁸⁹

A filtration experiment was conducted to reveal if the observed activity originated from homogeneous species. The experiment was done by filtering a reaction after 1 hour and 40 min inside a glovebox where a small part of the filtered liquid was analyzed by NMR and the remaining was reheated to 60 °C and stirred for 1 hour and 20 min before also being analyzed by NMR. The resulting yields were close to identical with 62% and 64% yield, respectively, and demonstrated that the observed activity originated from heterogeneous species in the mixture that could be filtered away.

The formation of nanoparticles have been an undesired phenomenon in the two previous projects using POP-based catalysts. Therefore, both POP catalysts were recovered and analyzed under a TEM microscope to detect if nanoparticles had formed in this project as well. The resulting images are shown in Figure 8.5 and demonstrated the formation of nanoparticles (image a and c). At the same time, there were also areas without any profound examples of nanoparticles where the presence of single atomic iridium could not be ruled out (image b and d).



Figure 8.5. TEM images of the recovered Ir/POP system with either bpy-PS-POP (a and b) or bpy-^tBuPS-POP (c and d). Adapted from Kegnæs *et al.*¹⁸⁹

Attempts to reuse the Ir/bpy-PS-POP system as an active catalyst were carried out with the conditions from Table 8.1 entry 1 (benzene, 0.10 mmol B₂pin₂, 5 mol% bpy-PS-POP, 0.5 mol% [Ir(cod)Cl]₂, 60 °C). The reaction time was reduced to 3 hours after it was demonstrated that the reaction reached completion at that point of time (Figure 8.4). In the initial attempt, the Ir/POP-catalyst was recovered outside the glovebox before being replenished with a new stock-solution of B₂pin₂ in benzene (0.1 M) inside a glovebox. However, no product formation was observed after 3 hours at 60 °C. In the next attempt, all recovery and reuse of the POP were conducted inside a glovebox for air-free recycling. Under these conditions, it was possible to recycle the catalyst as demonstrated in Table 8.4. 200% product yield was observed during the first three consecutive reactions (entries 1-3), whereas the activity dropped heavily at the third recycle (entry 4) and no activity was seen after the fourth recycle (entry 5). The drop in product yield was found in the extracted hexane phase after the first reaction. Nevertheless, these results demonstrated that the active catalyst in the reaction mixture deactivated when exposed to atmospheric air. This also indicated that the nanoparticles observed in the TEM images in Figure 8.5 may not be formed under the catalytic conditions but rather doing recovery and exposure to atmospheric air.

		$B_2 pin_2$	$ \begin{array}{c} \text{0.5 mol\% [Ir(cod)CI]}_2 \\ \xrightarrow{5 \text{ mol\% bpy-PS-POP}} 2 \\ \xrightarrow{4 \text{ H}_2} \\ \text{H}_2 \end{array} $
S	olvent (0	.1M) 0.1 mmol	
E	ntry ^a	Recycles	Yield ^b
1		0	200%
2		1	200%
3		2	200%
4		3	4%
5		4	0%

Table 8.4. Results of recycling the Ir/POP catalytic systems. Adapted from Kegnæs et al.¹⁸⁹

^a The iridium precursor and POP are premixed for 5 min in benzene before additing B_2pin_2 . ^b Yields are quantified by NMR using 1,3,5-trimethoxybenzene as standard.

A potential critical flaw of using PS-based POPs for C(sp²)-H borylation is that the polymer backbone consists of reactive C-H bonds that potentially can be borylated as well. Thus, the recovered POPs from the scale-up reaction using toluene as substrate were analyzed by ¹¹B MAS NMR to examine if borylation have occurred on the POP as well. The resulting spectra are presented in Figure 8.6 and showed the presence of boron species at a chemical shift of 25.6 ppm for both POPs and a signal at 10 and -5 ppm for bpy-^tBuPS-POP as well. The interpretation of these signals turned out to be very difficult as the difference between boronic species can be very small.²⁸⁹ In an attempt to elucidate the origin of the signals in the spectra, a reference experiment with B₂pin₂ was done and gave a clear signal at 24.3 ppm. Boroncontaining species such as HBpin and Ir-complexes were possible in the mixture as well based on the mechanism from Scheme 8.2. However, HBpin has been reported at 28.2 ppm and derivatives of possible Ir(bpy)-complexes have had signals at chemical shifts around ≈ 32 ppm.^{290,291} Based on these observations, it was assumed that the signals at 25.6 ppm originated from borylation of the POP due to its deviation from other potential species. Moreover, the intensity of the signal was highest from the bpy-PS-POP indicating that the more sterically hindered bpy-^tBuPS-POP inhibited the borylation of the backbone. The signals at 10 and -5 ppm were still inconclusive even when the signals originating from the rotor and probe was ruled as they were subtracted from the spectra.



Figure 8.6. ¹¹B MAS NMR of recovered POP from scale-up experiment with bpy-PS-POP to the left and bpy-^tBuPS-POP to the right. Adapted from Kegnæs *et al.*¹⁸⁹

8.4 Summary

Two different PS-based POPs with bpy functionality were synthesized with either styrene or 4-*tert*butylstyrene in the polymer backbone. Both POPs demonstrated excellent activity for various arenes capable of borylating twice per molecule B₂pin₂. Unfortunately, the incorporation of bpy into the POP backbone did not provide any altered regioselectivity as hoped. In general, the more bulky bpy-^tBuPS-POP was less activity than the less sterically hindered bpy-PS-POP. Nevertheless, the systems seemed to proceed through an Ir^{III}/Ir^V catalytic cycle where the precatalyst ([Ir^I(cod)Cl]₂) has to be activated to form the actual catalytic specie. This was showcased by the formation of gaseous H₂ from the reaction mixture, its capability to borylate with both B₂pin₂ and HBpin, and the presence of an induction period. The ratelimiting step seemed to be the C-H activation by oxidative addition based on the observation of a primary KIE of 3.7. The system was recycled successfully with full product formation in the first three consecutive reactions, albeit the catalytic activity was completely lost reaching the fifth consecutive reaction. Solidstate ¹¹B MAS NMR of the recovered catalyst indicated that borylation can also occur at the polymer backbone, which is a drawback of the system.

