Polymer precursors from catalytic reactions of natural oils

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A thesis submitted in fulfilment of the requirements for the degree of Doctor of Philosophy in the David J. Cole-Hamilton Research Group School of Chemistry

May 2013
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I, Marc R. L. Furst, hereby certify that this thesis titled, 'Polymer precursors from catalytic reactions of natural oils', which is approximately 38,000 words in length, has been written by me, that it is the record of work carried out by me and that it has not been submitted in any previous application for a higher degree. I was admitted as a research student in October 2009 and as a candidate for the degree of Doctor of Philosophy in August 2010; the higher study for which this is a record was carried out in the University of St Andrews between 2009 and 2013.

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“The most exiting phrase to hear in science, the one that heralds new discoveries, is not *Eureka!* but That’s funny…”

Isaac Asimov
The bidentate ligand $1,2\text{-bis(ditertbutylphosphinomethyl)benzene}$ has been shown to be a very efficient catalyst for operating the alkoxy carbonylation of alkenes and unsaturated esters and carboxylic acids giving a very high selectivity to the linear product with very few exceptions to this general rule.

Due to the increasing prices of petroleum feedstock and petroleum-derived chemicals, the preparation of chemicals starting from renewable resources and waste products from the industry becomes an interesting alternative. Fatty acids and fatty esters, due to the existence of one or more unsaturation in their alkyl chain are subjected to the alkoxy carbonylation reactions in presence of $1,2\text{-bis(ditertbutylphosphinomethyl)benzene}$, palladium, methane sulfonic acid, carbon monoxide and methanol, yielding diesters with a long carbon chain (up to 19 carbon atoms). The diesters are shown to be readily prepared from unpurified olive, rapeseed or sunflower oils as well as from tall oil. In the last case triesters are also formed. The diesters are subjected to hydrogenation in the presence of $1,1,1\text{-tris(diphenylphosphinomethyl)ethane}$, ruthenium and hydrogen, in a mixture of dioxane and water at high temperature, yielding the corresponding diols. The resulting products of the reactions are monomers for preparing polyesters having the potential to replace some existing petroleum-based polymers (for instance polyethylene).

The aminocarboxylation reaction in the presence of the same palladium/$1,2\text{-bis(ditertbutylphosphinomethyl)benzene}$ catalyst, in the presence of aniline, 2–naphthol and potassium iodide in diethylether, is employed for preparing esteramides, which are subjected to hydrogenation. Aromatic polyamides are prepared by melting together an aromatic diamine and diacids obtained from methoxycarbonylation.

Finally, $N$–Heterocyclic Carbene (NHC) ligands are employed for preparing new palladium complexes which are used in the Suzuki-Miyaura cross-coupling reaction in a water/isopropanol mixture. Other complexes based on copper are employed for developing an inexpensive transmetallation reaction for transferring a NHC ligand from copper to palladium and gold.
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<th>Abbreviation</th>
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<tbody>
<tr>
<td>ADMET</td>
<td>Acyclic diene metathesis</td>
</tr>
<tr>
<td>Amu</td>
<td>Average mass unit</td>
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<tr>
<td>DCM</td>
<td>Dichloromethane</td>
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<td>Dino</td>
<td>Dimethyl 1,19–nonadecanedioate</td>
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<td>DMF</td>
<td>Dimethylformamide</td>
</tr>
<tr>
<td>DTBPMB</td>
<td>1,2–bis(ditertbutylphosphinomethyl)benzene</td>
</tr>
<tr>
<td>GC–FID</td>
<td>Gas chromatography – flame ionisation detector</td>
</tr>
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<td>GC–MS</td>
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<tr>
<td>HDTC</td>
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<td>Infrared</td>
</tr>
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<td>Maldi–Tof</td>
<td>Matrix-assisted laser desorption/ionisation – Time-of-flight mass spectrometer</td>
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<td>Mes</td>
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<td>MSA</td>
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<td>Maldi–Tof mass spectrometry</td>
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<tr>
<td>Triphos</td>
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Pour Maman et Papa. En mémoire de Grand-Mère.
Chapter 1

General Introduction

As the title of this manuscript declares, the topic of this thesis is to develop some polymer precursors from catalytic reactions of various natural oils. Therefore, the main pillar of the thesis is the alkoxy carbonylation reaction of various triglycerides and some of their derivatives. In this general introduction the reader will have an overview of the concept of sustainable Chemistry: an overview that will focus on the utilisation of biomass, and especially of triglycerides, as starting materials for Chemistry. An insight into the alkoxy carbonylation reaction will be given in the second part. Due to the principal use of the 1,2–bis(diterbutylphosphinomethyl)benzene ligand in the Chemistry that was developed during the studies described in this thesis, the versatility of this ligand will be outlined in the last part of this introduction.

1.1 Biomass as a starting material for Chemistry

1.1.1 General overview on sustainable Chemistry

Sustainable Chemistry, also known as Green Chemistry concerns in “the design of chemical products that reduce or eliminate the use of hazardous substances”. As for chemical research in general, sustainable Chemistry focuses on minimising the hazards and optimising the efficiency of a chemical process. The concept of green Chemistry should not be confused with the one of “environmental Chemistry” which deals with the studies of Chemistry occurring in the natural processes. The twelve principles of Green Chemistry
defined by Anastas and Warner in 1991 play a central role by giving a guideline for developing new ways of synthesis for a Chemistry that is more effective, more efficient and more elegant.

1.1.2 The conversion of biomass

Throughout History, biomass was not only used for providing food (e.g. cereals from crops) or energy (e.g. wood from forests) but also to extract some valuable products such as drugs and flavours from plants. During the twentieth century, the industrial-scale production of chemicals involved for instance the synthesis of flavours from terpenes and the conversion of vegetable oils into surfactants. However, as the conventional route for synthesising chemicals from hydrocarbons was much cheaper than the preparation from biomass, the hydrocarbon route was obviously the preferred one. Converting biomass into chemicals can be achieved in two different approaches depending on the chemicals that are targeted. The first approach consists of targeting a specific chemical obtained from hydrocarbon feedstock and finding the most efficient synthesis to produce it from biomass. This approach, however, needs the identification of platform molecules that

\begin{figure}[h]
\centering
\includegraphics[width=0.8\textwidth]{figure1}
\caption{Different strategies for converting biomass\cite{5,8,9}}
\end{figure}
1.2 The interest in vegetable oils

Fats and oils originating from both vegetable and animal sources are currently the most important renewable feedstock employed by the chemical industry. The world global production of vegetable oils was 133 Mt in 2011, among them 11 Mt were used for producing bio-diesel and 15 Mt were dedicated to the chemical industry. Even if it has been shown that oleochemicals can be produced in an quantity sufficient enough for industrial applications without competing with arable land for food – the consumption ratio food:feed:chemistry being 74:6:20 – the amount of vegetable oils available for the industry competes with the quantity absorbed by the production of bio-diesel. Value enhancement of triglycerides leads to the preparation of industrial products and mainly to surfactants, lubricants and polymers. For instance, the production of surfactants being efficient and presenting interesting properties such as biocompatibility and biodegradability is a successful example of industrial conversion of vegetable oils into valuable chemicals. The area of industrial conversion of oils into chemicals being wide, the reader’s attention will now be focused only in the field of polymers.

1.2.1 Triglycerides

Triglycerides are the main constituents of vegetable oils and are made of glycerol bearing three fatty acids. Most of the fatty acids consist of a linear carbon chain, with an even number of carbon atoms in this chain. The chain length can be short (butyric acid, 4 C, found in milk) or very long (cerotic acid, 26 C, found in beeswax), saturated or unsaturated. Most of the unsaturated fatty acids have a cis C=C bond. Some fatty acids have a functional group on the carbon chain. For instance, ricinoleic acid (originating
from castor oil) has a hydroxyl group on the carbon chain. The existence of one or more unsaturations and functional groups on fatty acids makes them of interest for realising chemical reactions.

![General structure of a triglyceride](image)

**Figure 1.2:** General structure of a triglyceride ($R^1$, $R^2$, $R^3$: various carbon chains)

### 1.2.2 Polymerisation

Triglycerides and fatty acids can undergo many chemical and catalytic transformations for preparing oil-based polymers.

#### 1.2.2.1 Metathesis polymerisation

The olefin metathesis reaction\(^{24}\) and the well-performing existing catalysts\(^{25–30}\) designed for it represent a very interesting toolbox\(^{31}\) for using fatty acids, due to the existence of one or more unsaturations on the carbon chain. The preparation of oil-based polymers can be achieved using the ring-opening metathesis polymerisation (ROMP) and the acyclic diene metathesis (ADMET).

ROMP works with monomers having a strained ring which is not existing in natural fatty acids. Therefore, a fatty acid needs a modification of its structure for bearing such a ring. Castor oil is very suitable for such a purpose due to the existence of the hydroxyl group.\(^{32,33}\) A bicyclic castor oil derivative has been prepared from bicyclo[2.2.1]hept–5–ene–2,3–dicarboxylic anhydride (Monomer **A**, Figure 1.4).\(^{34}\) This monomer is highly viscous due to the hydrogen bonds between the carboxylic acids. This derivative has been polymerised with cyclooctadiene using a Hoveyda-Grubbs second generation catalyst, yielding a thermoset, with a maximum degradation temperature of 500°C. Two variations

![Grubbs first generation catalyst](image) ![Grubbs second generation catalyst](image) ![Hoveyda-Grubbs second generation catalyst](image)

**Figure 1.3:** Grubbs and Hoveyda-Grubbs metathesis catalysts
of this monomer have been prepared by reacting the triglyceride and its fatty alcohol with norbornene carbonyl chloride yielding a norbornenyl-functionalised castor oil (Monomer B, Figure 1.4) and norbornene-functionalised castor fatty alcohol (Monomer C, Figure 1.4) which were reacted together through ROMP with the Grubbs second generation catalyst (Figure 1.5). The obtained material has an increased cross-link density which improves its thermal stability.

ADMET does not need to modify the fatty acid for using it as a reagent, as the C=C bond of the carbon chain is used for the metathesis reaction. For instance, soy bean oil
and corn oil have been used for preparing material ranging from very viscous oils to rubbers, using the Grubbs first generation catalyst a low loading (0.1%).\textsuperscript{36,37} Low pressure favours the polymerisation by removing the alkene generated during the metathesis reaction. Even if the oil can be directly used for the ADMET, oil-derived monomers can be employed as well. For instance, an \(\alpha,\omega\)-diene containing hydroxyl groups derived from undecenoic acid (which is derived from castor oil) was subjected to the ADMET with a plant-derived phosphorus containing \(\alpha,\omega\)-diene, yielding linear polyesters containing phosphorus.\textsuperscript{38,39} The obtained polymers have shown to be good flame-retardants. Finally, it has been shown that polyamides can be prepared \textit{via} ADMET polymerisation, using castor oil-based \(\alpha,\omega\)-diene with two symmetrically spaced amide segments.\textsuperscript{40} A variation of the ADMET known as ATMET (for “acyclic triene metathesis”) has been shown to be an efficient method for preparing cross-linked polyesters from an artificial triglyceride, by the application of methyl acrylate as a chain stopper. The triglyceride used in this study was prepared from glycerol and methyl 10-undecenoate.\textsuperscript{41} However, natural triglycerides have been used, such as high oleic content sunflower oil. The Grubbs second generation catalyst was employed for the ATMET and methyl acrylate was used as a chain stopper. Variation of the ratio of triglyceride and methyl acrylate permits the tuning of the molecular weight of the final cross-linked polyester.\textsuperscript{42}

1.2.2.2 Condensation polymerisation

Condensation polymerisation is used for the preparation of polyurethanes, polyesters and polyamides.

The \textbf{polyurethanes} market represents several products such as adhesives, foam and coatings at a multi-million ton scale.\textsuperscript{43} Polyurethanes are traditionally obtained from the condensation of isocyanates and polyols originating from petroleum,\textsuperscript{44} and the use of polyols derived from fatty acids and esters constitutes an interesting alternative. The interest of natural oil based polyurethane relies on the biodegradability of the material. Even if limited in the case of cross-linked polyurethanes, the bio-degradation is higher than for polyurethanes from petroleum origins.\textsuperscript{45} Polyurethanes from natural origins lead to applications as various as from medical implants to flame retardants.\textsuperscript{46} Castor oil, due to the existence of the hydroxyl group, has been used without any further modification for preparing polyurethanes,\textsuperscript{47,48} which can have interesting properties such as wood-to-wood adhesives.\textsuperscript{49} However, not only castor oil has been used for preparing polyurethanes. Thus, the C=C bond on various triglycerides can be epoxidised and ring-opened for preparing suitable polyurethanes precursors.\textsuperscript{50} The precursors lead to various materials with different properties which are more a consequence of the crosslinking densities and less from the position of the cross-link in the chain.\textsuperscript{51}
The isocyanate needed for a polyurethane synthesis can be prepared from oleic acid, via the ozonolysis of the C=C bond followed by an oxidation yielding to 1,9–nonanedioic acid, which is converted to 1,7–heptamethylene diisocyanate (Curtius rearrangement, Figure 1.6). The diisocyanide can be reacted with 1,9–nonanediol prepared from oleic acid, yielding a polyurethane.

Finally, water-borne polyurethanes dispersions (WPUD) have been used from making the modification of starch, yielding to biodegradable materials. WPUD are attractive due to the absence of solvent emission and have been used for preparing adhesives, coatings, packings and other products.

Polyesters from natural oils can be obtained in three different ways. The fatty acid has to undergo some transformations for being reactive. Thus, polyesters can be obtained either by condensation of a diacid with a diol, self-condensation of an hydroxyacid, or ring-opening polymerisation of a lactone. An interesting example of self-condensation is made from 9–hydroxynonanoic acid. This hydroxy-acid is prepared in a two step reaction, involving the oxidative ozonolysis of the C=C bond of castor oil, followed by the methanolysis of the remaining triglyceride. The resulting polymer presents properties very similar to polycaprolactone and might become of interest for replacing it. However, castor oil does not need necessarily to be converted, and its fatty acid (ricinoleic acid) has been used directly for preparing polyesters. Ricinoleic acid has been copolymerised with lactic acid in different ratios, yielding copolymers, some of them being liquid at room temperature, and might be used in the future as drug carriers. Vegetable oils such as sunflower oil have been employed for preparing dimethyl 1,19–nonadecanedioate via methoxycarbonylation, and its corresponding alcohol was prepared via catalytic hydrogenation with ruthenium. The monomers yield long-chain polyesters with properties very similar to polyethylene and might represent a potential replacement for it. Finally, polyesters from natural oils can be obtained from biologically-based reactions. However, these processes are out of the scope of the present introduction.

Polyamides find applications in many areas. Probably the best known oil-based polyamide is nylon–11. Its monomer, 11–aminoundecanoic acid originates from castor
oil, thermally cracked and then chemically transformed.\textsuperscript{71} The product exhibits good dimensional stability, good electrical properties and a good chemical resistance. Offices wastepaper printed with a polymer-based toner is very challenging to de-ink. Therefore, soy-based copolyamides have been developed and processed into dual component toners,\textsuperscript{72} exhibiting performances similar to those of classical commercial toners.

### 1.2.2.3 Cationic polymerisation

An efficient way to achieve the polymerisation of oils is to start from their epoxide derivatives. For instance, epoxidised castor and soybean oils have been polymerised using a latent thermal initiator, $\textit{N}$–benzylpyrazinium hexafluoroantimonat.\textsuperscript{73} Interestingly, epoxidised castor and soybean oils have been copolymerised with the diglycidyl ether of bisphenol A, yielding polymer with enhanced mechanical properties. For instance, an addition of 10\% of epoxidised soybean oil in the diglycidyl ether of bisphenol A yields epoxy resins with better mechanical properties.\textsuperscript{74–76} The “soft” segments in the soybean oil epoxide reduces the crosslinking density an increases the toughness.

### 1.2.3 Plasticisers

Plasticisers, also known as dispersants, are polymer additives that increase the flexibility of the desired final material. The dominant applications (90\% of the market) are for polyvinyl chloride (PVC). The most common plasticiser used for this purpose is bis(2–ethylhexyl) phthalate which is suspected to cause health troubles,\textsuperscript{77} therefore the use of this compound and other phthalates is now restricted. Due to this restriction research was carried out in order to develop replacement materials originating from triglycerides. For instances, epoxidised plasticisers from natural oils have been prepared,\textsuperscript{78} and the origin of the oils that are used for preparing these biocompatible epoxidised plasticisers are as various as castor oil,\textsuperscript{79} seed oil,\textsuperscript{80} soybean oil,\textsuperscript{81} sunflower oil\textsuperscript{82} and tall oil.\textsuperscript{83} Moreover, if the oxirane ring from the epoxidised oil is opened using acetic anhydride, the final product can be added to PVC. The resulting material shows properties similar to the PVC having phthalate additives,\textsuperscript{84} showing that these new plasticisers derived from natural feedstock are a valuable option.