8.5 Experimental

Chemicals

All chemicals were reagent grade and used as received without further purification. NaCl and benzene was purchased from TCI. B₂pin₂ and 4,4'-dibromo-2,2'-bipyridine were obtained from Fluorochem. Toluene was obtained from a solvent purification system (Puresolv MD-7). The remaining chemicals were obtained from Sigma Aldrich; [Ir(cod)Cl]₂, [Ir(cod)OMe]₂, HBpin, anisole, trifluorotoluene, fluorobenzene, chlorobenzene, iodobenzene, 1-methylpyrrole, benzofuran, d₆-benzene, potassium vinyltrifluoroborate, PPh₃, Pd(OAc)₂, Cs₂CO₃, acacia gum, styrene, divinylbenzene, 4-*tert*-butylstyrene and 0.2 M AIBN in toluene.

Equipment

TEM images were obtained using a Technai T20 G2 microscope from TEI. Samples were deposited on 300 mesh Cu grids with no prior treatment. XPS was done with a spot size of 400 μ m with an Al alpha X-ray source with 10 scans per element. XRF analysis was conducted on a PANalytical Epsilon3 system. Liquid ¹H NMR was measured on a Bruker Ascend 400 (400 Hz). ¹¹B MAS NMR experiments were conducted using a Bruker Avance III spectrometer (B₀ = 11.75 T, v_L(¹¹B) = 192.546 MHz) equipped with a 4 mm CP/MAS Probe. The spectra were acquired with the Hahn echo pulse sequence ($\pi/2 - \tau - \pi - \tau - ACQ$) using a spinning frequency of 8000 Hz, a "solid $\pi/2$ " pulse of 3 us ($\pi/2$ (NaBH₄) = 6 μ s), and an interscan delay of 30 seconds. High-power SPINAL64 ¹H decoupling was applied during acquisition. Chemical shifts are reported relative to F₃B·O(C₂H₅) ($\delta_{iso} = 0$ ppm) using neat NaBH₄ as a secondary reference ($\delta_{iso} = -42.06$ ppm). An ¹¹B spectrum of an empty rotor has been subtracted for all presented spectra to eliminate any background signals from the probe. The Topspin module SOLA was used for simulating the quadrupolar lineshapes.

Vinylation of 4,4'-dibromo-2,2'-bipyridine adapted from Zhong et al.²⁸⁸

4,4'-dibromo-2,2'-bipyridine (0.32 mmol, 100 mg), potassium vinyltrifluoroborate (1.27 mmol, 170 mg), Pd(OAc)₂ (0.0064 mmol, 1.4 mg), PPh₃ (0.020 mmol, 5.0 mg), and Cs₂CO₃ (0.96 mmol, 311 mg) were weighed into a Schlenck tube where a magnetic stir bar was added. The mixture was made inert by 3 vacuum/N₂ cycles. Next, degassed THF (4.8 mL) and degassed H₂O (0.2 mL) were added to the solids and inside a N₂-filled plastic bag the Schlenck tube was sealed. The reaction mixture was heated to 85 °C for 48 h behind a blast shield. Next, the mixture was cooled down to rt. and H₂O (15 mL) was added before the organic phase was extracted with dichloromethane (20 mL) four times. The organic phase was washed with brine (50 mL) and dried over MgSO₄. The solvent was removed and the product was purified over silica gel chromatography in a mixture of hexane, EtOAc and Et₃N (90:10:2) providing a white powder (48 mg, 70% yield).

Polymerization procedure

 H_2O (60 mL), NaCl (26 mmol, 1.5 g), and acacia gum (2.4 g) were mixed into a 250 mL round-bottom flask with a magnetic stir bar. The mixture was stirred to create a clear solution and before being bubbled with N₂. In a 10 mL round-bottom flask, 4,4'-divinyl-2,2'-bipyridine (0.31 mmol, 65 mg), styrene (15 mmol, 1.71 mL, 1.55 g) or 4-*tert*-butylstyrene (15 mmol, 2.75 mL, 2.4 g), divinylbenzene (0.31 mmol, 43.5 μ L, 39.7 mg), and chlorobenzene (3 ml) were mixed and a magnetic stir bar was added. The mixture was sealed with a rubber septum and bubbled with N₂. After being bubbled, 0.2 M AIBN in toluene (0.3 mmol, 1.5 mL) was added and the whole content was mixed with the aqueous mixture in the 250 mL round-bottom flask by a syringe. The combined mixture was emulsified by stirring the mixture at 600 rpm for 1 h before being heated to 80 °C by an oil bath to start the polymerization. The mixture was left to stir overnight at 80 °C. The next day, the POP was collected on a glass funnel and washed 3x times with H₂O (50 mL), methanol (50 mL), THF (50 mL), and toluene (50 mL) before being dried in a vacuum oven. The procedure yielded white/off-white small beads.