### 1.3 The alkoxy carbonylation reaction

The systems described in this thesis are essentially based on the use of triglycerides, fatty acids and fatty esters that are subjected to the alkoxy carbonylation reaction. Therefore,
1.3 The alkoxy carbonylation reaction

the reader will find in this section all the necessary information for having a better understanding of the next chapters.

1.3.1 The carboxylation reactions

The alkoxy carbonylation reaction is a specific case of the most general reactions known as carboxylation. The carboxylation reactions rely on the formation of a carbonyl group in a carbon chain through the introduction of carbon monoxide. The first reaction of this kind is the “oxo synthesis”: hydroformylation. It was discovered by Roelen in 1938.\(^{85}\) Hydroformylation involves the formation of propanal by the reaction of syngas (mixture of carbon monoxide and hydrogen) with ethylene through a catalytic process.

In the carboxylation reactions, the function that is formed (as various as aldehyde, ketone, ester, carboxylic acid, lactone, amide...) is of great importance due to its high reactivity in organic syntheses.\(^{86}\) The probably greatest interest of the carboxylation reactions is the efficiency towards the concept of atom economy. Indeed, since all the atoms involved in the reaction (C and O from the carbon monoxide and atoms from the other reagents) end up in the final product the atom economy is 100%. The carboxylation reactions can involve the regioselectivity with the formation either linear or branched products from terminal alkenes. Examples of the most encountered carboxylation reactions are outlined in Table 1.1.

1.3.2 The alkoxy carbonylation

In 1953 a variation on the hydroformylation type reaction was reported. During the course of this year, Reppe discovered the hydroxycarbonylation and alkoxy carbonylation reactions of acetylene.\(^{87}\) The reaction of acetylene with carbon monoxide and water (or an alcohol) was shown to produce carboxylic acids or esters using a nickel catalyst. During the following years improvement were achieved for carrying out the reaction under milder conditions. Indeed, the original harsh conditions led to the desired products but were promoting the production of undesired side-products. Milder conditions were achieved by using cobalt catalysts.\(^{88}\) However, the high toxicity of this metal led the research to concentrate on palladium. The first palladium catalysts developed in the 1960’s were shown to be active at much lower temperature (about 100°C) than cobalt catalysts.\(^ {89-93}\) The introduction of phosphine ligands into the palladium system by Drent and co-workers in the 1980’s led to a major progress in the field of alkoxy carbonylation.\(^ {94}\) The reader will now have an overview of a diphosphine ligand that shows outstanding activities towards the alkoxy carbonylation reaction.
Table 1.1: Variety of functions obtained through the carbonylation reaction

<table>
<thead>
<tr>
<th>Reaction</th>
<th>Function built</th>
<th>Scheme</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hydroformylation$^{85,95-97}$</td>
<td>aldehyde</td>
<td><img src="https://via.placeholder.com/150" alt="Diagram" /></td>
</tr>
<tr>
<td>Copolymerisation$^{98}$</td>
<td>copolymer</td>
<td><img src="https://via.placeholder.com/150" alt="Diagram" /></td>
</tr>
<tr>
<td>Alkoxycarbonylation</td>
<td>saturated ester</td>
<td><img src="https://via.placeholder.com/150" alt="Diagram" /></td>
</tr>
<tr>
<td>Alkyne carbonylation$^{99}$</td>
<td>unsaturated ester</td>
<td><img src="https://via.placeholder.com/150" alt="Diagram" /></td>
</tr>
<tr>
<td>Alkyne carbonylation$^{99}$</td>
<td>diester</td>
<td><img src="https://via.placeholder.com/150" alt="Diagram" /></td>
</tr>
<tr>
<td>Pauson-Khand reaction$^{100,101}$</td>
<td>cyclohexone</td>
<td><img src="https://via.placeholder.com/150" alt="Diagram" /></td>
</tr>
<tr>
<td>The Monsanto process$^{102}$</td>
<td>carboxylic acid</td>
<td><img src="https://via.placeholder.com/150" alt="Diagram" /></td>
</tr>
</tbody>
</table>

1.4 1,2–bis(ditertbutylphosphinomethyl)benzene

The diphosphine 1,2–bis(ditertbutylphosphinomethyl)benzene (shortened as DTBPMB, Figure 1.7) was first reported in 1976 by Moulton and Shaw. In 1992, Crascall and Spencer showed that the degree of interaction with the metal centre depends on the bite angle and the steric hindrance of the substituents on the diphosphine.

![Figure 1.7: 1,2–bis(ditertbutylphosphinomethyl)benzene](https://via.placeholder.com/150)

1.4.1 The alkoxycarbonylation of simple alkenes

To the best of our knowledge, no catalytic studies have been reported before the work of Tootze and co-workers on the methoxycarbonylation of ethylene for the production of methyl propanoate in 1996, which was rapidly followed by numerous patents from
The ligand, once complexed to palladium has shown very high activity towards the methoxycarbonylation of ethylene with turnover numbers >100,000. As outlined by the authors, the obtained methyl propanoate was suggested to be a possible intermediate for the synthesis of methyl methacrylate. Indeed, the catalytic system patented by the Lucite company is nowadays used in the “Alpha Process” for the production of methyl propanoate leading to the synthesis of methyl methacrylate. A system describing the continuous process for the methoxycarbonylation of ethylene was recently patented by Eastham and Tindale, and a system comprising zwitterions added to the reaction mixture for enhancing the performances of the reaction was recently patented by Riisager and co-workers. The field of hydro/methoxycarbonylation of ethylene to methyl propanoate using BTDPMB-based systems and variations of the ligand has been recently reviewed by Fanjul and co-workers. Drent and Jager have shown the BTDPMB/palladium system to give methyl pentanoate from 2–butene in 97% selectivity at 65 bar and 100°C, showing the methoxycarbonylation of a carbon chain longer than ethylene was possible. The same authors desired to increase the selectivity to the linear ester and found that using a mixture anisole/methanol : 2/1 as a solvent for the methoxycarbonylation of 2–butene and 1–octene yielded a full conversion to the ester with high selectivity to the linear species (97%). However this system did not shown any real improvement in comparison to the one without anisole and was still using relatively harsh conditions (T > 100°C, P > 60 bar). An efficient system was reported by Cole-Hamilton and co-workers for the methoxycarbonylation of 1–octene in 97.8% conversion under very mild conditions (1 bar of CO and 20°C). The authors reported in the same paper that increasing the CO pressure to 4 bar, a 100% conversion of 1–hexene was possible at room temperature.

1.4.2 Mechanism of the reaction

1.4.2.1 Alkoxy carbonylation

Mechanistic studies carried out by Toniolo and Cavinato in 1990 on the new (at the time) phosphine/palladium systems suggested that two mechanisms were possible for the alkoxy carbonylation reaction. Other studies, including the copolymerisation of olefins with carbon monoxide, confirmed that both mechanisms can occur. The two suggested mechanistic paths (Figure 1.8) involve either a carboalkoxy-palladium species or a hydro-palladium species. In the first mechanism, the alkene is inserted in the carboalkoxy-palladium bond and an alcoholyis releases the ester, while the active catalyst is regenerated by coordination of carbon monoxide. The second mechanism involves the insertion of the alkene in the palladium-hydride bond, followed
by a second insertion from carbon monoxide, while alcoholysis releases the ester and regenerates the active catalytic species. In both mechanisms, the rate-determining step is the nucleophilic attack of the alcohol. Originally it has been suggested that the methoxycarbonylation of ethylene leads to methyl propanoate using monodentate phosphine ligands and to copolymers using bidentate ligands. However this simple relationship ligand/product does not hold, and this was remarkably outlined by Knight, Doherty and co-workers who have shown that catalyst systems based on cis- and trans-1,2-bis(diphenylphosphinomethyl)cyclohexane are selective for copolymerisation of ethylene with carbon monoxide. On the other hand, catalyst systems based on exo,endo-2,3-bis(diphenylphosphinomethyl)norbornane are selective for producing methyl propanoate. In contrast, catalyst mixtures formed from endo,endo-2,3-bis(diphenylphosphinomethyl)norbornane are selective for making the copolymer, with a productivity similar to that of trans-1,2-bis(diphenylphosphinomethyl)cyclohexane.

It has been suggested that the methoxy cycle is dominant if oxidants are present. This was explained using the fact that palladium–hydride species oxidise in the presence of oxidant in methanol to give the palladium–methoxy complexes. Tooze and co-workers later found evidence that actually the hydride mechanism was occurring during the methoxycarbonylation of ethylene while using palladium–triphenylphosphine complexes.

Further investigations have been made for a better understanding of the mechanism of the alkoxycarbonization while specifically using the BTDPMB ligand. Thus, Heaton and co-workers were the first to isolate all the intermediates involved in the methoxycarbonylation of ethylene. The authors found that, contrary to what was previously suggested, the palladium–hydride species was stable in the presence of oxygen at temperatures as high as 80°C or in the presence of an excess of benzoquinone. No evidence of the palladium-methoxy complex was found. These observations gave strong support...
to the hypothesis that the methoxycarbonylation of ethylene follows the hydride catalytic cycle (cycle B in Figure 1.8). Cole-Hamilton and co-workers gave other evidences in support of the hydride mechanism by carrying out labelling experiments in MeOD under CO starvation conditions.\textsuperscript{131} In support of the hydride mechanism, the authors suggested that the high rate of D\textsuperscript{0}–methyl propanoate formation at the beginning of the reaction suggests that under conditions of CO starvation, the rate of ethylene exchange between A (Figure 1.9) and the gas phase competes with the rate of CO coordination. The carboxyethyl mechanism is unable to explain the formation of the large amounts of D\textsuperscript{0}–methyl propanoate at low reaction times. Indeed, the termination step has to transfer deuterium from MeOD to end up in the formed methyl propanoate (see Figure 1.10). In both mechanisms, the authors suggest that the vacant sites on palladium might be stabilised by coordination of MeSO\textsubscript{3}– (as they use methane sulfonic acid), methyl propanoate or even the solvent. The role of the solvent and of methane sulfonic acid was studied and explained by Heaton and co-workers.\textsuperscript{132} They proposed that methanol fulfils two key roles in addition of being a reagent. First, methanol is involved in the formation of the key intermediate for the methoxycarbonylation of ethylene: [Pd(DTBPMB)H(MeOH)]. And second, methanol stabilises the hydride species. Indeed, when the hydride species is in solution in THF, the reaction yields dihydrogen while nothing happens in methanol. However the stability of the hydride is surprising.
and may be explained by the role of methane sulfonic acid. The use of MeSO₃H instead of TfOH enhances the stability of the hydride which is stable in solution at 80°C for several hours.

The final step of the alkoxycarbonylation consists of the nucleophilic attack of the alcohol. Van Leeuwen and co-workers gave evidence that the alcoholysis is the rate-determining step of the alkoxycarbonylation,¹³³ which was suspected by Heaton.¹³⁴ The authors also showed well that the pressure of carbon monoxide does not have any influence on the rate of the alcoholysis.¹³³

### 1.4.2.2 Isomerisation

The Pd/DTBPMB system has been shown to be efficient for alkoxycarbonylation of terminal alkenes. In the case of internal alkenes, one could have expected that alkoxycarbonylation would lead to branched esters. However the system is efficient for the alkoxycarbonylation of internal alkenes with high selectivity to the linear esters. For instance, for 2–octene the selectivity was >97% (99% at room temperature) and 94% in the cases of 3– and 4–octene.¹¹⁷ Obviously the catalyst has proven to be efficient for the isomerisation of alkenes to the terminal position. This seems quite surprising at first sight due the thermodynamically disfavored existence of terminal alkene vs internal alkene.¹³⁵ Studies made using MeOD instead of MeOH on the alkoxycarbonylation of 1–octene in a mixture MeOD/toluene : 1/4 showed that all isomers with 0–15 D atoms exist.¹¹⁷ The existence of the deuterated isomers was the first evidence to the ability of the catalyst to isomerise the C=C bond (Figure 1.11). It was usually considered that the high steric

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**Figure 1.10:** Proposed carbomethoxy mechanism for the formation of various deuterated methyl propanoate from CO, ethylene and MeOD catalysed by Pd/DTBPMB system.¹³¹ (P=P=DTBPMB)
hindrance from the tertbutyl group was the cause of the selectivity to the linear esters. However, the real origin of this unusual and interesting selectivity remained unclear until very recently and the work of Mecking and co-workers on this phenomenon\textsuperscript{136} using methyl oleate as a model substrate and 1,3–bis(ditermbutylphosphino)propane as model ligand for DTBPMB. The authors realised the direct experimental observation at low temperature of the intermediates involved in the reaction and proposed key mechanistic features (Figure 1.12). In the isomerisation equilibrium the terminal linear alkyl species \textbf{1} is predominant, the branched species not being observed. However, the branched species \textbf{2} exists in similar amount that the linear species due to the chelating stabilisation of the adjacent ester group. Both linear and branched species \textbf{1} and \textbf{2} can insert CO. The methanolysis of the linear product \textbf{3} yields the linear diester. However, species \textbf{4} is resistant to methanolysis. The authors showed that the path leading to \textbf{4} does not constitute a dead end, but preferentially a resting state which can convert...
again to species 2 by loss of CO, and isomerises to the “productive” catalytic cycle (left cycle on Figure 1.12). Finally, the full mechanism of the reaction methanolysis/isomerisation/methoxycarbonylation yielding a linear diester from sunflower oil was entirely described by Walther and co-workers. 137

1.4.3 Tolerance towards different functional groups

The DTBPMB ligand has been shown to be efficient for the alkoxycarbonylation of alkenes whatever the position of C=C bond in the carbon chain. However, this ligand has shown to be successfully involved in the alkoxycarbonylation of other substrates and in some other reactions. Otherwise stated, the term “ligand” designates in the following section the DTBPM ligand.

1.4.3.1 Alkoxycarbonylation of norbornene

The Pd/DTBPMB system has been shown to give high linear selectivity on alkene methoxycarbonylation. However, Ruiz, Claver and co-workers have demonstrated another highly selective ability of this system toward the carbonylation of norbornene. 138 Indeed, they showed that the catalyst based on PdCl₂/DTBPMB affords excellent conversions (>99%) and selectivity (>99%) to the exo-ester (Figure 1.13). 139

![Figure 1.13: Methoxycarbonylation of norbornene](image)

1.4.3.2 Isomerisation, Alkoxycarbonylation and Hydroxycarbonylation of unsaturated esters and carboxylic acids

The case of unsaturated esters: The methoxycarbonylation of unsaturated esters with high selectivity towards the linear diesters was reported in 2005. 140 The catalyst Pd/DTBPMB was then shown to be versatile for utilisation of alkenes bearing a functional group on their carbon chain. The phenomenon of isomerisation of the C=C bond has been recently used for the alkoxycarbonylation of unsaturated fatty esters where the C=C bond is deep buried in the carbon chain. 64,65,67,141 In these studies, the authors
showed that the one-pot methanolysis/isomerisation/methoxycarbonylation of triglycerides originating from natural oils was possible, yielding to long chain diesters with high selectivity to the linear species. One exception to the linear selectivity has been reported, however this is valid only in a specific case, while the C=C bond is trapped between two unreactive functions towards the methoxycarbonylation, and for the methoxycarbonylation of styrene and vinyl acetate (see 1.4.3.3).

The efficiency of the Pd/DTBPMB system for isomerising the C=C bond was employed by Sereining and co-workers for preparing methyl 12-oxostearate from ricinoleic acid. The C=C bond is isomerised next to the hydroxyl group, resulting in a keto-enol equilibrium yielding 100% conversion to the desired oxoester product. Moreover, the catalyst used on monounsaturated cardanol has been shown to be efficient for isomerising the C=C bond to the benzylic position, yielding isocardanol. However, the conversion was only 40%, the remaining products being random isomers of cardanol. Finally, the isomerising olefin metathesis using a bi-catalytic system Ru/Pd was carried out by Goossen and co-workers. However, in this case the Pd/DTBPMB system showed very poor activity for isomerising the C=C bond.

Finally, the methoxycarbonylation reaction was employed for making the preparation of 1,3,5,7,9,11,13,15-octakis[methylpropanoate]octasiloxane (OMPO, Figure 1.14).

Preparation of adipic acid: Adipic acid and its ester equivalent are involved in the synthesis of polymers, therefore an efficient synthesis for obtaining them is important. The production of adipic acid led to numerous patents, however the syntheses can be linked in three groups. The first kind of synthesis involves the methoxy/hydroxycarbonylation of pentenoic acid isomers. This leads to the production of the diacid. Another multi-step process starts from γ-valerolactone, originating from levulinic acid. The lactone is ring-opened, yielding to pentenoic acid which is then methoxycarbonylated.

Finally, the last group of syntheses involve the hydroxycarbonylation of butadiene in a
two step reaction. A first hydroxycarbonylation is carried out at a low water concentration (<3% in weight to the liquid reaction medium), while a second hydroxycarbonylation is made at higher water amounts (between 3% and 50%). A continuous flow process yielding adipic acid has been developed. Eastham and Tindale claim that in the hydroxycarbonylation reaction, an excess of the ligand over the metal is advantageous, as the ligand may play the role of a base to buffer the acid level and prevent the degradation of the substrate.

1.4.3.3 Alkoxycarbonylation of vinyl acetate and styrene

The methoxycarbonylation of vinyl acetate has been reported yielding up to 78% selectivity to the branched product, to methyl 2–(acetyloxy)propanoate, a potential source of lactic acid and its esters (Figure 1.15). As well as being involved in the carbonylation process, it appeared that the ligand played the role of stabiliser towards vinyl acetate, preventing its degradation to methyl acetate and 1,2–dimethoxyethene due to transesterification with methanol catalysed by methane sulfonic acid. In most reactions a large excess of acid is employed, but in this case the reactions were carried out using an excess of DTBPMB over acid. NMR studies showed that all the acid was present in the form of the diphosphonium salt, $[C_6H_4(CH_2 PH_{tBu}^2)_2]^{2+}$ but that this quaternary phosphonium salt is able to oxidatively add P–H across the palladium centre to generate the catalytically active hydrido complex. The tying up of the acid in this way removed free acid and prevented the transesterification of vinyl acetate by methanol. The authors screened a range of diphosphine ligands where the tBu groups on DTBPMB were successively replaced by iPr groups in order to try to improve the branched:linear ratio by reducing the steric demand of the ligand, but DTBPMB ligand showed the best activity. Ooka and co-workers have reported the methoxycarbonylation of vinyl acetate using a polymeric sulfonic acid instead of methane sulfonic acid. The sulfonate group was attached to a polymeric resin, with an optimal ratio $SO_3H/Pd = 4.5$. This heterogenised catalyst is potentially capable of recycling. The same system has shown a high

![Figure 1.15: The methoxycarbonylation of vinyl acetate as a step reaction in the production of methyl lactate.](image)
efficiency for the methoxycarbonylation of styrene, again with a high selectivity (88%) to the branched product (Figure 1.16).

![Figure 1.16: Methoxycarbonylation of styrene](image)

1.4.3.4 Hydroxycarbonylation and alkoxycarbonylation of alkynes

The methoxycarbonylation of alkynes, and especially propyne, has been reported yielding methyl methacrylate. However, to the best of our knowledge, the DTBPMB ligand was reported being involved in hydroxycarbonylation and methoxycarbonylation of alkyne only once in the literature. Contrary to the methoxycarbonylation of styrene which can give high selectivity to branched saturated ester, the hydroxycarbonylation of phenylethyne provides a 99% selectivity to the linear unsaturated ester (88% yield). Small amounts of the dicarbonylation product (9%) were shown to have arisen from the branched hydroxycarbonylation product (Figure 1.17). This confirms the generally high preference for linear hydroxycarbonylation provided by the Pd/DTBPMB/MSA system.

![Figure 1.17: Hydroxycarbonylation of phenylethyne](image)

The reaction carried out with linear aliphatic alkynes in presence of methanol yields isomerised unsaturated esters in the case of 1–butyne, pentyne and octyne, only when the reaction is carried out over a short reaction time or with low catalyst loading. A longer reaction time gives saturated diesters with a predominance of the linear species. Indeed, a cascade reaction happens, so that the initially formed unsaturated diester, which predominantly has the double bond in the $\alpha,\beta$–position conjugated to the double bond, undergoes isomerisation of the double bond all along the chain, but the double bond is only trapped by methoxycarbonylation when it is in the least thermodynamically favoured terminal position. The selectivity to the $\alpha,\omega$–diesters is >99% for dimethyl...
adipate from butadiene, 92% for dimethyl heptanedioate from 1–pentyne and 87% for dimethyl decanedioate formed from 1–octyne, where the double bond has to travel out of conjugation and seven positions along the chain. Internal alkynes generally give mono-methoxycarbonylation at one end of the triple bond (e.g. methoxycarbonylation of 4–octyne, Figure 1.18), although longer reaction times lead to products that have one terminal ester function and one internal.99

![Figure 1.18: Methoxycarbonylation of 4-octyne](image)

1.4.3.5 Obtention of 5–cyanovaleric acid

Obtaining 5–cyanovaleric acid from the methoxycarbonylation of pentenenitriles would provide a significant improvement in the preparation of this important intermediate which can give ε–caprolactam on hydrogenation (Figure 1.19).160,161 The 5–cyanovaleric acid is reduced to 6–aminocaproic acid which undergoes cyclisation leading to ε–caprolactame. In the presence of methanol, the carbonylation of 3–pentenenitrile gives, after 5 hours at 100°C, methyl 5–cyanovalerate (conversion > 97%, 98% linear selectivity).162,163 The stability of the nitrile function towards the methoxycarbonylation is remarkable. Conversely, it is noticeable that the ligand/Pd system is inert towards the nitrile function, showing its versatility and tolerance for reactive functional groups.

![Figure 1.19: 5–cyanovaleric acid: an ε–caprolactam precursor](image)

1.4.3.6 Other reactions involving palladium

Apart the methoxycarbonylation of alkene or alkyne species, the Pd/DTBPMB system has been involved in various reactions with different kinds of substrates.

For instance, Beller and co-workers carried out the oxidative homocoupling of various benzyl and heterobenzyl alcohols, giving the corresponding benzoate esters in 60 to 85% yields (Figure 1.20).164 The authors demonstrated the feasibility of this reaction using an aliphatic alcohol, 1–octanol in a 72% conversion.
Cross-coupling reactions have been attempted as well. For instance, the C–C and C–N bond-forming reaction was tried by Wills and co-workers,\textsuperscript{165} however they showed that the DTBPMB ligand was not the most efficient ligand for making such a coupling. Nevertheless, the Suzuki-Miyaura reaction catalysed by Pd/DTBPMB has been described by McNulty and co-workers.\textsuperscript{166} The scope of the Suzuki-Miyaura cross-coupling reaction is shown to be quite broad and it is efficient with aryl iodides, bromides, and activated aryl chlorides. However, deactivated aryl chlorides are less reactive. The authors have shown as well the possibility of making carbonylative coupling reactions involving aryl bromides, carbon monoxide and a nucleophile (\textit{e.g.} an alkyl alcohol, water and diethyl amine) with yields up to 97\% (Figure 1.21).

Such carbonylation reaction have been attempted on aryl chlorides.\textsuperscript{167} However, the reaction was only shown to be efficient when the aromatic ring was electron poor. The opposite reaction (decarboxylation) was shown to be efficient on 4–hydroxybenzoic acid at relatively high temperature (85\% conversion at 140\textdegree C, Figure 1.22).\textsuperscript{168}

The preparation of aqueous poly(arylacetylene) dispersions was done using bidendate phosphine/palladium catalysts.\textsuperscript{169} DTBPMB gave very high activity towards the phenylacetylene polymerisation (96\% conversion). However, it was not shown to be the best ligand for the catalytic system, \textsuperscript{4}Bu\textsubscript{2}P(CH\textsubscript{2})\textsubscript{3}P\textsuperscript{4}Bu\textsubscript{2} yielding full conversion and a higher turnover number.
1.4.3.7 Other reactions involving rhodium

All the systems previously described deal with palladium. However, the ligand was not only used with this metal and was for instance complexed to rhodium for promoting the hydroformylation reaction.\(^{170}\) The Rh/DTBPMB system was shown to be efficient towards the hydroformylation of 1–hexene (100%) and 1–octene (89%). However, contrary to what is seen with the methoxycarbonylation of unsaturated alkyl esters, the selectivity to the desired linear aldehyde is very poor (maximum 55%).

Another reaction involving the Rh/DTBPMB system was described for the carbonylation of methanol for the production of acetic acid.\(^{171}\) The process of methanol carbonylation is traditionally carried out with cis–[Rh(CO)\(_2\)I\(_2\)]\(^{-}\) in the Monsanto process.\(^{102}\) The authors showed that a catalytic system based on [RhCl(CO)\(_2\)]\(_2\)/DTBPMB, with added methyl iodide, gives higher initial rates for the reaction than the Monsanto catalyst at 150–180°C. However, the active species is not stable under the reaction conditions and rapidly decomposes to a species identified as the Monsanto catalyst. Only the promoting effect of the added methyl iodide seems explaining the initial observed higher carbonylation rates. However, it is more likely that the rhodium forms a complex with DTBPMB, which gives a higher rate of oxidative addition, but that the complex is unstable towards quaternisation of the DTBPMB.

1.5 Conclusion

Biomass presents many possibilities in which a transformation (chemical, catalytic) can occur for producing valuable chemicals or end-products. Among all the starting materials available from biomass, vegetable oils and triglycerides represent a great reservoir for developing new processes, yielding especially monomers and polymers. Among the processes that can be used, the methoxycarbonylation of natural oils represents an interesting choice. Indeed, due to the great versatility and the powerful tool that is represented by the Pd/DTBPMB catalytic system, a large range of various alkoxy carbonylation reactions can be attempted.

The bidentate ligand 1,2–bis(di tertbutylphosphinomethyl)benzene has been shown to be a versatile ligand that can be employed in very many reactions (carbonylation and its derivatives, and cross-coupling reactions). The interest in this ligand relies essentially on its high selectivity towards the terminal alkoxy carbonylation of alkenes, with the exception of styrene and vinyl acetate leading to the branched products. This interesting selectivity is used in the next chapters for the alkoxy carbonylation and aminocarbonylation of various natural oils and some of their derivatives for the preparation of linear diesters and esteramides, that can be used for the preparation of polymers.
Chapter 2

Polyester precursors from catalytic reactions of natural oils

The work presented in this chapter was partially published in Green Chemistry in 2012.65

Dimethyl 1,19–nonadecanedioate is produced from the methoxy-carbonylation of commercial olive, rapeseed or sunflower oils in the presence of a catalyst derived from [Pd₂(dba)₃], 1,2–bis(ditert-butylphosphinomethyl)benzene and methane sulfonic acid. The diester is then hydrogenated to 1,19–nonadecanediol using Ru/1,1,1–tris–(diphenylphosphinemethyl)ethane. From this diester 1,19–nonadecadienoic acid is synthesised and hydrogenated to short chain oligoesters using the same ruthenium-based catalyst, oligoesters that can themselves be hydrogenated to 1,19–nonadecanediol in the presence of water.

2.1 Introduction

As oil feedstock dwindle, there will be a need to find alternative fuels and also alternative feedstock that can be used to produce the many chemicals that enhance our living conditions. Polymeric materials have revolutionised how mankind lived over the last hundred years, not only replacing scarce, expensive and sometimes toxic metals or clothing, but also allowing the development of wholly new applications that were not contemplated until plastics were introduced on a large scale.172 Cellulose esters, used as thermoplastic materials, and vulcanised natural rubber173 were amongst the first man made plastics
to be re-discovered, being already know in ancient Mesoamerica. These polymers were based on sustainable feedstock, but they were soon superseded in importance by petroleum derived polymers. A return to new polymer feedstock, once again based on natural raw materials, may occur in the very long term. This applies, amongst others, to polyesters and polyamides as well as polyethylene, a small portion of which is already produced from renewable resources. Polyamides and polyesters are usually derived from monomers which are functionalised in the \( \alpha \) and \( \omega \) positions, so one possible route to bio-derived analogues would be to make such monomers from fatty acid esters, such as methyl oleate. One way to do this is to use metathesis. Self-metathesis gives the \( \text{C}_{18} \) diester, while cross-metathesis with dimethyl maleate or methyl propenoate gives difunctionalised \( \text{C}_{11} \) products. In a similar way, cross-metathesis of methyl 10–undecenoate (derived from castor oil) with acrylonitrile followed by an hydrogenation step gives the difunctionalised \( \alpha, \omega \)-aminoester. However, in all of these reactions only half the carbon atoms from methyl oleate will end up in the desired diesters, the remainder giving hydrocarbons (by self-metathesis) or monofunctionalised products (by cross-metathesis). An alternative is to use a reaction in which the double bond in an unsaturated ester – for instance methyl oleate – is isomerised to the thermodynamically least favoured terminal position in the hydrocarbon chain, where this double bond will be trapped by a tandem reaction. Attempts to use hydroformylation as the trapping reaction have only been partially successful with low \( \omega \) selectivity, but it has been recently reported that, using methoxycarbonylation as the trapping reaction, very high selectivity (\( > 95\% \)) towards dimethyl 1,19–nonadecanedioate can be obtained.

This methoxycarbonylation reaction was eventually employed as part of a route leading to aliphatic polyesters, with melting and crystallisation temperatures in the range of typical thermoplastics starting from the nature-derived ester, methyl oleate. This process involves the methoxycarbonylation of methyl oleate to give dimethyl 1,19–nonadecanediol with very high selectivity and isolated yields of over 90%. The key to this remarkable reaction, which involves isomerisation of the double bond backwards and forwards along the chain, but is only being trapped by carbonylation when it is in the thermodynamically least favoured \( \omega \) position relative to the ester group, is the use of a palladium based catalyst modified by the ligand 1,2–bis(diterbutylphosphino-methyl)benzene (DTBPMB) (Figure 2.1). Dimethyl 1,19–nonadecanediolate was reduced to 1,19–nonadecanediol using LiAlH\(_4\) or by catalytic hydrogenation. Condensation of the diester with the diol gave the polyester with ester groups separated by

\[
\begin{array}{c}
\text{P}^\text{Bu}_2 \\
\text{P}^\text{Bu}_2
\end{array}
\]

**Figure 2.1**: DTBPMB
17 carbon atoms on the carboxylic acid side and 19 carbon atoms on the alcohol derived side. The obtained polyesters have similar properties to low-density polyethylene. For this reasons, this new kind of polyester would represent a real possibility for replacing the non-biodegradable and petroleum-derived polyethylene (Figure 2.2). A similar Chemistry was carried out starting from the unsaturated C\textsubscript{23} ester, methyl erucate.

![Figure 2.2: Comparison between a polyethylene chain (bottom) and its possible replacement by a long carbon chain polyester (top).](image)

In this chapter are reported the attempts to render the syntheses of these monomers even more bio-compatible. In particular, the synthesis of dimethyl 1,19–nonadecanedioate (shortened as “Dino”) was realised directly from biological feedstock such as olive, rapeseed and sunflower oils, removing the need for extraction and purification of methyl oleate. The catalytic hydrogenation of the diester to 1,19–nonadecanediol has developed as a cleaner alternative to LiAlH\textsubscript{4} reduction. Finally, the synthesis of oligomers of 19–hydroxynonadecanoate by partial hydrogenation of 1,19–nonadecanedioic acid will be described. All these reactions are outlined in Figure 2.3.