General borylation procedure in 0.1 mmol scale

Inside an argon filled glovebox, a stock solution of either [Ir(cod)Cl]₂ or [Ir(cod)OMe]₂ (0.0017 mmol, 1.2 mg) in arene or heterocycle (3.5 mL) was initially prepared in a 4 mL vial. In another 4 mL vial, bpy-POP

(0.0015-0.005 mmol bpy, 2.8-9.2 mg) was weighed off and a magnetic stir bar was added before 1 mL of the iridium-stock solution was mixed with the POP. The resulting mixture was premixed for 5 min before B_2pin_2 (0.05-0.1 mmol, 12.7-25.4 mg) was added and the vial was sealed with a PTFE-lined screw cap. Outside the glovebox, the vial was put into an aluminum heating block at either 60 or 100 °C for the specified time at 1200 rpm. After the specified time, the reaction mixture was cooled down to rt. before a stock solution of 1,3,5-trimethoxybenzene in dichloromethane was added as a NMR standard (0.5 mL of a 0.2 M stock solution). Afterwards, 1 mL hexane was added and the reaction was mixed thoroughly before approximately 0.4 mL was being filtered through a 0.22 μ m syringe filter and concentrated on vacuum. The resulting mixture was analyzed by NMR using CDCl₃ as solvent.

Procedure for 2.0 mmol scale

Inside an argon filled glovebox, [Ir(cod)Cl]₂ (0.01 mmol, 6.69 mg), bpy-POP (0.1 mmol bpy, 185.2 mg) and toluene (20 mL) was mixed in a 50 mL round-bottom flask with a magnetic stir bar. The resulting mixture was premixed for 5 min before B₂pin₂ (2.0 mmol, 508 mg) was added and the vial was sealed with a rubber septum. Outside the glovebox, the round-bottom flask was put into an oil bath and heated to 60 °C for 24 h at 1000 rpm. Thereafter, the reaction mixture was cooled down to rt. before hexane (20 mL) was added to the mixture. The solid catalysts was collected on a glass funnel and washed with 20% EtOAc in hexane (150 mL). The solid catalyst was dried in a vacuum oven for *post* characterization whereas the solvent was removed from the filtrate to yield a clear viscous oil of borylated toluene.

Competition study

Inside an argon filled glovebox, a stock solution of $[Ir(cod)Cl]_2$ (0.0017 mmol, 1.2 mg) in a 1:1 mixture of benzene and an arene (1.75 mL each) was initially prepared in a 4 mL vial. In another 4 mL vial, bpy-POP (9.2 mg, 0.005 mmol bpy) was weighed off and a magnetic stir bar was added before 1 mL of the iridium-stock solution was mixed with the POP. The resulting mixture was premixed for 5 min before B₂pin₂ (0.1 mmol, 25.4 mg) was added and the vial was sealed with a PTFE-lined screw cap. Outside the glovebox, the vial was put into an aluminum heating block at 60 °C for 24 h at 1200 rpm. Next, the reaction mixture was added as a NMR standard (0.5 mL of a 0.2 M stock solution). Afterwards, 1 mL hexane was added and the reaction was mixed thoroughly before approximately 0.4 mL was being filtered through a 0.22 μ m syringe filter and concentrated on vacuum. The resulting mixture was analyzed by NMR using CDCl₃ as solvent.

Kinetic isotope effect

Inside an argon filled glovebox, a stock solution of $[Ir(cod)Cl]_2$ (0.0017 mmol, 1.2 mg) in d₆-benzene (3.5 mL) was initially prepared in a 4 mL vial. In another 4 mL vial, bpy-PS-POP (0.005 mmol bpy, 9.2 mg) was weighed off and a magnetic stir bar was added before 1 mL of the iridium-stock solution was mixed with the POP. The resulting mixture was premixed for 5 min before B₂pin₂ (25.4 mg, 0.1 mmol) was added and the vial was sealed with a PTFE-lined screw cap. Outside the glovebox, the vial was put into an aluminum heating block at 60 °C for the specified time at 1200 rpm. After the specified time, the reaction mixture was cooled down to rt. before a stock solution of 1,3,5-trimethoxybenzene in dichloromethane was added as a standard (0.5 mL of a 0.2 M stock solution). Afterwards, 1 mL hexane was added and the reaction was mixed thoroughly before approximately 0.4 mL was being filtered through a 0.22 µm syringe filter and concentrated on vacuum. The resulting mixture was analyzed by GC-FID-MS using EtOAc as solvent.

Test with HBpin

Inside an argon filled glovebox, a stock solution of $[Ir(cod)Cl]_2$ (1.2 mg, 0.0017 mmol) in benzene (3.5 mL each) was initially prepared in a 4 mL vial. In another 4 mL vial, bpy-POP (9.2 mg, 0.005 mmol bpy) was weighed off and a magnetic stir bar was added before 1 mL of the iridium-stock solution was mixed with the POP. The resulting mixture was premixed for 5 min before either B₂pin₂ (12.7 mg, 0.05 mmol) and HBpin (12.8 mg, 11.3 µL, 0.1 mmol) or HBpin (25.6 mg, 22.6 µL, 0.2 mmol) were added and the vial was sealed with a PTFE-lined screw cap. Outside the glovebox, the vial was put into an aluminum heating block at 60 °C for 6 h at 1200 rpm. Next, the reaction mixture was cooled down to rt. before a stock solution of 1,3,5-trimethoxybenzene in dichloromethane was added as a NMR standard (0.5 mL of a 0.2 M stock solution). Afterwards, 1 mL hexane was added and the reaction was mixed thoroughly before approximately 0.4 mL was being filtered through a 0.22 µm syringe filter and concentrated on vacuum. The resulting mixture was analyzed by NMR using CDCl₃ as solvent.

Filtration experiment

Inside an argon filled glovebox, a stock solution of $[Ir(cod)Cl]_2$ (0.0017 mmol, 1.2 mg) in benzene (3.5 mL) was initially prepared in a 4 mL vial. In another 4 mL vial, bpy-PS-POP (0.005 mmol bpy, 9.2 mg) and 1,3,5-trimethoxybenzene (16.8 mg, 0.1 mmol) were weighed off and a magnetic stir bar was added before 1 mL of the iridium-stock solution was mixed with the POP. The resulting mixture was premixed for 5 min before B_2pin_2 (25.4 mg, 0.1 mmol) was added and the vial was sealed with a PTFE-lined screw cap. Outside the glovebox, the vial was put into an aluminum heating block at 60 °C for 1 hour and 40 min at 1200 rpm. Next, the reaction mixture was taken into the glovebox again, filtered through a 0.22 µm syringe filter and added to a new 4 mL vial with a magnetic stir bar. A small part of the liquid was taken for one NMR sample before the vial was sealed with a new PTFE-lined screw cap again. Outside the glovebox, the vial was put into an aluminum heating block at 60 °C for 1 hour and 40 min at sealed with a magnetic stir bar. A small part of the liquid was taken for one NMR sample before the vial was sealed with a new PTFE-lined screw cap again. Outside the glovebox, the vial was put into an aluminum heating block at 60 °C for 1 hour and 20 min at 1200 rpm. Afterwards, the mixture was concentrated on vacuum and was analyzed by NMR using CDCl₃ as solvent.

Recycling experiment

Inside an argon filled glovebox, a stock solution of $[Ir(cod)Cl]_2$ (0.0017 mmol, 1.2 mg) in benzene (3.5 mL) was initially prepared in a 4 mL vial. In another 4 mL vial, bpy-PS-POP (0.005 mmol bpy, 9.2 mg) was weighed off and a magnetic stir bar was added before 1 mL of the iridium-stock solution was mixed with the POP. The resulting mixture was premixed for 5 min before B₂pin₂ (25.4 mg, 0.1 mmol) was added and the vial was sealed with a PTFE-lined screw cap. *Outside the glovebox, the vial was put into an aluminum heating block at 60 °C for 3 hours at 1200 rpm. Then, the reaction mixture was taken into the glovebox and placed under vacuum to remove excess benzene. The resulting solids was extracted with hexane (3x2 mL) where 1,3,5-trimethoxybenzene (16.8 mg, 0.1 mmol) was added to the combined hexane phase. To the remaining solids, a solution of 0.1 M B₂pin₂ in benzene (1 mL) was added before the vial was sealed with a PTFE-lined screw cap and was taken out of the glovebox to repeat the procedure as described above from the asterisk(*). The combined hexane phase was concentrated under vacuum and analyzed on NMR using CDCl₃ as solvent.

9 Summary and conclusions

In **Chapter 3**, the successful formation of an alloy catalyst between cobalt and nickel was achieved by carbonizing a nickel impregnated ZIF-67. The methodology was novel and had many advantages as other combinations of alloys could be readily made as well. The alloy nanoparticles were stabilized on a nitrogen-doped carbon structure. The catalyst did not leach metal during the reaction and had a porous structure evident by N₂-physisorption. The material was assessed in the hydrosilylation of ketones where it showed to be easy to recover and recycle due to its magnetic properties. The catalyst demonstrated good activity towards different cyclic aliphatic ketones and derivatives of acetophenone whereas aliphatic ketones and ketones with bulky functional groups only provided limited activity. The reaction pathway was believed to be an Ojima-type mechanism as the transformation proceeded unaffected by different radical inhibitors and had strong dependency on steric hindrance.

Chapter 4 covered the α -alkylation of ketones with alcohols as masked electrophiles using commercially available Pd/C as catalyst. The reaction proceeded under very mild conditions compared to similar heterogeneous Pd catalysts. The system tolerated both alcohols and ketones with electron donating and withdrawing functional groups excellently. Albeit, a secondary alcohol was completely inactive, and aliphatic alcohols required a temperature increase to proceed adequately. The system showed to be heterogeneous in nature, did not leach metal, and the catalyst could be recycled three times without any significant loss of activity or selectivity. The mechanism was elucidated with stoichiometric experiments and *in-situ* IR where it was found that a hydrogen-borrowing pathway fitted nicely with the results. The tests also demonstrated reversibility in the dehydrogenation step, that the catalyst was not inhibited or poisoned during the reaction conditions, and that the rate-limiting step was the base catalyzed aldol condensation. This meant that the expensive palladium did not play a part in the rate limiting step and that the metal loading could be decreased without effecting the activity.

In **Chapter 6**, a POP-based catalytic system was investigated in the hydrogenation of CO_2 to FA where five different PP-based POPs were synthesized. All POPs containing ligands did not show any porosity during N₂-physisorption analysis. However, changing to CO_2 as adsorbate provided a clear adsorption trend with PP-POP and bpy-PP-POP being the most porous. In the catalytic assessment, the bpy-PP-POP achieved a TON-value >20,000, which was one of the highest for a POP-based system over one reaction. Attempts to recreate the catalytic activity with homogeneous analogues were unsuccessful. It was assumed that the incorporation of ligand into the POP prevented the formation of inactive species that otherwise would be formed such as dimers and saturated complexes. The catalytic system could be recycled, but the activity decreased during reuse probably due to metal leaching and/or formation of metal nanoparticles. The system was also active in the reversible reaction, dehydrogenation of FA to H₂ and CO₂, which can help the implementation of H₂ as a renewable energy source.