![Figure 2.3: (a) Formation of dimethyl 1,19–nonadecanedioate by methoxycarbonylation of some natural oils catalysed by Pd / MSA / DTBPMB; (b) Hydrogenation step using Ru / Triphos; (c) Hydrolysis of dimethyl 1,19–nonadecanedioate.](image)
Polyester precursors from catalytic reactions of natural oils

sunflower oil directly to Dino. However, the work described in this chapter shows that it is not necessary to use high oleate oils to obtain pure materials. This makes the process described in this chapter potentially much cheaper and much eco-friendly, and could provide a high added value outlet for surplus oil stocks. The same communication\textsuperscript{64} also briefly describes the hydrogenation of the diester to the diol using a catalyst devised by Milstein and co-workers.\textsuperscript{181} Finally, the hydrogenation has been proven to work by using the Saudan’s ruthenium catalyst.\textsuperscript{141,182}

2.2 Synthesis of dimethyl 1,19–nonadecanedioate from triglycerides

Previous studies on the methoxycarbonylation of unsaturated C\textsubscript{18} esters\textsuperscript{140} opened the path to investigate whether Dino could be obtained from oils that contain substantial amounts of C\textsubscript{18} fatty acid esters with different amounts of unsaturation, reasoning that methanolysis of the triglyceride esters and methoxycarbonylation should occur in tandem under the reaction conditions. The oils were obtained from a local supermarket and were chosen for their different proportions of oleic, linoleic and linolenic acid esters (Table 2.1). Using a method very similar to that described previously\textsuperscript{67,141} for the methoxycarbonylation of methyl oleate, a one-pot synthesis of Dino from natural oils has been successfully achieved, affording the desired product as an analytically pure snowy white powder, with NMR spectra as reported earlier.\textsuperscript{67,141} This one-pot process represents a significant enhancement in production of Dino since it starts from standard quality natural oils with no extra purification and avoids the multiple reaction and purification steps usually required for high purity methyl oleate as a feedstock. The yields obtained from 10 mL of the different oils, as well as the conversion of C\textsubscript{18} chains are shown in Table 2.1.

The isolated yield of the desired Dino reaches its maximum with olive oil, followed by a similar yield for rapeseed oil. Sunflower oil as a feedstock provided the lowest isolated yield – these data reflect the differing amounts of triglyceride oleate present in the starting oils. Nevertheless, it is noticeable that the isolated yield, in the case of olive oil and rapeseed oil, is slightly higher 100%. At first sight, this very interesting, but impossible result led to consider whether not only the oleate part of the oil was reactive, but also the linoleate part. As shown in previous studies,\textsuperscript{140} the linoleate part will react through methoxycarbonylation, leading to different isomers of dimethyl 1,19–nonadecenedioate. This compound may afterwards react through transfer hydrogenation from the methanol, giving the Dino (Figure 2.4). In this way, the overyield of 2% in the case of olive oil and 8% for rapeseed oil would be easily explained. Actually, this
2.2 Synthesis of dimethyl 1,19–nonadecanedioate from triglycerides

<table>
<thead>
<tr>
<th>Compositiona</th>
<th>Methyl oleate</th>
<th>Olive oil</th>
<th>Rapeseed oil</th>
<th>Sunflower oil</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oleate</td>
<td>&gt;99%</td>
<td>73%</td>
<td>64%</td>
<td>38%</td>
</tr>
<tr>
<td>Linoleate</td>
<td>–</td>
<td>2%</td>
<td>19%</td>
<td>50%</td>
</tr>
<tr>
<td>Linolenate</td>
<td>–</td>
<td>3%</td>
<td>6%</td>
<td>2%</td>
</tr>
<tr>
<td>Dino(^b)</td>
<td>&gt;9.0 g</td>
<td>6.5–6.9 g</td>
<td>6.3–6.4 g</td>
<td>2.8–3.4 g</td>
</tr>
<tr>
<td>Isolated yield</td>
<td>71–74%</td>
<td>61–69%</td>
<td>28–36%</td>
<td></td>
</tr>
<tr>
<td>(from oleate)(^c)</td>
<td>(up to 102%)</td>
<td>(up to 108%)</td>
<td>(up to 96%)</td>
<td></td>
</tr>
</tbody>
</table>

\(^a\) Unsaturated C\(_{18}\) fraction only, the remaining fatty acid residues are from different chain lengths (mainly C\(_{16}\) and C\(_{23}\)) and from stearic (saturated C\(_{18}\)) acids.

\(^b\) Dimethyl 1,19–nonadecanedioate obtained from 10 mL of oil.

\(^c\) Yields are calculated assuming the molecular mass of the starting material is equivalent to glycerol trioleate (885.43 amu).

Overyield is too easily explained. Further studies, described in Chapter 3, show that this hypothesis of transfer hydrogenation from the methanol is inadequate, for the simple reason it does not occur – at least under the present reaction conditions – and it seems that only the oleate is reacting. As an exact and accurate composition of the oils is difficult to obtain, it is believed that such overyields are due to a small underestimation of the oleate amount in the different oils. Moreover, evidence that the Dino arises mainly from the oleate chains in the oils is supported by GC–MS analysis of the crude reaction products. Nonetheless, due to the multitude of compounds present and the often similar or identical masses and similar fragmentation patterns, full assignments from GC–MS

![Diagram](image_url)

Figure 2.4: Possible transfer hydrogenation from methanol to the alkene
Polyester precursors from catalytic reactions of natural oils

are problematic. An example of the various composition of the crude mixture obtained after the methoxycarbonylation of sunflower oil is given in Figure 2.5. However, the main impurities are glycerol and methyl esters of saturated fatty acids of different chain lengths which are present as glycerol esters in the feed oil. For instance, peak A in the GC–FID trace shown in Figure 2.5, which is much more intense in the trace obtained from olive oil, with a slightly shorter retention time than that for Dino (peak B) and a parent ion at 354 amu (GC–MS), can be assigned tentatively to 1,19-dimethyl nonadecenedioate isomers. This is relevant in view of the significant linoleate content of many feedstocks (Table 2.1), and shows that this material is also carbonylated to linear products. Some of the different minor side-products obtained after methoxycarbonylation of olive oil are tentatively identified by GC–MS as methyl hexadecanoate 1, methyl stearate 2, methyl eicosanoate 3 and methyl tetracosanoate 4 (Figure 2.5).

The methoxycarbonylation of the different oils leads to various conversion to Dino. Moreover, an efficient way has been found which avoids the use of time-consuming and solvent-wasting column chromatography for isolating Dino. Among all the products obtained after the reaction, it seems that the desired product is the only linear saturated diester present in the crude mixture. Dino was observed not to be soluble in ice-cold methanol. Therefore, all the products from the crude mixture but Dino remain solubilised in cold methanol. A simple filtration over a Büchner funnel yielded the expected product with a 99% purity. Higher purity can be easily reached by recrystallisation from ice-cold methanol. This utilisation of cold methanol renders the synthesis of the desired compound even more eco-friendly and economically valuable. The monomer is eventually obtained as a white snowy powder, whereas the remaining side-products present the appearance of a highly viscous liquid, whatever the starting oil (olive, rapeseed or

![Figure 2.5: GC–FID trace of the methoxycarbonylation of sunflower oil](image)
sunflower) used for the reaction (Figure 2.6). Potential uses of the remaining oil as a lubricant or even a perfume additive could be considered.

Further studies on the methoxycarbonylation of methyl linoleate are reported separately in Chapter 3.

Figure 2.6: After the methoxycarbonylation of olive oil: the monomer is obtained as a white powder (right), the side-products as an orange liquid (left)

2.3 Hydrogenation of dimethyl 1,19–nonadecanedioate

The hydrogenation of esters and carboxylic acids, which are amongst the more difficult hydrogenations to have been reported,\textsuperscript{183} has traditionally been carried out using copper chromite at high pressures and temperatures. The first homogeneous catalysts for this reaction, ruthenium complexes of 1,1,1–tris–(diphenylphosphinemethyl)ethane (Triphos, Figure 2.7) were described by Elsevier and co-workers.\textsuperscript{184–186} Initially, the reactions only worked with activated acids such as oxalic acid, which could be hydrogenated to 1,2–ethanediol with high selectivity.\textsuperscript{184} Further developments by the same group,\textsuperscript{185,186} but also by-workers at Davy Process Technology\textsuperscript{187,188} extended the substrate scope to cover other acids including simple aliphatic carboxylic acids. High activities towards primary alcohols were achieved by adding water (10% volume) and working at high temperature (220°C).\textsuperscript{187,188} Reductive hydrogenation of an acid is shown on the left half of Figure 2.8. It is thought that the harsh conditions (such as high temperatures) required to obtain good rates lead to the decarbonylation of an aldehyde or any other reaction intermediate to give the species [RuH\textsubscript{2}(CO)(Triphos)], which is catalytically inactive.

Figure 2.7: 1,1,1–tris–(diphenylphosphinemethyl)ethane (Triphos)
Ruthenium carbonyl complexes are sometimes synthesized by decarbonylation of alcohols and the mechanism is quite well understood. In addition, the complex [RuH$_2$(CO)(Triphos)] has been isolated from a reaction of [Ru(acac)$_3$] and Triphos in methanol under hydrogen, and others have isolated the same complex from the hydrogenation of levulinic acid under similar conditions. Water is then required to return the catalyst into an active form by water-gas shift type chemistry (right hand of Figure 2.8). Furthermore, this may explain the presence of products bearing a methyl end group, which would arise from the reaction leading to a release of an alkane species (top right of Figure 2.8). An alternative method for hydrogenating simple esters using the Ru/Triphos system involves carrying out the hydrogenation in methanol in the presence of zinc powder, where good activities could be obtained at 100°C. Original suggestions that Triphos is active because it coordinates in a facial manner have been challenged by the discovery of several other catalysts, which do not contain facially coordinating ligands but which are active for ester and acid hydrogenation. Indeed, it has been reported that 1,19–nonadecanediol as well as 1,23–tricosanediol can be formed in high yields and with more than 99% purity, using dichlorobis(2–(diphenylphosphino)ethylamine) ruthenium as the catalyst (Figure 2.9).
2.3 Hydrogenation of dimethyl 1,19–nonadecanedioate

Table 2.2: Hydrogenation of Dino with the Ru/Triphos/Zn system

<table>
<thead>
<tr>
<th>Entry</th>
<th>Time (h)</th>
<th>Temperature (°C)</th>
<th>Yield(^b)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>20</td>
<td>100</td>
<td>20%</td>
</tr>
<tr>
<td>2</td>
<td>115</td>
<td>100</td>
<td>85%</td>
</tr>
<tr>
<td>3</td>
<td>1</td>
<td>140</td>
<td>&lt;1%</td>
</tr>
<tr>
<td>4</td>
<td>3</td>
<td>140</td>
<td>&lt;1%</td>
</tr>
<tr>
<td>5</td>
<td>20</td>
<td>140</td>
<td>&gt;99%</td>
</tr>
</tbody>
</table>

\(^a\) Conditions: Dino 1.103 mmol (393 mg), Ru(acac)\(_3\) 0.011 mmol (4.5 mg), Triphos 0.022 mmol (14 mg), Zn 0.132 mmol (8.6 mg), \(P(H_2) = 70\) bar, MeOH (10 mL).

\(^b\) \(^1\)H NMR

2.3.1 First attempts at hydrogenation

The first attempts at the hydrogenation of Dino were based on the use of zinc powder as an additive to the Ru/Triphos system.\(^{184}\) The reacting conditions were originally designed for the hydrogenation of dimethyl oxalate to ethylene glycol. Therefore, the system was applied in an attempt to hydrogenate Dino to 1,19–nonadecanediol, which results are reported in Table 2.2. It was noticeable that the same conditions as Elsevier (Table 2.2, entry 1) led to some conversion, though much lower than expected. Indeed, the \(^1\)H NMR conversion was only 20%. Increasing the reaction time to 115 h – nearly five days – increased the conversion rate up to 85% (Table 2.2, entry 2). However, a small amount of saturated end group was noticed in the \(^1\)H NMR spectrum, which leads to the conclusion that such a long reaction time leads to a degradation of the starting Dino via a decarboxylative mechanism. Moreover, such a long reaction time cannot be considered as economically valuable. For these reasons, it was decided to increase the working temperature, reasoning that the kinetics of the reaction would substantially improve. This gave full conversion to the desired 1,19–nonadecanediol after 20 h at 140°C (Table 2.2, entry 5). No saturated end groups were seen on the \(^1\)H NMR spectrum, showing the reaction was running properly without any degradation of the materials. Shorter reaction times show the existence of an induction period (Table 2.2, entry 3 and 4). However, on receipt of a new batch of Triphos caused the reaction to stop working.

2.3.2 The Ru/Triphos/Zn system fails

Once the batch of Triphos ran out, another had to be used. It became troublesome to notice that the new batch did not allow the reaction to be as performing as with the
Table 2.3: Failure of the Ru/Triphos/Zn system

<table>
<thead>
<tr>
<th>Entry</th>
<th>Time (h)</th>
<th>Temperature (°C)</th>
<th>Yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>20</td>
<td>140</td>
<td>16%</td>
</tr>
<tr>
<td>2</td>
<td>16</td>
<td>140</td>
<td>&lt;1%</td>
</tr>
<tr>
<td>3</td>
<td>20</td>
<td>140</td>
<td>10%</td>
</tr>
<tr>
<td>4</td>
<td>20</td>
<td>140</td>
<td>25%</td>
</tr>
<tr>
<td>5</td>
<td>25</td>
<td>140</td>
<td>0%</td>
</tr>
<tr>
<td>6</td>
<td>20</td>
<td>180</td>
<td>19%</td>
</tr>
</tbody>
</table>

\( ^a \) Conditions: Dino 1.103 mmol (393 mg), \( \text{Ru(acac)}_3 \) 0.011 mmol (4.5 mg), Triphos 0.022 mmol (14 mg), Zn 0.132 mmol (8.6 mg), \( P(H_2) = 70 \text{ bar, MeOH (10 mL)} \).

\( ^b \) \text{^1H NMR}

\( ^c \) \( H_2O 1\% \) (0.1 mL added to the methanol)

previous batch. Indeed, while with the original batch the reaction was providing a full conversion to 1,19–nonadecanediol (Table 2.2, entry 5), the other batch of Triphos only gave a poor conversion of 16% (Table 2.3, entry 1). The first hypothesis in such a case is the poisoning of the catalyst by some impurities which could be present in the new batch of ligand. Therefore, it was decided to add some water to the solvent (Table 2.3, entry 2) for promoting the regeneration of the catalyst to the active species. Nevertheless, this attempt failed and only provided a conversion below 1%. The batch of Triphos was then recrystallised from THF to remove the possible impurities. Once the recrystallised ligand was used, it only gave non reproducible results, the conversion to the desired product oscillating between 0% and 25% (Table 2.3, entries 3, 4 and 5). Eventually, a last attempt was tried by increasing the reaction temperature to 180°C, which only led to a conversion of less than 20% (Table 2.3, entry 6). Afterwards, this very promising Ru/Triphos/Zn system has been abandoned. It seemed that the new batch of Triphos used in the new series of experiments did not contain any impurities. This suggests that the previous batch contained some impurities, whatever kind, that probably played the very important role of a promoter. If the first batch really contained any promoter, its nature is unknown. Indeed, the first batch was totally used in previous experiments.

2.3.3 Enhancement of the catalytic activity of the Ru/Triphos system

2.3.3.1 Utilisation of methanesulfonic acid

Leitner and co-workers have reported the successful hydrogenation of levulinic acid using the Ru/Triphos system under different conditions to the one previously described and
Table 2.4: Production of 1,19-nonadecanediol by hydrogenation of Dino

<table>
<thead>
<tr>
<th>Entry</th>
<th>Solvent</th>
<th>( \text{H}_2\text{O} ) (mmol)</th>
<th>MSA (mmol)</th>
<th>Temperature (°C)</th>
<th>Yield GC–(isolated)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1(^{b})</td>
<td>methanol</td>
<td>0</td>
<td>0.111</td>
<td>140</td>
<td>99%–(81%)</td>
</tr>
<tr>
<td>2(^{c})</td>
<td>methanol</td>
<td>0</td>
<td>0.111</td>
<td>140</td>
<td>99%–(63%)</td>
</tr>
<tr>
<td>3</td>
<td>dioxane</td>
<td>0</td>
<td>0.111</td>
<td>220</td>
<td>&lt;1%</td>
</tr>
<tr>
<td>4</td>
<td>dioxane</td>
<td>10</td>
<td>0.111</td>
<td>220</td>
<td>&lt;1%</td>
</tr>
<tr>
<td>5</td>
<td>dioxane</td>
<td>10</td>
<td>0</td>
<td>220</td>
<td>99%–(73%)</td>
</tr>
<tr>
<td>6</td>
<td>dioxane</td>
<td>50</td>
<td>0</td>
<td>220</td>
<td>99%–(76%)</td>
</tr>
<tr>
<td>7</td>
<td>dioxane</td>
<td>0.6</td>
<td>0</td>
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<td>18%</td>
</tr>
<tr>
<td>8</td>
<td>dioxane</td>
<td>0</td>
<td>0</td>
<td>220</td>
<td>13%</td>
</tr>
</tbody>
</table>

\(^{a}\) Conditions: Dino 1.103 mmol (393 mg), Ru(acac)\(_3\) 0.011 mmol (4.5 mg), Triphos 0.022 mmol (14 mg), \( P(\text{H}_2) = 40 \text{ bar} \), Dioxane + Water = 10 mL

\(^{b}\) Zn 0.132 mmol (8.6 mg), \( P(\text{H}_2) = 70 \text{ bar} \)

\(^{c}\) Absence of Zn

have shown that the acid is successfully reduced to 1,4-pentanediol, itself reduced to 2-methyltetrahydrofuran. In some of their reactions they used ammonium hexafluoroorthophosphate \([\text{NH}_4^+\text{PF}_6^-]\) as an additive, which will undoubtedly react with water to give hydrofluoric acid and \([\text{O}_2\text{PF}_2^-]\). This interesting result led us to investigate whether addition of acid might enhance the hydrogenation reactions carried out in our work, which had shown very variable reproducibility depending upon the batch of Triphos employed. Some tests were then carried out by adding methane sulfonic acid (MSA) to the reaction. The previous system Ru/Triphos/Zn but with added MSA was successful in reducing Dino into the desired product with high conversion (Table 2.4, Entry 1). Moreover, it was very noticeable that the same reaction led to a high conversion if zinc was omitted (Table 2.4, Entry 2). Moreover, the solvent effect was dramatic. In the presence of MSA the hydrogenation of Dino was successful, but swapping the solvent for dioxane led to a conversion below 1% (Table 2.4, Entry 3). Furthermore, carrying out the reaction in the presence of water (10% in volume) provided a very similar result (Table 2.4, Entry 4). Nevertheless, it is also noticeable that the latter reaction, without MSA, led to full hydrogenation of Dino to the expected 1,19-nonadecanediol (Table 2.4, Entry 5). From this point, it was decided to start further studies of the role of water. Indeed, if it were possible – as it seems – to sway the reactivity of the catalyst towards hydrogenation by replacing MSA with water, this could be very interesting from the economical and ecological point of view.
2.3.3.2 About the role of water

As suggested in Figure 2.8, the role of water is to regenerate the poisoned catalyst into an active species by a water-gas shift type reaction. Nevertheless, according to the previously described results, it may be possible that water has roles. In order to investigate more about the role of water during the reaction, the amount of water was successively decreased from 5 mL to 1 mL, 0.06 mL and 0 mL. Full conversion to diol was observed when a large excess of water (10% to 50%) in dioxane was employed (Table 2.4, Entries 5 and 6). However, the conversion of Dino to the corresponding diol decreased dramatically if only a negligible amount of water was added (0.6%, Table 2.4, Entry 7) or if water was omitted entirely (Table 2.4, Entry 8).

The large amounts of water required for hydrogenation reactions in dioxane may suggest that it is not only required for catalyst regeneration as in Figure 2.8. Indeed, such a large amount would suggest an hydrolysis of the diester into a diacid, which would be the active species being hydrogenated. In order to test this hypothesis, the corresponding diacid was synthesised by a hydrolysis of Dino, and was then hydrogenated in the absence of both water and MSA (conditions as for Table 2.4, Entry 8). 1,19-nondecanediol was not obtained as expected. Surprisingly, we observed the production of a white solid, for which NMR spectroscopy, MALDI–TOF Mass Spectrometry (MTMS) and infrared (IR) analyses suggest that a partial hydrogenation of the diacid to 19-hydroxynonadecanoic acid occurs, and that this intermediate undergoes a condensation esterification to give short chain oligoesters (Figure 2.10). The IR spectrum shows that both hydroxy (ν(OH) = 3450 cm$^{-1}$) and ester carbonyl groups (ν(CO) = 1735 cm$^{-1}$) are present. Hydroxy end groups are also observed in the $^1$H NMR spectrum. The latter spectrum (Figure 2.11) shows that the average chain length of the isolated polymer seems to be three monomeric units. Moreover, the presence of a small amount of saturated end group(s) on the $^1$H NMR spectrum shows the existence of a decarboxylative reaction, most probably due to the high temperatures used in the process, but also giving some evidence about the proposed mechanism of regeneration of the catalyst into the active species. Even if the major products obtained after this hydrogenation are these oligomers, the crude product also contains 1,19-nondecanediol, in low amount (Table 2.4, Entries 7 and 8).

![Figure 2.10: The formation of a short chain oligoesters](image-url)
The MTMS suggests that the oligomers are mostly short chains (up to four monomer units). Detailed analysis of the MTMS shows that each chain of oligomer can have several different end groups. The MTMS peaks corresponding to oligomers of chain lengths with four monomer units are shown in Figure 2.12. The assignment of the peaks is represented in Figure 2.13. Well defined clusters of peaks are also observed and are separated by 14 mass units. The main signals arise from oligoesters in which the terminal units are diol (2×OH) hydroxyacid (OH, CO₂H), or diacid (2×CO₂H). Since hydrogenation of the 1,19–nonadecanedioic acid produced an oligomeric material in the absence of water, the possibility has been considered that a further role of water might be to hydrolyse the oligomers formed, allowing their successful hydrogenation. In order to see if these oligoesters could be intermediates in the formation of the expected 1,19–nonadecanediol, a sample of the oligomers was hydrogenated in a mixture of 50% dioxane and 50% water, without any addition of MSA. Complete conversion to 1,19–nonadecanediol was obtained, confirming the previous hypothesis that water can aid the depolymerisation reactions. Three approaches to the hydrogenation of dimethyl 1,19–nonadecanedioate have now been described using three different catalytic systems, which are depicted in Figure 2.14. Each of them has some disadvantages. Catalysts 1¹⁴¹ and 2⁶⁴,¹⁸¹ both require fairly sophisticated ligands, and 1 requires a large amount of base (MeONa). However, they both operate under relatively mild conditions. For instance,
requires 50 bar, 100°C and 2 has a need for only 10 bar, 115°C, whereas the simpler catalyst system 3 – the work presented here – is formed \textit{in situ} from readily available materials, but requires rather higher temperatures (up to 220°C).

The projects introduced in this chapter are of interest and can be improved. For instance, once a 1,19–nonadecanediol is obtained from the Dino, a polyester can be obtained by a condensation reaction. However, a system will be described here that makes
use directly of methyl oleate and a diol for obtaining a polyester by an alkoxycarbonylation chain reaction.

### 2.4.1 Principle of the reaction

The long-carbon chain polyesters described in this chapter are produced via the condensation reaction between dimethyl 1,19–nonadecanediolate and 1,19–nonadecanediol catalysed by Ti(O⁻ Bu)₄. However, another path for obtaining the polyester could be achieved using another catalyst. Indeed, observing the mechanism of the methoxycarbonylation reaction suggests that the polymerisation can be achieved using the Pd/DTB-PMB/MSA catalytic system. Methoxycarbonylation is only a particular case of the alkoxycarbonylation, which involves the reaction of an alkene, carbon monoxide and an alcohol. The hypothesis is based on the fact that any kind of alcohol will react. Therefore 1,19–nonadecanediol can in principle be involved in the alkoxycarbonylation reaction.

![Diagram of the reaction process](Image)

**Figure 2.15:** One-pot Polymerisation/Alkoxycarbonylation of methyl oleate and 1,19–nonadecanediol. 1: Initiation 2 & 3: Propagation 4 & 5: Termination
of methyl oleate. Moreover, the presence of an acid would allow the transesterification of methyl oleate. Both functions of methyl oleate are then involved in a chain reaction leading to the desired polymerisation reaction (Figure 2.15).

2.4.2 Attempts at preparing the polyester and various tests

The solvent used for the reaction must not be an alcohol, because it would compete with the 1,19–nonadecanediol for the alkoxycarbonylation. Dioxane was chosen because it solubilises both monomers. The first attempt was to directly polymerise 1,19–nonadecanediol with methyl oleate (Table 2.5, Entry 1). A $^1$H NMR spectrum of the crude sample once the solvent was removed showed only the the unreacted mixture of both reagents. The reason for the monomers not reacting together might be the too high dilution in dioxane. Alkoxycarbonylation is normally carried out using the alcohol as the solvent. Therefore, we carried out some tests aimed at checking the feasibility of the reaction in a diluted environment. For instance, butan–1–ol was selected for replacing 1,19–nonadecanediol in the test (Table 2.5, Entry 2). However, the GC–MS trace shows the existence of a peak at 338 amu. The expected product of the reaction, 1–butyl 19–methyl nonadecanedioate should provide a peak at 398 amu, corresponding to butyl oleate isomers. The peaks present on the GC–MS reveal the existence of unreacted methyl oleate and the presence of butyl oleate in the same proportions, so only the transesterification occurred during the reaction.

In order to promote the butoxycarbonylation of methyl oleate, two equivalents of butan–1–ol were added (Table 2.5, Entry 3). In this case, if the reaction works, no polymerisation can be carried out leading to polyester alternating carbon chains of 4 and 19 carbons, simply because butan–1–ol is not a diol. Unfortunately, once again only the transesterification product and unreacted methyl oleate were obtained. Therefore, we decided to increase the concentration of the reagents by varying the amount of solvent (Table 2.5, Entry 4). Nevertheless, the main difference compared to the previous experiment (Table 2.5, Entry 3) was an insignificant increase in the amount of butyl oleate compared to methyl oleate. The expected 1,19–butyl nonadecanedioate was obtained in low yield with some 1–butyl 19–methyl nonadecanedioate (Table 2.5, Entry 4). This encouraging result shows that the reaction is feasible.

Another attempt was tried using butan–1,4–diol as the solvent (Table 2.5, Entry 5). Obviously, in this case the chances that the polymerisation might occur are restricted, the solvent playing the role of a “parasite” (Figure 2.15, Step 4): the alkoxycarbonylation is highly favoured, but at both ends, hence preventing polymerisation. The GC–MS analysis of the mixture does not show any of the expected compound bis(4–hydroxybutyl) nonadecanedioate. Traces of tetrathydrofuran and but–3–en–1–ol were detected, as well
Table 2.5: Test-reactions for the one-pot Polymerisation/Alkoxycarbonylation

<table>
<thead>
<tr>
<th>Entry</th>
<th>Alcohol</th>
<th>Solvent</th>
<th>Conversion</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1,19–nonadecanediol</td>
<td>dioxane</td>
<td>0%</td>
</tr>
<tr>
<td>2</td>
<td>butan–1–ol</td>
<td>dioxane</td>
<td>0%</td>
</tr>
<tr>
<td>3</td>
<td>butan–1–ol</td>
<td>dioxane</td>
<td>0%</td>
</tr>
<tr>
<td>4</td>
<td>butan–1–ol</td>
<td>dioxane</td>
<td>&lt;1%</td>
</tr>
<tr>
<td>5</td>
<td>butan–1,4–diol</td>
<td>butan–1,4–diol</td>
<td>100%</td>
</tr>
</tbody>
</table>

*a Conditions: Methyl oleate (1 mL, 2.93 mmol), alcohol (3.08 mmol), Pd$_2$(dba)$_3$ (54 mg, 0.059 mmol), DTBPMB (232 mg, 0.586 mmol), Methanesulfonic acid (76 µL, 1.17 mmol), dioxane (10 mL), CO (40 bar), 80°C, 16 h.

*b Two equivalents of butan–1–ol

*c As Entry 3 but higher concentrations (1.6×, 2×, 2.5×, 3.3× more)

as traces of an unknown product at 190 amu, which could arise from the methoxy-carbonylation of but–3–en–1–ol leading to 4–hydroxybutyl 5–hydroxypentanoate. The proposed mechanism for obtaining these three products is shown in Figure 2.16.

Interestingly, methyl oleate was not found in the crude mixture, suggesting its full conversion to a new product. The logical conclusion is that bis(4–hydroxybutyl) nonadecanedioate cannot be seen on the GC–MS trace, because its boiling point is far too high. A Maldi-Tof analysis was then run on the dried crude mixture. Surprisingly and gratifyingly, the spectrum showed the existence of oligomers bearing two C$_{19}$ and three C$_{19}$ units (Figure 2.17 and 2.18).
2.4.3 Conclusion about the polymerisation

The one-pot polymerisation/alkoxycarbonylation of methyl oleate with dimethyl 1,19-nonadecanediol is an interesting concept. Even if the expected polymerisation of methyl oleate and 1,19-nonadecanediol was not successful, some tests have proven the feasibility of connecting butan-1,4-diol to methyl oleate for obtaining very short chain oligomers. The polymerisation reaction is certainly highly dependent on the concentration of the monomers in the solvent. For the moment, it is very difficult to realise the opportunity to obtain long-chain polyester through this method. However, those promising results definitively open the way for further investigations. For instance, we
can consider the preparation of a polyester for which the structure is an alternation of C₁₉ and C₄ units.

2.5 General Conclusion

Dimethyl 1,19–nonadecanedioate can be conveniently prepared in high purity from the methoxycarbonylation of cheap and readily available olive, rapeseed or sunflower oils. The diester can be hydrogenated using a Ru/Triphos system in the presence of water to give 1,19–nonadecanediol. 1,19–nonadecanedioic acid can be hydrogenated in the absence of MSA and water but only to short chain oligoesters. Such oligoesters can be hydrogenated to 1,19–nonadecanediol if water is added. Here, water may have three key roles: first, it may recycle inactive carbonyl compounds formed from the active catalyst by water-gas shift type chemistry; second, it may hydrolyse the starting diester to the carboxylic acid, generating the acid required to promote the reaction; and finally it may assist in hydrolysing the intermediate oligoesters that might otherwise precipitate during the reaction.
Chapter 3

Tall Oil Fatty Acids as inexpensive renewable feedstock

The work presented in this chapter was partially published in Green Chemistry in 2013.142

Tall Oil Fatty Acids, one of the side products from the paper industry, containing mainly oleic and linoleic acids, are used for producing dimethyl 1,19–nonadecanedioate by methoxycarbonylation in the presence of $[\text{Pd}_2(\text{dba})_3]$, 1,2–bis(2,6-dimethylphenylphosphinoethyl)benzene and methane sulfonic acid in methanol. The methoxycarbonylation of methyl linoleate was used as a model reaction in order to identify other products formed. Approaches to the minimisation of the formation of side products were developed. The question of whether or not polyunsaturated esters can give saturated diesters or even triesters is addressed.

3.1 Introduction

As described in the previous chapter, because of dwindling petroleum feedstocks and increasing prices, the need for renewable resources for producing the polymers that are ubiquitous in enhancing our lives is becoming more and more evident. Ideally, from an ecological and economic point of view, the monomers required for such polymers would be derived from non-toxic wastes or side products from plant based feedstocks. In chapter 2, the synthesis of a new long carbon chain polyester precursor, Dino, and its hydrogenation to 1,19–nonadecanediol has been described. Mecking and co-workers
have shown that these precursors can be copolymerised to aliphatic polyesters with properties very similar to those of polyethylene.\textsuperscript{66,67,141} It was subsequently shown that unpurified olive, rapeseed and sunflower oils, could provide much cheaper alternatives to purified methyl oleate for achieving the synthesis of the Dino.\textsuperscript{65} Walther and co-workers employed a variety of sunflower oil with a high oleic acid content.\textsuperscript{64} All of these oils are used for food, so any process that starts from them would be in competition with food crops, a situation that has to be avoided. The Kraft process for the production of pine wood pulp, produces a side product known as Tall Oil (2 M tonnes per year), which is rich in Tall Oil Fatty Acids (Tofa, mainly oleic and linoleic acids).\textsuperscript{194} Tofa has traditionally been used in inks, rubbers and adhesives.\textsuperscript{195}

In this chapter are reported the studies to render the synthesis of Dino economically attractive and ecofriendly by using Tofa as the feedstock. Furthermore, suspecting a possible transfer hydrogenation from the methanol to the unsaturated isomers of dimethyl 1,19–nonadecenoate to form the saturated equivalent,\textsuperscript{140} the studies on this phenomenon using pure linoleic acid are reported. The possible formation of triesters from a methoxycarbonylation of dimethyl 1,19–nonadecenedioate isomers will be described. 2–Undecenoic acid, for which the methyl ester is available from metathesis of methyl oleate with dimethyl maleate,\textsuperscript{177} undergoes isomerising methoxycarbonylation to the nylon–12,12 precursor, dimethyl 1,12–dodecanedioate, which is also made from methyl 10–undecenoate, available from cracking castor oil.\textsuperscript{32} We also show that the double bond can be selectively moved 13 steps along a chain to form dimethyl 1,17–heptadecanedioate from 2–hexadecenoic acid.