Chapter 7 described the first POP active in the asymmetric C(sp³)-H functionalization. The POP swelled in *m*-xylene and created a quasi-homogeneous environment that made it possible to mimic homogeneous catalytic systems. Enantioselectivity was achieved by incorporating chiral phosphoramidites in the POP, which acted as a heterogeneous ligand. The presence of these ligands was verified by solid-state NMR and a signal could even be detected in liquid ³¹P-NMR using d₈-toluene as solvent due to the swelling properties of the POP. A substrate scope demonstrated that the reaction could proceed with different 3-arylpropanamides with high ee. In contrast, only electron rich aryl iodides provided adequate activity.

Recycling of the catalyst only showed limited success as both the product yield and ee decreased for each new recycle even with the addition of fresh Pd. *Post* characterizations showed that the phosphoramidite had been oxidized and Pd nanoparticles had formed as well.

In **Chapter 8**, the borylation of arenes was investigated using two different PS-based POPs with bpy acting as a heterogeneous ligand. The PS-POPs were synthesized with either styrene or 4-*tert*-butylstyrene as part of the backbone to create differences in steric hindrance. Both POPs were active in the direct $C(sp^2)$ -H borylation of arenes by forming an active Ir/bpy complex *in-situ*, but the more sterically hindered bpy-^tBuPS-POP showed to be less active than the bpy-PS-POP. Unfortunately, the incorporation of bpy into a PS-based POP did not achieve any regioselectivity as the observed trends follow the arene rather than the POP. The systems seemed to proceed through an Ir^{III}/Ir^{V} catalytic cycle that was capable of borylating twice per B₂pin₂ molecule leading to a release of hydrogen. A primary KIE was found strongly indicating that the C-H bond played a central role in the rate-determining step and competitive studies revealed that electron deficient arenes reacted faster than electron rich ones. The system was recyclable providing quantitative yields over three consecutive reactions. However, ¹¹B MAS NMR indicated that the polystyrene backbone was borylated as well demonstrating an undesired flaw in the use of PS-based POPs.

Overall, this dissertation has shown the high potential heterogeneous catalysis can have in organic synthesis. The first two projects used stabilized nanoparticles on carbon as an active catalyst. These catalysts were either easily accessible by a carbonization step or commercially available. Neither of the catalysts leached metal, which makes it easier to get access to highly pure chemical products and demonstrates one of the advantages of heterogeneous catalysis. Yet, for processes requiring high selectivity it may not be ideal to have nanoparticles as an active phase. Thus, the formation of heterogeneous SAMCs was investigated in three different projects by using POPs as the support material. These materials showed that they were able to mimic known homogeneous catalytic system while being heterogeneous in nature even in challenging and complex stereoselective reactions. Two of the projects utilized swollen POPs swelled to get the desired properties, which were incredible potent as the catalysts showed excellent activity and selectivity. However, the use of swelling can also restrict POP-based catalysts as conditions where the POP does not swell cannot be applied. In contrast, porous POPs do not have the same limitation as exemplified in the hydrogenation of CO₂ with a PP-based POP. Yet, investigations of porosity by physisorption experiments showed to be non-trivial as N_2 as adsorbate gave misleading results compared to using CO₂. It was also demonstrated that the amount of ligand in the POP heavily affected the catalytic performance with the less concentrated ones being superior in activity. Moreover, the anchoring of the catalytic system to a POP provided unique catalytic performance as homogeneous analogues were not able to provide the same activity. It was believed that the anchoring prevented deactivation commonly associated with homogeneous catalysts and thereby making POPs superior in some setups. Recycling of these POP-based catalysts were more challenging than when applying metal nanoparticles as the active phase. The undesired formation of metal nanoparticles for these SAMCs showed to be an issue for all the setups, but also metal leaching and ligand oxidation were observed, which demonstrate some of the issues relating to POP-based catalytic systems. Despite this, with the research presented in this dissertation and ongoing research within the scientific group of Prof. Søren Kegnæs, I believe that POPs can play an important role for catalysis in the future as they have shown excellent catalytic performance in different types of reactions.

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11 Appendix

11.1 Conferences and presentations

May 2018	Participation in the "5 th International School-Conference on Catalysis for Young Scientists – From Molecular to Industrial Level" in Moscow, Russia, with an oral presentation. Awarded with the best oral presentation.
August 2018	Attended the annual meeting for Danish Chemical Society in Odense, Denmark.
November 2018	Oral presentation at the annual PhD symposium organized by the Department of Chemistry, Technical University of Denmark. Poster presentations in 2017 and 2019.
November 2018	Attended the "Lundenser" gathering between University of Copenhagen, Lund University, and Technical University of DTU with a poster presentation at University of Copenhagen, Denmark.
August 2019	Participated at EuropaCat 2019 in Aachen, Germany, with a poster presentation.
January 2020	Participated in the Thorkild Holm symposium in Copenhagen, Denmark.

11.2 Publications

Bennedsen, N. R.; Kramer, S.; Mielby, J. J.; Kegnæs, S. Catal. Sci. Technol., 2018, 8, 2434–2440.

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Bennedsen, N. R.; Mortensen, R. L.; Kramer, S.; Kegnæs, S. J. Catal., 2019, 371, 153–160.

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Kramer, S.; Bennedsen, N. R.; Kegnæs, S. ACS Catal., 2018, 8, 6961–6982.

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Bennedsen, N. R.; Christensen, D. B.; Wang, B.; Wang, R.; Kramer, S.; Kegnæs, S. (submitted)

Bennedsen, N. R.; Kramer, S.; Kegnæs, S. (submitted)

Bennedsen, N. R.; Yang, F.; Kramer, S.; Kegnæs, S. (in progress)

The publications are presented with their respective front pages next.