### 3.2 Composition of the Tofa

The Tofa was analysed using GC–MS and \textsuperscript{1}H NMR techniques. At first sight, the MS spectrum shows a single major peak with the library offering a good match of the MS for linoleic acid (m/z = 280). However there was also a peak in the MS at m/z = 282 possibly arising from oleic acid. The quantitative ratio of oleic vs linoleic acids was obtained from a literature method\textsuperscript{196} based on a \textsuperscript{1}H NMR analysis of the crude mixture. This showed the Tofa to contain 72% of linoleic acid and 28% oleic acid.

### 3.3 The methoxycarbonylation of linoleic acid

In order to identify the products from and hence to optimise the methoxycarbonylation of Tofa as well as to address the question of whether or not transfer hydrogenation
of dimethyl 1,19–nonadecenedioate esters to Dino occurs, the methoxycarbonylation of pure linoleic acid was carried out in methanol under an atmosphere of CO (30 bar) at 90°C over 48 h using the palladium-based catalyst described in Chapter 2. GC analysis of the crude product showed several components (Figure 3.1).

Compound 3 was readily identified as the expected 1,19–dimethyl nonadecenedioate, existing as a mixture of esters with the double bond at different positions in the chain. It is clear that there is little, if any of the saturated diester, Dino (4), which has a retention time slightly longer than that of the unsaturated diesters and is observed in the methoxycarbonylation products of Tofa (Figure 3.3). It has been previously suggested that dimethyl 1,19–nonadecenedioate could be produced from methyl linoleate or linolenate by methoxycarbonylation followed by transfer hydrogenation from methanol. The work on natural oils described in chapter 2 as well as work on methyl linoleate by Mecking and co-workers suggested that this transfer hydrogenation does not occur to any large extent, and these new results confirm that significant transfer hydrogenation does not occur. In order to identify the other products formed during the methoxycarbonylation of linoleic acid, they were separated by column chromatography and fully characterised. Compounds 1 and 2 are known C19 keto esters, with 2 being methyl 17–oxooctadecanoate and 1 being a mixture of isomers of methyl n–oxooctadecanoate with the keto group at different positions along the chain. Compound 5 has not been fully identified but appears to be a mixture of methyl methoxyoctadecanoates. Finally, compound 6 was isolated (19 % yield, 44 % if the reaction was carried out in the presence of MgSO4) and fully characterised as a mixture of trimethyl heptadecane–1,n,17–tricarboxylate, where “n” indicates that the extra carboxymethoxy group is at any position along the chain. These triesters are discussed in more detail later on, but arise from methoxycarbonylation of the double bonds in the various isomers of dimethyl

![Figure 3.1: GC–FID trace of the crude mixture from the methoxycarbonylation of linoleic acid. The numbered peaks arise from compounds shown in Figure 3.2](image)
1,19–nonadecenoate. We surmised that compounds 1 and 2 might arise from addition of water to linoleic acid or methyl linoleate followed by isomerisation of the enol to the ketone (Figure 3.2). Possible isomerisation of the double bonds into conjugation catalysed by the Pd complex might enhance this reaction. 1 and 2 do not appear previously to have been synthesised by hydration of linoleic acid or its methyl ester, but they have been formed by bacterial oxidation of oleic acid in an aqueous environment. Under the same conditions, linoleic acid gives unsaturated keto esters, which can dehydrate to give conjugated dienoic acid esters. Drying the reagents did not reduce the amount of these products, but water is formed from esterification of linoleic acid by methanol and this water might then add across the methyl linoleate. To test this, a reaction was carried out under identical conditions to those used for the methoxycarbonylation of methyl linoleate, but under N₂ in place of CO. 1 and 2 were the major products confirming that this reaction is independent of the methoxycarbonylation. Interestingly, in this reaction, some methyl oleate was formed, suggesting that transfer hydrogenation is possible in the absence of CO. The origin of the various products is shown in Figure 3.2.

### 3.4 Methoxycarbonylation of Tofa

The methoxycarbonylation of Tofa using the same catalytic system as was used for linoleic acid, leads to a variety of different products as seen on the GC–FID trace in Figure 3.3. Most of the major products are the same as those produced from linoleic acid, except that Dino (4) from methoxycarbonylation of methyl oleate is a significant component. The methoxycarbonylation of Tofa followed by hydrogenation using Pd/C
Figure 3.2: Products obtained from the methoxycarbonylation and hydrogenation of TOFA and linoleic acid.
led to the desired Dino in very good purity and good yields (Figure 3.2, Table 3.1), proving the Tofa can be a valuable source of the polymer precursor. The GC–MS trace of the crude mixture before hydrogenation showed a significant amount of dimethyl 1,19–nonadecenedioate isomers$^{65,66}$ in addition to the desired saturated product. Hydrogenation of this mixture using Pd/C led to the desired Dino in very good purity and 32% isolated yield. When the methoxycarbonylation was carried out using syngas in place of pure CO, it led to a similar ratio between saturated and monounsaturated diesters, proving the reaction does not need a high purity CO grade, but works with lower and much less expensive CO grades. This reaction also shows that the palladium catalyst does not promote hydrogenation. In addition, a peak with a longer retention time was observed in the GC–MS (Product 6, Table 3.1). An identical peak was observed from the methoxycarbonylation of methyl linoleate and its origin is discussed below.

Knowing that compounds 1 and 2 are formed from a reaction between methyl linoleate and water produced during the initial esterification of linoleic acid by methanol and that the proportion of compound 6 increases with longer reaction times, we attempted to increase the yield of the desired 4 from Tofa. Methyl linoleate was stirred for 3 h in
methanol containing the amount of MSA required for the subsequent methoxycarbonylation reaction and MgSO$_4$. GC analysis showed that complete conversion of the acids to methyl oleate and methyl linoleate occurred. After filtration, this solution was used for methoxycarbonylation under the standard conditions, but for 10 h in an attempt to reduce the amount of triester 6 formed. GC analysis showed mainly compounds 3 and 4 with some 6 (Figure 3.4). Hydrogenation of this solution (Figure 3.5) gave, in addition to methyl stearate and 6, predominantly the desired 4, isolated in 32% yield.

### 3.5 Triesters

Compound 6 gave a large peak on the GC–MS trace with a a parent ion of m/z = 415. This molecular mass corresponds to that of a triester, trimethyl heptadecane–1, n,17–tricarboxylate (HDTC, “n” designates any position within the hydrocarbon chain) (Figures 3.2 and 3.6), which could be formed from methoxycarbonylation of dimethyl 1,19–nonadecenedienoate. Moreover, the GC–MS provided a fragment that would fit with the loss of a methoxy group from the supposed triester. Another fragment was identified to be possibly coming from a decarboxylation of the triester. These fragments are reported in the Table 3.2. We did further investigations to discover whether this was the identity of this product. Apart from reactions of styrene$^{99,158}$ and vinyl acetate,$^{156,157}$ which

![Figure 3.6: An example of a triester: trimethyl heptadecane–1,7,17–tricarboxylate](image)
Table 3.2: Main fragments obtained on GC–MS and proposed assignment

<table>
<thead>
<tr>
<th>m / z</th>
<th>Fragment</th>
</tr>
</thead>
<tbody>
<tr>
<td>415</td>
<td>[M]+</td>
</tr>
<tr>
<td>383</td>
<td>[M - OMe]+</td>
</tr>
<tr>
<td>355</td>
<td>[M - CO₂Me]+</td>
</tr>
</tbody>
</table>

give predominantly branched products, all other studies using Pd/DTBPMB/MSA for methoxycarbonylation have shown very high selectivity to carbonylation at the terminus of carbon chains, even if the double bond is buried deep in the chain (methyl oleate, methyl erucate) or conjugated to an ester function (see section 3.6 and second carbonylation of alkynes). However, all of the substrates we have examined have the possibility of isomerisation of the C=C bond to the C terminus where it can be trapped by methoxycarbonylation. The one exception to this generalisation is the carbonylation of internal alkynes, where the first carbonylation occurs at one end of the triple bond because triple bond isomerisation does not occur. In the case of dimethyl 1,19–nonadecendioate, the double bond cannot migrate to the end of the chain because both ends are already esterified, so there is the possibility of adding a third ester group wherever the double bond is in the chain.

3.5.1 NMR analysis of the proposed product

Figure 3.7: HSQC spectrum of trimethyl heptadecane–1, n, 17–tricarboxylate
A triester could explain the different fragments seen on the mass spectrum (Table 3.2), so we isolated the proposed HDTC from the crude mixture, obtained from the methoxycarbonylation of linoleic acid, by column chromatography and analysed it by $^1$H NMR and $^{13}$C NMR techniques. In the $^{13}$C NMR spectrum, there are at least three resonances near $\delta$ 46 ppm, which are upside down compared with the signals from methylene groups. These resonances correlate (Figure 3.7) with $^1$H NMR resonances near $\delta$ 2.30 ppm, slightly upfield from the resonance arising from the methylene groups next to the terminal $-\text{CO}_2\text{Me}$ functions ($\delta$ 2.32 ppm). These resonances are exactly where the resonances from the CH attached to a mid-chain $-\text{CO}_2\text{Me}$ would be expected to appear. The fact that there are at least 3 C signals near $\delta$ 46 ppm suggests that at least 3 different isomers are present. Given that the methoxycarbonylation catalyst is also a good double bond isomerisation catalyst, it seems likely that the dimethyl 1,19–nonadecendioate will exist as various isomers with double bonds in different positions along the chain and that methoxycarbonylation will then place the third ester group in a variety of positions along the chain. In support of this, there is also more than one methoxy resonance near $\delta$ 3.70 ppm. The triester which has two geminal carboxylate groups at one end would be expected to show resonances near $\delta$ 3.30 ppm ($^1$H) and $\delta$ 50 ppm ($^{13}$C) for the methine group. Although the $^1$H NMR spectrum of the isolated triester does have very weak peaks in the region near $\delta$ 3.30 ppm, they appear to be singlets and do not correlate with appropriate $^{13}$C resonances. This suggests that very little of the triester containing a geminal diester is formed, as expected since the amount of $\alpha,\beta$-unsaturated diester has been measured as 3–5%.

These triesters may be important as cross linkers in polymerisation reactions using naturally derived monomers.

### 3.5.2 Methoxycarbonylation of dimethyl maleate as a model reaction

To confirm the suggestion that Pd/DTBPMB/MSA could catalyse the methoxycarbonylation of a trapped internal double bond, we carried out the methoxycarbonylation of dimethyl maleate. The reaction led efficiently to trimethyl ethane–1,1,2–tricarboxylate (TET) (Figure 3.8), together with some dimethyl fumarate, formed by Z–E isomerism of dimethyl maleate.

![Figure 3.8: Synthesis of TET from methoxycarbonylation of dimethyl maleate](image)
3.6 Shorter diesters from natural resources

The diesters described in this chapter and the previous carbonylation work on methyl oleate and natural oils all contain 19 carbon atoms, with the advantage that all the C atoms of the oleate end up in the product. However, there is considerable interest in diesters of different chain lengths, also derived from natural resources. It is well established that dimethyl 1,18-octadecanediol can be formed by self-metathesis of methyl oleate followed by hydrogenation, but in this case, half the C atoms end up in a long chain hydrocarbon. In order to improve the atom efficiency for obtaining shorter chain diesters from methyl oleate and related compounds, the metathesis of methyl oleate with dimethyl maleate to produce dimethyl 1,11-undec-2-endioate, a C<sub>11</sub> diester and methyl 2-undecenoate, an α,β-unsaturated ester, was proposed and demonstrated. In order to make the C<sub>12</sub> diester, we attempted the methoxycarbonylation of methyl 2-undecenoic acid, which requires the double bond to move eight bonds into the least thermodynamically favoured position before being trapped there by methoxycarbonylation. Previously the maximum distance for isomerisation that we had observed in this Chemistry was 8 bonds (for methyl oleate or methyl erucate) or 7 bonds where the double bond was conjugated to an ester (second carbonylation of 1-octyne to give dimethyl 1,10-decanedioate). Gratifyingly the reaction worked well and produced dimethyl 1,12-dodecanedioate with high selectivity. The same product, which is an important component of nylon-12,12 was also prepared by the methoxycarbonylation of methyl 11-undecenoate, which is available from cracking castor oil, although shorter reaction times could be used in this case. This reaction has previously been demonstrated using other catalysts. To test the isomerising ability of the catalyst still further, 2-hexadecenoic acid, which requires the double bond to move 13 places to make the α,ω-diester, was successfully methoxycarbonylated to dimethyl 1,17-heptadecanedioate in high selectivity (Table 3.3). These reactions are summarised in Figure 3.9.

![Figure 3.9: Methoxycarbonylation of unsaturated C<sub>11</sub> (n = 1) and C<sub>16</sub> (n = 6) esters](image-url)
3.7 Optimisations and further work

By using Tofa, the synthesis of diesters and triesters can be carried out using bio-derived resources which do not compete with food crops for land. We have described an efficient batch synthesis of dimethyl 1,19–nonadecanedioate. Transferring this synthesis to a continuous flow reactor would represent a major improvement in the utility of this synthesis and for this reason, a possible design of a rig will be outlined in this section. The rig was not built for reasons of time.

3.7.1 General overview on continuous flow Chemistry

The two main parameters that vary while comparing batch and flow reactions are the stoichiometry and the residence time:

- **Stoichiometry:** in a batch reaction, it is defined by the concentration of the reagents and the surface area to volume ratio. In a flow reaction, stoichiometry relies on the concentration of the reagents and their flow rate across the reactor.

- **Residence time:** in a batch reaction, it is defined by the time a reactor is maintained at a target temperature. In a flow reaction, it relies on the ratio of the reactor volume and the flow rate.

Continuous flow reactors, despite being widely used in industry only appeared recently in laboratories. In the laboratory, micro-reactors are mostly employed and offer numerous advantages. Safety is increased by using continuous flow reactions instead of batch reactions: thermal runaway is less likely, due to the dominance of the thermal mass of the system. Moreover, continuous flow reactions allow the use of smaller reactors. The mixing of the reagents occurs only by diffusion due to the dominance of

# Table 3.3: Methoxycarbonylation of 2–undecenoic acid and 2–hexadecenoic acid

<table>
<thead>
<tr>
<th>Substrate</th>
<th>Methyl 10–undecenoate</th>
<th>2–undecenoic acid</th>
<th>2–hexadecenoic acid</th>
</tr>
</thead>
<tbody>
<tr>
<td>Conversion (GC FID)</td>
<td>83%</td>
<td>84%</td>
<td>79%</td>
</tr>
<tr>
<td>Selectivity linear diester</td>
<td>89%</td>
<td>92%</td>
<td>90%</td>
</tr>
<tr>
<td>Selectivity $\omega$–2 branched di.</td>
<td>6%</td>
<td>4.3%</td>
<td>3.5%</td>
</tr>
<tr>
<td>Selectivity $\omega$–3 branched di.</td>
<td>1.5%</td>
<td>1%</td>
<td>1%</td>
</tr>
<tr>
<td>Other branched diester</td>
<td>3.5%</td>
<td>2.6%</td>
<td>5.5%</td>
</tr>
<tr>
<td>Isolated yield</td>
<td>58%</td>
<td>43%</td>
<td>58%</td>
</tr>
</tbody>
</table>

*Uncalibrated*
laminar flows. In micro-reactors, temperature changes can be monitored almost in real time thanks to the importance of the surface-to-volume ratio.

Finally, a variety of reactions can be achieved by the mean of continuous flow Chemistry, such as hydroformylation and alkene metathesis. According to Seeberger, micro-reactors are the round bottom flask of this new century.

### 3.7.2 A possible rig

Despite being efficient in a batch reaction, methoxycarbonylation of alkenes has proved difficult using continuous flow Chemistry. The reaction was performed using a supported ionic liquid phase (SILP) catalyst and supercritical CO$_2$. The DTBPMB ligand was tuned to have a sulfonated backbone in order to immobilise the catalyst into the ionic liquid. Despite many attempts, the continuous flow methoxycarbonylation of 1–octene was in general unsuccessful and the system had to be abandoned. Dimethyl 1,19–nonadecanedioate (Dino) is soluble in warm methanol but insoluble in ice-cold methanol (see Chapter 2 and Appendix A). This property is used for isolating Dino in high purity (>99% GC–FID) by crystallisation and filtration. To obtain high purity Dino in a continuous flow system the four following criteria must be satisfied:

![Figure 3.10: Design of the proposed rig](image-url)
3.7 Optimisations and further work

1. The amount of side-products has to be minimised
2. The catalyst has to be homogeneous
3. The system has to be warmed up to 90°C
4. The extraction vessel has to be at 0°C for isolating the Dino

Criterion 1 can be achieved by a partial hydrogenation of Tofa for reducing the amount of linoleic acid. Partial hydrogenation of fatty acids is an efficient process that has been abandoned by the food industry for health reasons, but it can increase the amount of oleic acid in Tofa. Therefore, production of ketoesters can be avoided as well as production of triesters.

Criterion 2 is reached by using methanol as the reaction and carrying solvent. The system is warmed up to 90°C but at the extraction vessel were the temperature is maintained at 0°C. Therefore, the reaction is carried out at the optimal temperature and the dimethyl 1,19–nonadecanedioate will crash out in the extraction vessel. This vessel is designed like a cartridge containing a filter for maintaining the dimethyl 1,19–nonadecanedioate inside. A possible design for a rig able to perform such continuous flow methoxycarbonylation is represented in Figure 3.10.

3.7.3 Principle

The system is a closed circuit which is maintained at 30 bar of CO. It is supplied in substrate thanks to a liquid pump (LP1, Figure3.10). The substrate consists in methyl oleate and the stoichiometric amount of methanol necessary for the methoxycarbonylation. Indeed, the close circuit contains methanol as the carrying solvent. The more the rig runs the more the methanol consumed. This consumption of methanol has to be

![Diagram](image.png)

**Figure 3.11:** Accumulation of the sample in the first cartridge
compensated. The substrate is introduced into the close circuit containing methanol (carrying solvent), methane sulfonic acid and the catalyst. The reaction occurs in a reactor: it contains a spiral-shaped tube heated to 90°C. This shape is for maximising the contact time between the substrate and the catalyst. The mixture arrives in cartridge 1 (CA1, Figure 3.11) which is cooled to 0°C. The formed dimethyl 1,19-nonadecanediolate precipitates in the cartridge due to its insolubility in cold methanol and a filter (F, Figure 3.11) holds the solid in the cartridge, and prevents it entering the circuit. Methanol, the catalyst and the methane sulfonic acid (MSA) (and possibly unreacted methyl oleate) continue to the two way valve (TWV1, Figure 3.11) and are pumped through the circuit by a second liquid pump (LP2, Figure 3.11) which maintains the circulation of the fluid in the whole circuit.

3.7.4 Recovery of the product

The second cartridge (CA2, Figure 3.12) is empty (no solvent, no gas pressure). The liquid pump (LP2, Figure 3.12) is stopped and the valve (SV2, Figure 3.12) is closed. A pressure of CO is applied in the cartridge (CA1, Figure 3.12) via the flow controller ((MFC, Figure 3.12), which purges the mixture, leaving the solid. The methanol (containing remainder of the mixture of catalyst, MSA and maybe some unreacted methyl oleate) is sent to the second cartridge (CA2, Figure 3.12) which is filled. Once the second cartridge is full of the mixture purged from the first cartridge, the valve (SV2, Figure 3.13) is opened, the two way valve (TWV1, Figure 3.13) is oriented to the second cartridge and the liquid pump (LP2, Figure 3.13) restarted. The first cartridge is disconnected, the product is removed from it and eventually the empty cartridge is re-installed. The whole operation is repeated when the second cartridge is full of solid.

![Figure 3.12: Purge of the first cartridge](image-url)
3.8 General Conclusion

Tall oil fatty acids, which contain out of minor products mainly oleic acid and linoleic acid, have been methoxycarbonylated to a mixture of 1,19–nonadecanedioate and 1,19–nonadecenedioate (mixture of isomers). Some of the latter is converted into a mixture of isomers of trimethyl 1,\(n\),17–heptadecanetricarboxylate, which may be of interest as cross-linkers in polyesters prepared from plant based diesters. The methoxycarbonylation of linoleic acid shows that esters containing two double bonds give unsaturated diesters and triesters only, with no transfer hydrogenation to give saturated diesters.

Undecenoic acids or esters with the double bond conjugated to the carbonyl group (available from metathesis of methyl oleate with dimethyl maleate)\(^{177}\) or in the terminal position (avaible from castor oil) can both be methoxycarbonylated to dimethyl 1,12–dodecanediaote, a component of nylon–12,12 whilst the conjugated double bond

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3.7.5 (Dis)advantages of this system

The great advantage of the system is to keep the catalyst in solution and to permanently avoid any contact with the atmosphere. Moreover, thanks to the purging system, the amount of catalyst is kept constant in the system. This way the catalyst is long lasting, with no contact with air and a continuous feed of substrate. Finally, the extracted diester is of very high purity. However, the main disadvantage would be the packing of the solid in the cartridge. Indeed, if it packs to strongly, it might prevent the circulation of the liquid and then prevent the system from working. Moreover, during the purge of the cartridge, the sudden packing of the solid might block the purge system and dangerously blow up the cartridge. Finally, for safety reasons, as on any rig a pressure relief valve is installed on the system at the critical node (PRV, Figure 3.10).
in 2-hexadecenoic acid can be moved 13 bonds along the chain to the least thermodynamically favoured terminal position before methoxycarbonylation to furnish dimethyl 1,17-heptadecanedioate.

Finally, an extension to continuous flow Chemistry using tall oil fatty acids is suggested and might, if such a system is built and tested in the future, be of interest from an industrial point of view. Indeed, Tofa is a very cheap resource with few applications and the process described in this chapter would provide a value enhancement of this natural feedstock.
Chapter 4

Amides and polyamides from unsaturated esters

Reaction of long chain alkenes with CO and aniline in the presence of palladium complexes of 1,2-bis(ditertbutylphosphinomethyl)-benzene produces amides with high linear selectivity, with much higher rates and catalyst stability if 2-naphthol and potassium iodide are added. Unsaturated esters give mixed ester amides, whereas reactions in diethyl ether lead to high selectivity to the linear amide. Finally, aromatic polyamides are synthesised by condensation reactions of paraphenylenediamine and polyacids derived from castor oil and tall oil.

The results presented in the following chapter are grounded on the early-stage work developed by C. Jiménez-Rodriguez and A. Núñez-Magro, former PhD Students in the Group of Prof. D. J. Cole-Hamilton at the University of St Andrews. A summary of their results is presented in section 4.2.1 for a better comprehension of my own work.

4.1 Introduction

Amides are important industrial chemicals finding uses in detergents and as thickeners. Amides are usually prepared in the laboratory by the Schotten-Baumann reaction involving the condensation reaction of an amine with an acyl chloride, which is highly wasteful as chloride has to be introduced and then removed for disposal. It is also hazardous, because acyl chlorides are unstable on exposure to atmospheric or other moisture and produce fumes of HCl. Several amide syntheses have been developed
over the past century, among them the Schmidt reaction\textsuperscript{225} involving a ketone and an azide, the Ugi reaction\textsuperscript{226} producing bis-amides by using a ketone (or an aldehyde), an isocyanide, a carboxylic acid and an amine, and the Chapman thermal rearrangement\textsuperscript{227} of aryl imino ethers. More recently, in 1997 Milstein and co-workers\textsuperscript{228} developed a ruthenium-based catalyst for producing an amide directly from an alcohol and an amine.

An interesting synthesis of amides involving the aminocarbonylation of alkenes has been developed, but has found use mainly in cyclisation reactions\textsuperscript{229–231} The system that has been developed for the methoxycarbonylation of aromatics,\textsuperscript{167} unsaturated compounds,\textsuperscript{117,140,156} and fatty acids\textsuperscript{64,65,141} usually with very high selectivity towards the linear products, is also highly active for aminocarbonylation using aniline. This is the system which is described below.

4.2 Aminocarbonylation and hydrogenation of unsaturated esters

4.2.1 Aminocarbonylation of alkenes

The results presented in the section 4.2.1 are courtesy of C. Jiménez-Rodriguez\textsuperscript{232} and A. Núñez-Magro\textsuperscript{190}.

4.2.1.1 First reactions

Carbonylation of 1–octene in the presence of aniline and a catalyst, prepared in situ from PdCl\textsubscript{2} and 1,2–bis(di tert butylphosphinomethyl)benzene (DTBPMB), at 100°C and under CO (30 bar) for 3 h produces the linear amide, N–phenyl nonanamide as the only amide product in 38% yield. Extending the reaction time to 6 h allows quantitative conversion to a linear amide in a 98% yield. Aminocarbonylation of 1–hexene proceeded smoothly to yield the desired linear amide (>99.9%). Lowering the temperature to ambient inhibited the reaction and the isomerisation of the 1–octene, but lowering the pressure to 10 bar increased the conversion after 3 h to 100%, with rather poorer linearity (65%). Lowering the pressure (2 bar) still further inhibited the reaction despite an extended reaction time. The fact that the linearity of the product can be so high, despite extensive alkene isomerisation being observed when the reaction is incomplete, suggests that, as with methoxycarbonylation,\textsuperscript{117} internal alkenes isomerise to terminal alkenes which are trapped by carbonylation.
4.2.1.2 Addition of a promoter

Although the reactions described above produce amides with good conversion and good linear selectivity, the catalyst loadings are high (2 mol%), the reaction times long (3 to 6 h) and the catalyst is found to have decomposed when the autoclave is opened. Drent has reported\textsuperscript{233} that the addition of 1–naphthol and NaI allows the successful amidocarbonylation of 1–octene with 3–dimethylaminopropylamine, when using [Pd(OAc)\textsubscript{2}] in the presence of 1,2–P,P–bis(9–phosphabicyclo[3,3,1 or 4,2,1]nonyl)ethane as the catalyst precursor: turnovers in 1 h can be as high as 1500 and linearities reach 98.5%. Accordingly, the addition of the same additives to the Pd/DTBPMB catalyst system was investigated. Gratifyingly much higher rates of reaction, and catalyst stability, can be obtained than with PdCl\textsubscript{2} when using either aniline or 3–dimethylaminopropylamine as the nucleophile.

A plausible explanation for the role of 1–naphthol involves the attack of the aryl alcohol onto the acylpalladium species to generate the aryl ester and the hydridopalladium complex which restarts the catalytic reaction (Figure 4.1). Reaction of the arylester with the amine regenerates the aryl alcohol and produces the observed amide. Interestingly, the less acidic phenol was not effective in this type of reaction and 1–naphthol was less effective than 2–naphthol. In order to prove this hypothesis, a reaction without amine was run and in this case, no conversion to the intermediate was observed. Moreover, according to this hypothesis only catalytic amounts of 2–naphthol are necessary for promoting the reaction. However, stoichiometric amounts of promoter seem necessary for fast rates of the reaction, probably due to an existing equilibrium highly favouring species 1. We note that a reaction carried out in the presence of 1–naphthol, but with no aniline does not give conversion to the intermediate.

\begin{center}
\textbf{Figure 4.1:} The aminocarbonylation promoted by 2–naphthol
\end{center}
Table 4.1: Products from the aminocarbonylation of methyl acrylate with aniline

<table>
<thead>
<tr>
<th>Entry</th>
<th>T (°C)</th>
<th>t (h)</th>
<th>Conv. (%)</th>
<th>Li. (%)</th>
<th>Br. (%)</th>
<th>Michael (%)</th>
<th>Others (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>85</td>
<td>3</td>
<td>27%</td>
<td>1</td>
<td>3</td>
<td>22</td>
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</tr>
<tr>
<td>2</td>
<td>115</td>
<td>3</td>
<td>45%</td>
<td>0</td>
<td>0</td>
<td>45</td>
<td>0</td>
</tr>
<tr>
<td>3</td>
<td>70</td>
<td>16</td>
<td>52%</td>
<td>4</td>
<td>7</td>
<td>41</td>
<td>0</td>
</tr>
<tr>
<td>4</td>
<td>85</td>
<td>16</td>
<td>75%</td>
<td>7</td>
<td>13</td>
<td>54</td>
<td>1</td>
</tr>
<tr>
<td>5</td>
<td>115</td>
<td>16</td>
<td>87%</td>
<td>0</td>
<td>0</td>
<td>82</td>
<td>5</td>
</tr>
<tr>
<td>6</td>
<td>85</td>
<td>64</td>
<td>93%</td>
<td>9</td>
<td>8</td>
<td>69</td>
<td>7</td>
</tr>
</tbody>
</table>

Li.: Linear product; Br.: Branched product; Michael: Product from the Michael addition

*Conditions: methyl acrylate (1.14 mL, 12.7 mmol), aniline (1.16 mL, 12.7 mmol), Pd\(_2\)(dba)\(_3\) (114 mg, 0.0125 mmol), DTBPMB (251 mg, 0.0637 mmol), 1,4-dioxane (10 mL), MSA (10 µL), 2-naphthol (1368 mg, 9.5 mmol), KI (10 mg, 0.064 mmol), P (CO) = 30 bar

4.2.2 Aminocarbonylation of unsaturated esters

4.2.2.1 First attempts with ethyl 3-hexenoate

I want to acknowledge Thomas Seidensticker for his help in the section 4.2.2.1.

The goal is to achieve the aminocarbonylation of natural fatty esters for preparing a range of esteramides that could be reduced to esteramines, precursors to bio-derived polyamides. For this, the reaction conditions have to be adapted to optimise the yields and the conversions to the desired linear products. Our first attempt using methyl acrylate was unsuccessful, as can be seen in Table 4.1. We thought that the very low efficiency of the reaction was possibly due to the conjugation of the C=C bond with the C=O bond of the ester function, preventing the reaction from occurring. We then decided to use another substrate which does not bear such a conjugated double bond and presents a more similar appearance to fatty esters: ethyl 3-hexenoate. The reaction conditions previously used with methyl acrylate failed to produce the desired linear and branched amidoester. Only low conversion was observed and mainly the amidation of the ester was observed (Table 4.2, entry 1). Moreover, no selectivity to any amidoester (linear or branched) was observed. It seemed the conjugation of the double bond was not the source of the inefficiency of the reaction. Therefore, the conditions needed to be altered. Using toluene as a solvent led to an improved selectivity for some amidoester isomers (Table 4.2, entry 2). Unfortunately, warming to 115°C did not increase the conversion to the esteramide but led to a higher conversion of the undesired amide (Table 4.2, entry 3). However, leaving the reaction running for 64 h increased the conversion of the esteramide, with increased selectivity to the desired linear product (27:1) (Table 4.2,
4.2 Aminocarbonylation and hydrogenation of unsaturated esters

Table 4.2: Products from the aminocarbonylation of ethyl 3-hexenoate with aniline

<table>
<thead>
<tr>
<th>Entry</th>
<th>T (°C)</th>
<th>t (h)</th>
<th>Conv. (%)</th>
<th>Li. (%)</th>
<th>Br. (%)</th>
<th>Am. (%)</th>
<th>Mi. (%)</th>
<th>Ot. (%)</th>
</tr>
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<tbody>
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<td>17</td>
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<td>2</td>
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<td>16</td>
<td>52%</td>
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<td>28</td>
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<td>3</td>
<td>115</td>
<td>16</td>
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<td>27</td>
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<tr>
<td>5</td>
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<td>89%</td>
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<td>22</td>
</tr>
<tr>
<td>6</td>
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<td>16</td>
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<td>94%</td>
<td>15</td>
<td>14</td>
<td>40</td>
<td>5</td>
<td>20</td>
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</tbody>
</table>

Li.: Linear; Br.: Branched; Am.: Amide; Mi.: Michael addition; Ot.: Others

*a Conditions: ethyl 3-hexenoate (2.02 mL, 12.7 mmol), aniline (1.16 mL, 12.7 mmol), Pd₂(dba)₃ (114 mg, 0.0125 mmol), DTBPMB (251 mg, 0.0637 mmol), toluene (10 mL), MSA (10 µL), 2-naphthol (1368 mg, 9.5 mmol), KI (10 mg, 0.064 mmol), P (CO) = 50 bar
*b Dioxane was used instead of toluene
*c Without promoter

entry 4), although producing a high yield of amide. To further optimise the conditions, we attempted to alter the kinetics of the reaction by heating to 140°C. However, while the conversion stayed the same, the selectivity to the linear esteramide dropped dramatically (Table 4.2, entry 5). A test reaction using no promoter under the same conditions, dramatically decreased the conversion to the amidoester. This showed the 2-naphthol to be necessary as a promoter of the reaction (Table 4.2, entry 6). Finally, a reaction with the promoter at high temperature gave a lower selectivity to the linear product than at lower temperature (Table 4.2, entry 7).