Catalysis Science & Technology

PAPER

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Cobalt-nickel alloy catalysts for hydrosilylation of ketones synthesized by utilizing metal-organic framework as template[†]

Niklas R. Bennedsen, Søren Kramer, Jerrik J. Mielby and Søren Kegnæs 😳*

In this article, we report an approach to synthesize alloy Co-Ni nanoparticles encapsulated in carbon by utilization of the MOF, ZIF-67, as a sacrificial template. The alloy CoNi materials are synthesized by incipient wetness impregnation of cobalt-containing ZIF-67 with nickel(ii) nitrate followed by carbonization. The formation of alloy nanoparticles was verified by XRD and TEM analysis showed that they are distributed evenly throughout the entire material. The carbon encapsulating the alloy nanoparticles is N-doped and graphitic according to XPS analysis. Further characterization by ICP, N₂-physisorption, and SEM imaging was also performed. The CoNi materials exhibited promising activity in the catalytic hydrosilylation of ketones. A carbonization temperature of 800 °C provided the best catalyst for this transformation. The reaction conditions were optimized, different silanes tested, a time study conducted, and the heterogeneity of the catalysis assessed with different tests. Finally, a substrate scope of various ketones was examined.

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Introduction

Metal-organic frameworks (MOFs) have attracted much attention due to their high porosity, surface area, and easily tunable chemical structure.¹⁻⁴ As a consequence of these features, MOFs have found applications in various fields such as chemical sensoring,⁵ gas storage,^{6,7} photocatalysis^{8,9} and catalysis.^{3,10} One of the remaining challenges associated with the use of MOFs as catalysts is their often moderate thermal stability. Accordingly, as an alternative approach to catalyst synthesis, MOFs have been used as structural templates and source of carbon for the formation of metal nanoparticles encapsulated in a porous matrix.¹¹ This process is facilitated by carbonization of the MOF. In contrast to the parent MOFs (non-carbonized), these encapsulated metal nanoparticles typically possess improved chemical and thermal stability required for catalytic reactions and efficient catalyst recycling. Most of the reported studies focus on carbonization of monometallic MOFs such as the isostructural Zn²⁺-containing ZIF-8 and Co2+-containing ZIF-67, where the metal ions are linked by 2-methylimidazole.12-14

Recently, the use of catalysts consisting of metal nanoparticles which are alloys of abundant, non-noble metals has received considerable attention due to the intriguing properties of these materials.¹⁵⁻¹⁷ Alloying non-noble metals together may achieve the desired activity and selectivity often observed by using precious metals as seen in the synthesis of ammonia with a cobalt/molybdenum alloy.¹⁸ In the case of alloy nanoparticles between cobalt and nickel, they have shown enhanced catalytic activity in CO₂ dry-reforming,^{19,20} water splitting,²¹ oxygen evolution reaction,²² and H₂ release.²³ However, in terms of their use in reactions for synthetic organic chemistry, very few examples exist. Recently, our group have published that alloy CoNi nanoparticle are active catalysts for a series of organic reactions, including silylative pinacol coupling reactions and double bond migrations.^{24,25}

In the synthesis of alloy CoNi nanoparticles, ZIF-67 is of interest due to its inherent cobalt content, which during carbonization facilitate the formation of cobalt nanoparticles encapsulated in porous N-doped carbon. These nanoparticles are ideal for heterogeneous catalysis.^{11,25} However, only few attempts to synthesize alloy metal nanoparticles by introducing additional metals into the ZIF prior to the carbonization process are reported and no CoNi alloys accessed from ZIF-67 are reported.²⁷

Reduction of ketones by hydrogenation or hydrosilylation is an important and widely used transformation in the production of fine chemicals, such as pharmaceuticals.²⁸ The hydrosilylation approach avoids the use of high pressures, which can be a requirement for hydrogenations. For ketone hydrosilylation, homogeneous precious metal catalysts have typically been used.²⁹ However, significant recent advances in homogeneous base metal catalysis has led to the development of highly efficient catalytic systems based on these inexpensive metals.³⁰ While selectivity and activity is often higher in homogeneous catalysis, heterogeneous catalysis offers



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Palladium on carbon-catalyzed α -alkylation of ketones with alcohols as electrophiles: Scope and mechanism



JOURNAL OF CATALYSIS

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ABSTRACT

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Keywords: Pd/C catalysis Reaction mechanism α -Alkylation Heterogeneous catalysis In-situ IR Kinetics C—C bond formation The α -alkylation of ketones with alcohols represents a green strategy for the formation of crucial carboncarbon bonds since it only produces water as byproduct. In terms of reaction mechanism, the evidence for homogeneous catalysis supports a catalytic hydrogen-borrowing pathway; however, the reaction mechanism has not been investigated for heterogeneous Pd/C catalysts. Here, we report an improved method for α -alkylation of ketones with alcohols using commercially available Pd/C, ubiquitous in organic synthesis labs, as catalyst. The reaction conditions are mild compared to state-of-the-art for both homoand heterogeneous catalysts, and the developed conditions produces quantitative yields for most ketones and alcohols. A hot filtration experiment and recycling of the catalyst supports the heterogeneous nature of catalysis. Importantly, the reaction mechanism is studied for the first time by a combination of stoichiometric experiments and kinetic analyses by in-situ IR (React-IR).

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1. Introduction

Methods for facile carbon-carbon bond formation are crucial for the synthesis of organic molecules such as pharmaceuticals, agrochemicals, and functional materials [1-4]. Accordingly, the formation of a new $C(sp^3)-C(sp^3)$ bond to the α -carbon of carbonyl compounds, termed α -alkylation, is an important transformation that has received considerable attention [5-10]. Conventional methods for α -alkylation reactions often have problems with undesired waste, e.g. salts from alkyl halides, and require strong metallic bases and cryogenic temperatures. These aspects limit the industrial implementation and decrease the atom efficiency and sustainability of the methodologies [11,12]. Recently, a different strategy where alcohols are used as masked electrophiles, leading to water as the only byproduct, has attracted attention due to its potential as a greener alternative [13-19]. A variety of transition-metals has been implemented as catalysts for the α -alkylation of ketones with alcohols in both homogeneous [20-30] and heterogeneous systems [31-41]. Typically, reaction temperatures above 100 °C and 1-2 mol% catalyst loadings are required.

For homogeneous systems, the reaction mechanism for α -alkylation of ketones with alcohols has been thoroughly examined and the general consensus is that the reactions proceed through a hydrogen-borrowing pathway (Fig. 1) [19,23,26,

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https://doi.org/10.1016/j.jcat.2019.01.034 0021-9517/© 2019 Elsevier Inc. All rights reserved. **30,34,42**]. The reaction is initiated by dehydrogenation of the alcohol forming the corresponding aldehyde, thus activating it as an electrophile. Next, aldol condensation, which is typically catalyzed by addition of base, reacts the produced aldehyde and the ketone affording an α , β -unsaturated ketone. Finally, the C–C double bond is hydrogenated by the hydrogen originally removed from the alcohol, hence the term "hydrogen-borrowing".

In contrast to the homogeneous reactions, limited mechanistic evidence has been accumulated for α -alkylation of ketones with alcohols using heterogeneous catalysis [37,39,41]. In particular, no thorough mechanistic investigation including kinetics has been performed on α -alkylation of ketones with alcohols using palladium on carbon catalysis. A reaction pathway similar to homogeneous catalysis is tempting to propose; however, it cannot always be assumed that the pathways with homogeneous and heterogeneous catalysts are the same [43,44]. A better understanding of the operating pathways is pivotal for advancement of the field and rational design of future reactions.

In 2005, Cho described the only existing methodology, which includes substrate scope investigation, where commercially available Pd/C is used as catalyst for α -alkylation of ketones with alcohols [31]. The catalytic system used for the reaction between acetophenone and benzyl alcohol (2 equiv) was comprised of 5 mol% Pd/C, 3 equivalents KOH, and 4 equivalents 1-decene in dioxane at 100 °C for 20 h and afforded 66% yield of the corresponding 1,3-diphenylpropan-1-one. Albeit, the use of a commercially available catalyst which is ubiquitous in organic synthesis

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Porous Organic Polymers Containing Active Metal Centers as Catalysts for Synthetic Organic Chemistry

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ABSTRACT: Porous organic polymers (POPs) containing catalytically active mononuclear metal centers can bridge the gap between homogeneous and heterogeneous catalysis. These materials offer catalysts with straightforward control over the active site analogously to homogeneous organometallic catalysts; however, just like classical heterogeneous catalysts, they are easy to separate from reaction mixtures and recycle. The main objective of this Review is to provide an overview of the different types of reactions for synthetic organic chemistry where metal-POP catalysts have been utilized. In addition, a brief description of different synthesis strategies for accessing metal-POPs is included. We also propose a uniform naming system for metal-POP catalysts. Finally, current challenges that could advance the field and facilitate industrial application are discussed.



KEYWORDS: heterogeneous catalysis, single-site catalysts, porous organic polymers, organic synthesis, metal catalysis, organometallic chemistry

1. INTRODUCTION

In view of the continuous environmental and economic challenges in the world, there is a pressing need to develop a more sustainable and efficient chemical industry by creating and implementing more efficient chemical transformations. This can be done by developing new highly selective catalysts with increased product yield and therefore lowered process costs. Ideally, catalysts are developed by catalyst design where the active sites are introduced so that the catalyst selectively drive the reaction to form only the desired products. The uniform active sites accessible in homogeneous catalysis often streamline this task and allow for rationalization based on computational simulations.¹ In contrast, heterogeneous catalysts may contain multiple active sites, which, historically, have led to a greater requirement for trial-and-error experiments in the production of numerous catalysts. Nonetheless, heterogeneous catalysts often display significant advantages over homogeneous catalysts in terms of sustainability, recyclability, robustness, and ease of catalyst separation.²⁻⁴ One of the reasons for the trial-and-error approach in synthesis of heterogeneous catalysts may be the difficulty in design and synthesis of well-defined uniform active sites in many types of heterogeneous catalysts. This is, for instance, illustrated in "classic" heterogeneous catalysts consisting of metal nanoparticles on a high-surface-area support, where several different types of active sites often exist on the metal particles.⁵ Catalyst design of heterogeneous catalysts has therefore often focused on reducing the size of the active metal particles in order to enhance catalytic performance and efficiency of the hetero-

geneous nanoparticle catalysts. A reduction of the size of the metal particles in general leads to a more efficient use of metal as the relative surface area of the particles is increased. The ultimate size-reduction of nanoparticles is when each metal "particle" consists of only a single metal atom and each single metal atom acts as active site. Ideally, this will give a highly efficient use of the metal but would also lead to more welldefined and uniform active sites, as known from homogeneous catalysis. However, the reduction of particle size enhances the tendency for particle sintering, leading to a decrease in the catalytic activity. Thus, the development of sintering-stable heterogeneous nanoparticle catalysts has attracted attention over the years, and many strategies have been developed to address the problem of sintering of nanoparticle catalysts.⁶⁻ Many synthesis strategies have also been developed in order to combine the advantages of molecular homogeneous catalysts and heterogeneous processes, aiming to obtain high reactivity and selectivity of the molecular catalysts while facilitating product recovery and catalyst recycling. $^{3,4,11-13}$

Herein, we will focus on the use of porous organic polymers (POPs) containing active mononuclear metal centers and how they are applied as single-site catalysts for synthetic organic chemistry (Figure 1). The solid nature of POPs and their high porosity make them attractive in heterogeneous catalysis.^{14,15} In addition, the possibility to incorporate ligands in the

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11.3 Co-author statements

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	Carried out all syntheses and a majority of the characterizations used in the article with corresponding interpretations and analysis in collaboration with the other authors.
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Title of article Palladium on Carbon-Catalyzed α -Alkylation of Ketones with Alcohols as Electrophiles: Scope and Mechanism Journal/conference Journal of Catalysis 2019 Author(s) Niklas Rosendal Bennedsen, Rasmus Lykke Mortensen, Søren Kramer & Søren Kegnæs Name (capital letters) and signature of PhD student NIKLAS ROSENDAL BENNEDSEN PhD student's date of birth 06/01-1993 Declaration of the PhD student's contribution For each category in the table below, please specify the PhD student's contribution to the article as appropriate (please do not fill in with names or x's) Minor contribution to the work Substantial contribution to the work Category (please specify the nature of the PhD (please specify the nature of the PhD student's contribution) student's contribution) Contributed with relevant scientific Formulation of the conceptual input during the catalytic testing and discussed the direction of the project framework and/or planning of with the other authors. the design of the study including scientific questions Carried out all catalytic tests and a majority of the characterizations used Carrying out of in the article. Contributed by experiments/data collection interpreting and analyzing majority of and analysis/interpretation of results the data in collaboration with the other authors. Wrote the initial draft of the Writing of the article/revising manuscript with a majority of the the manuscript for Figures, Schemes etc. Contributed continuously with input and helped intellectual content during revision of the draft. Signatures





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Category	Minor contribution to the work (please specify the nature of the PhD student's contribution)	Substantial contribution to the work (please specify the nature of the PhD student's contribution)
Formulation of the conceptual framework and/or planning of the design of the study including scientific questions		Planned the direction of the project and what experiments that should be done.
Carrying out of experiments/data collection and analysis/interpretation of results		Synthesized most of POPs and the homogeneous iridium-complex used in the article. Carried out physisorption experiments, test for metal leaching, and interpreted obtained results for the most techniques.
Writing of the article/revising the manuscript for intellectual content		Wrote the initial draft and made a majority of the Figures, Schemes etc. Made most of the revisions in the article.
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¹ International Committee of Medical Journal Editors – Recommendations for the Conduct, Reporting, Editing, and Publication of Scholarly Work in Medical Journals, updated December 2016

² DTU Code of Conduct for Research Integrity (E-book p. 19)

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Technical University of Denmark



A Chiral Porous Organic Polymer	as Heterogeneous Ligand for Enantiose	lective Pd-Catalyzed C(sp ³)–H
Functionalization		
lournal/conference		
Catalysis Science and Technolog	zy 2020	
Author(s)		
Niklas Rosendal Bennedsen, Søren Kra	mer & Søren Kegnæs	
Name (capital letters) and signa	ture of PhD student	
NIKLAS ROSENDAL BENNEDSEN		
PhD student's date of birth		
06/01-1993		
Declaration of the PhD student	s contribution	and seen and all and and arranged and
For each category in the table below not fill in with names or x's)	w, please specify the PhD student's contribu	tion to the article as appropriate (please of a second second second second second second second second second
Category	Minor contribution to the work (please specify the nature of the PhD student's contribution)	Substantial contribution to the work (please specify the nature of the PhD student's contribution)
Formulation of the conceptual framework and/or planning of the design of the study including scientific questions		Provided the concept and idea of the project. Planned and developed the used procedures including many of the tests carried out in collaboration with the other authors.
Carrying out of experiments/data collection and analysis/interpretation of results		Did all syntheses and catalytic tests. Carried out most of the characterizations with the interpretation and analyzes thereof i collaboration with the other authors.
Writing of the article/revising the manuscript for intellectual content		Wrote the initial draft for the article. Made a majority of the figures, schemes etc. used in the article. Contributed during revision of the article.





Title of article			
A Chiral Porous	Organic Polymer as Heterogen	eous Ligand for	Enantioselective Pd-Catalyzed C(sp ³)–H
Functionalizatio	on		
Journal/confer	ence		
Catalysis Scien	ce and Technology 2020		
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27/8-20	Niklas Rosendal Bennedsen	PhD student	Nilely Bennge

Technical University of Denmark



Title of article

Direct C(sp²)-H borylation of arenes with a heterogenized bpy ligand incorporated into a porous organic polymer Journal/conference

Journal

Author(s)

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PhD student's date of birth

06/01-1993

Declaration of the PhD student's contribution

For each category in the table below, please specify the PhD student's contribution to the article as appropriate (please do not fill in with names or x's)

Category	Minor contribution to the work (please specify the nature of the PhD student's contribution)	Substantial contribution to the work (please specify the nature of the PhD student's contribution)
Formulation of the conceptual framework and/or planning of the design of the study including scientific questions		Provided the concept and idea of the project. Planned and developed the used procedures including many of the tests carried.
Carrying out of experiments/data collection and analysis/interpretation of results		Carried out most of the characterizations and all of the catalytic tests with corresponding interpretation.
Writing of the article/revising the manuscript for intellectual content		Wrote the initial draft for the article. Made a majority of the figures, schemes etc. used in the article.
Signatures		





Title of article			
Direct C(sp ²)-H	borylation of arenes with a hete	erogenized bpy	igand incorporated into a porous organic polymer
Journal/confer	ence		
Journal			
Author(s)			
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