4.2.2.2 Optimisation with methyl 10-undecenoate

These first results with ethyl 3-hexenoate were encouraging. Therefore we decided to focus our attention on methyl 10-undecenoate, an unsaturated ester obtained from the thermal cracking of castor oil. Methane sulfonic acid (MSA) is necessary for building the palladium complex in situ. Nevertheless, due to the presence of aniline, MSA would react with the amine to form an ammonium salt before the complex can be synthesised. Following the conclusions obtained from the results of Table 4.2 (the higher the temperature the lower the conversion to the desired product) we decided to screen a range of temperature between 60°C and 140°C (Table 4.3). Thus, with same amount of MSA (10 µL) we found that high temperature promoted the amidation of the ester (Table 4.3, entry 1). The selectivity to the amidoester was slightly increased at 100°C and 120°C.
Table 4.3: Aminocarbonylation of methyl 10-undecenoate with aniline

<table>
<thead>
<tr>
<th>Entry&lt;sup&gt;a&lt;/sup&gt;</th>
<th>T (°C)</th>
<th>t (h)</th>
<th>Conv.</th>
<th>Li. (%)</th>
<th>Br. (%)</th>
<th>Am. (%)</th>
<th>Mi. (%)</th>
<th>Ot. (%)</th>
</tr>
</thead>
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<td>16</td>
<td>51%</td>
<td>7</td>
<td>1</td>
<td>41</td>
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<td>0</td>
</tr>
<tr>
<td>2&lt;sup&gt;b&lt;/sup&gt;</td>
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<td>32%</td>
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<td>16</td>
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<td>100</td>
<td>16</td>
<td>38%</td>
<td>7</td>
<td>3</td>
<td>26</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>9&lt;sup&gt;c&lt;/sup&gt;</td>
<td>100</td>
<td>64</td>
<td>&gt;99%</td>
<td>96</td>
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<tr>
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<td>74%</td>
<td>62</td>
<td>2</td>
<td>10</td>
<td>1</td>
<td>0</td>
</tr>
</tbody>
</table>

Li.: Linear; Br.: Branched; Am.: Amide; Mi.: Michael addition; Ot.: Others
<sup>a</sup>Conditions: methyl 10-decenolate (1.42 mL, 6.35 mmol), aniline (1.16 mL, 12.7 mmol), Pd(dba)<sub>2</sub> (115 mg, 0.2 mmol), DTBPMB (99 mg, 0.25 mmol), toluene (10 mL), MSA (100 µL), 2-naphthol (1368 mg, 9.5 mmol), KI (10 mg, 0.064 mmol), P (CO) = 50 bar
<sup>b</sup>MSA: 10 µL
<sup>c</sup>Solvent: dimethyl sulfoxide
<sup>d</sup>Solvent: diethyl ether

while amidation decreased (Table 4.3, entries 3 and 4). A good compromise between the conversion to the amidoester and the amide was found. Therefore, we decided to increase the amount of MSA, while maintaining the catalyst loading constant and varying the temperature of the reaction. At 100°C (Table 4.3, entry 5) the higher amount of MSA caused a dramatic drop in the conversion of the esteramide. On the other hand, when the reaction was carried out at 80°C over a longer time (64 h instead of 16 h, Table 4.3, entry 10) a significant increase in the conversion to the esteramide was observed. Moreover, replacing toluene by diethyl ether, the overall conversion to the esteramide was more than 99%, with a 96% selectivity to the linear product (Table 4.3, entry 11). It seemed that diethyl ether was the key solvent for the reaction. Despite a very high selectivity, the reaction time was very long (64 h) and the reaction kinetics needed to be improved. Two parameters can be changed for optimising the kinetics: the temperature and the amount of potassium iodide (KI). We decided to screen the range of temperature between 90°C and 110°C while increasing the amount of KI from 0.06 to 0.2 equivalent. Using 0.1 equivalent, the optimal temperature (95°C) gave a 70% selectivity to the linear product (Table 4.4, entry 2) while at 110°C the selectivity dramatically dropped to 10% (Table 4.4, entry 3). Nonetheless, the role of KI was shown to be very important. When its amount was increased to 0.2 equivalent, the selectivity reached 91% (Table
4.2 Aminocarbonylation and hydrogenation of unsaturated esters

Table 4.4: Aminocarbonylation of methyl 10-undecenoate with aniline in Et₂O

<table>
<thead>
<tr>
<th>Entry</th>
<th>T (°C)</th>
<th>t (h)</th>
<th>KI (eq.)</th>
<th>Li. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>90</td>
<td>16</td>
<td>0.1</td>
<td>10</td>
</tr>
<tr>
<td>2</td>
<td>95</td>
<td>16</td>
<td>0.1</td>
<td>70</td>
</tr>
<tr>
<td>3</td>
<td>110</td>
<td>16</td>
<td>0.1</td>
<td>21</td>
</tr>
<tr>
<td>4</td>
<td>95</td>
<td>16</td>
<td>0.2</td>
<td>91</td>
</tr>
<tr>
<td>5</td>
<td>95</td>
<td>16</td>
<td>0.2</td>
<td>13</td>
</tr>
<tr>
<td>6</td>
<td>110</td>
<td>16</td>
<td>0.2</td>
<td>99&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

Li.: Linear

<sup>a</sup>Conditions: methyl 10-decenoate (1.42 mL, 6.35 mmol), aniline (1.16 mL, 12.7 mmol), DTBPM (395 mg, 1 mmol), Et₂O (10 mL), MSA (100 µL), Pd₂(dba)₃ (92 mg, 0.1 mmol), 2-naphthol (1368 mg, 9.5 mmol), KI (17 mg, 0.1 mmol or 32 mg, 0.2 mmol), P (CO) = 30 bar

<sup>b</sup>Solvent: 20 mL

<sup>c</sup>isolated yield: 60%

4.4, entry 4). Moreover, when the selectivity dropped at 110°C for 0.1 equivalent of KI, the maximum was reached while using 0.2 equivalent (Table 4.4, entry 6). A hypothesis for explaining the role of KI is based on the assumption that KI would dissociate and the iodide will be associated to the palladium, forming a Pd–I bond. Iodide generates the highest electron-density of the halides via σ–bond donation.<sup>234,235</sup>

4.2.2.3 Attempts with methyl oleate

Having obtained excellent conversion to the C₁₂ amidoester, we tried some experiments using methyl oleate to check the possibility of obtaining the C₁₉ species. Unfortunately, the reaction conditions used for methyl 10-undecenoate were inefficient. The selectivity to the C₁₉ amidoester was only 35%, compared to more than 99% for the C₁₂ species. Only minor amount of branched product were detected and no amide (from amidation of the ester function) was detected. Increasing the temperature to 130°C only led to a minor increase in the conversion. Nevertheless, neither a shorter reaction time nor a longer one gave better conversion to the C₁₉ amidoester. The optimum conditions used for the aminocarboxylation of methyl 10-undecenoate are apparently not general for all the unsaturated esters, and are inappropriate for methyl oleate. A hypothesis would be the difficulty for the catalyst to efficiently isomerise the double bond to the end of the chain during the aminocarboxylation reaction.
4.2.3 Hydrogenation of the esteramide

The challenge was to selectively reduce the amide function to an amine without interfering with the ester group. In chapter 2 we described the reduction of an ester to an alcohol using a ruthenium/triphos catalyst in the presence of water. In the absence of water the reduction of the ester function fails. It is not worth making the hydrogenation of the esteramide using the ruthenium/triphos/water system. Indeed, the ester function will be reduced to the alcohol, and excess of water would hydrolyse the amide function to a carboxylic acid which will then reduce to an alcohol. However, a dry system will be inefficient in reducing the ester function and could possibly hydrogenate the amide function into an amine, leading to an esteramine. Following this hypothesis, we decided to run some tests for checking the feasibility of this hydrogenation.

The reaction was then carried out as in chapter 2 using the C_{12} amidoester in a dry solvent. The reaction appeared to produce very random results and there were major problems with making the reaction reproducible. The GC–FID yields oscillate between 0% and 32% maximum. The same reaction conditions (temperature, time, pressure) do not permitted a reproducibility of the hydrogenation reaction. When the reaction did occur, the GC–MS trace showed a peak at 305 amu corresponding to the expected methyl 12–(phenylamino)dodecanoate, and also side-products consistent with methyl dodecanoate and N–dodecylaniline, coming respectively from the decarboxylation and deamination of the starting material or of methyl 12–(phenylamino)dodecanoate. The desired product was isolated by column chromatography, although not in a complete purity. The $^1$H (Figure 4.2) and $^{13}$C NMR analyses could be done. The product was

![Figure 4.2: $^1$H NMR of methyl 12–(phenylamino)dodecanoate](image)
confirmed to be methyl 12–(phenylamino)dodecanoate. The specific hydrogenation of the amide function in the presence of an ester function is a very interesting phenomenon, even though the reproducibility is poor. The same reaction conditions applied to N–phenylacetamide did not show any hydrogenation of the amide. When N–phenylacetamide and methyl acetate were introduced in the system, the hydrogenation never occurred. There is maybe a link between the ester function and the amide function for permitting the specific hydrogenation of the amide function. Due to the difficulties of making this reaction reproducible, the study was stopped but deserves further studies and development in the future.

4.3 Preparation of aromatic polyamides

The aminocarbonylation leads to interesting products with potential value for preparing polyamides. Therefore, the synthesis of some polyamides was attempted and is described in the following section.

4.3.1 General overview on aramides

“Aramid” is the portmanteau word for aromatic polyamide. Aramide fibres belong to a class of heat-resistant and high strength synthetic fibres. The first example was introduced to the market in 1967 by the DuPont company under the trade name “Nomex” (Figure 4.3). It is synthesised by the condensation of m-phenylenediamine with isophthaloyl chloride. This polymer is the first example of a meta variant of the aramides. Nomex has very interesting properties: it is heat-resistant and flame-retardant and can be employed as a high-voltage electrical insulation. Unlike “Kevlar” which is a para aramide, Nomex cannot align during filament formation. Therefore, it has poorer strength compared to Kevlar, which was developed by Kwolek in 1964 and introduced by the DuPont company in the early 1970’s (Figure 4.4). Kevlar is synthesised via the condensation of terephthaloyl chloride with paraphenylenediamine. Its high tensile strength is due to the unique geometry of the monomeric units, i.e. the existence of the intermolecular hydrogen bonds (C=O/H–N) which gives the linear chain its strength, and the stacking interactions of the aromatic rings, giving rigidity to the final material. Due to its tensile strength and its thermal stability, Kevlar has numerous uses, among them sports equipment, fire protection clothes, bullet-proof jackets and helmets for soldiers. Kevlar has therefore outstanding advantages and applications. The Teijin company developed in the 1980’s an alternative material that has a property that Kevlar does not, flexibility. The Teijin company introduced a new polymer with highly-oriented co-polymeric chains named “Technora” (Figure 4.5).
4.3.2 The Reversed Nylon 12T: Revont

In the first part of this chapter, the aminocarbonylation of methyl 10-undecenoate was shown to be quantitatively possible. Even if the isolation of the final monomer still needs some improvement to be economically reliable, methyl 12-oxo-12-(phenylamino)dodecanoate catalytically reduced to methyl 12-(phenylamino)dodecanoate is intended to be used as polyamide precursor. However, it is noticeable that the phenyl ring, in such a polymer, acts as a substituent. This substituent might be randomly oriented in space or have a specific orientation. The orientation of the branched phenyl ring is unsure until the final material is prepared. In addition, the phenyl ring might inhibit polyamide formation. However, if the phenyl ring could be by any means included in the main polymeric chain, it would provide some stacking interactions between the polymeric chains. Therefore, by combining the intermolecular C=O/H–N hydrogen bonds, the stacking interaction of the phenyl rings and the non-rigidity of the carbon chain, the
properties might be a consistent tensile strength combined with a flexibility of the final material (Figure 4.6). The existing material that looks similar to the one presented here is nylon 12T. nylon 12T and the polymer we are designing here possess the property of being “reversed”: were the nylon 12T possesses an aromatic ring and a C$_{12}$ carbon chain, our polymer possesses a C$_{12}$ carbon chain and an aromatic ring (Figure 4.6). However, it is extremely difficult to find any literature dealing with nylon 12T. Nevertheless, nylon 6T is a very common material. The difference between nylon 6T and nylon 12T is the carbon chain length (6 carbons instead of 12). As nylon 6T has properties such as high melting temperatures, good impact resistance and good mechanical properties at high temperatures,$^{236}$ it becomes tempting to suppose that the proposed polymer, “Reversed Nylon 12T” (Revont), potentially has similar properties to nylon 6T.

### 4.3.3 Synthesis of the monomer

The path leading to such a material is to use benzene–1,4–diamine instead of aniline for synthesising the monomer. The final product will be methyl 12–(4–aminophenylamino)–12–oxododecanoate (Figure 4.7). An advantage of using this diamine is to spare the hydrogenation step: the amine function is readily available at the end of the chain for reacting with the ester function.

Surprisingly, the reaction conditions employed for the aminocarboxylation of methyl 10–undeceoate with aniline were inefficient when using benzene–1,4–diamine. Under
the same reaction conditions, the synthesis of the monomer occurs with a maximum yield of 20% (GC–FID). Changing the conditions (higher temperature or one equivalent of benzene–1,4–diamine or more solvent) only led to a poorer conversion. The reaction could occur on both amine functions, however the corresponding product was not observed at the end of the reaction.

![Figure 4.7: Synthesis of 12–(4–aminophenylamino)–12–oxododecanoate](image)

### 4.3.4 An easier way for obtaining the Revont

#### 4.3.4.1 Synthesis of the polymer

The proposed synthesis of Revont is based on the condensation reaction of 12–(4–aminophenylamino)–12–oxododecanoate on itself, the amine function reacting with the ester function. Indeed, the Revont can be considered to have 12–(4–aminophenylamino)–12–oxododecanoate as the repeat unit. However, due to the difficulty of synthesis of the monomer, another way of synthesising the polymer was attempted. In this way, dodecanedioic acid and benzene–1,4–diamine will be considered as the repeat units. It has been proven that dimethyl dodecanedioate can be easily synthesised via the methoxycarbonylation of methyl 10–undecenoate. The saponification of methyl 10–undecenoate followed by an acidic treatment produces dodecanedioic acid which can react with benzene–1,4–diamine by a condensation reaction. However, the goal was not to synthesise the Revont as it would be done in an industrial process, but only to generate some samples that can be studied. Two synthetic paths were used for preparing the polymer.

#### 4.3.4.2 Utilisation of the acyl chloride

The acyl chloride has a higher reactivity than the carboxylic acid towards the amine function for the condensation reaction. Therefore, dodecanedioyldichloride was synthesised from dodecanedioic acid. The synthetic path for obtaining dodecanedioyldichloride is represented in the Figure 4.8. The synthesis of the Revont was carried out in a biphasic system. Dodecanedioyldichloride was solubilised in dichloromethane and benzene–1,4–diamine was solubilised in slightly basic water. When the water phase was slowly poured over the dichloromethane phase, a white/yellow material formed at the interface and grew while slightly wiggling the flask. This method was abandoned.
4.3 Preparation of aromatic polyamides

4.3.4.3 Utilisation of the carboxylic acid

The condensation of an acid and an amine requires much harsher conditions than the condensation of an acyl chloride with an amine. Benzene–1,4–diamine and dodecanedioic acid were crushed together and melted a 170°C for one hour under vacuum. However, the acid sublimed and condensed on the neck of the flask. Therefore, the same reaction was carried out under air, which unfortunately led to a rapid degradation of the mixture, which turned to soot. The reaction was therefore done under nitrogen. The formation of water drops liquefying on the neck of the flask indicated the reaction was working. The obtained material is hard and its colour varies from pale brown to purple.

4.3.4.4 Analysis of the material

The material obtained after the condensation reaction at 170°C for one hour under nitrogen was analysed using FT–IR and Maldi–Tof techniques. The samples presented the same features on the FT–IR spectrum, which shows the presence of the following absorptions (Figure 4.9):

- Amide function: bands A (3300 cm\(^{-1}\)), E (1660 cm\(^{-1}\), C=O stretching) and G (1560 cm\(^{-1}\), NH bending, secondary amide).
- Alkyl chain: bands C (2920 cm\(^{-1}\), CH\(_2\) stretching), D (2850 cm\(^{-1}\), CH\(_2\) stretching), J (1400 cm\(^{-1}\), CH\(_2\) deformation) and L (720 cm\(^{-1}\), CH\(_2\) rocking).
- Phenyl ring: bands B (3030 cm\(^{-1}\), CH stretching), F (1610 cm\(^{-1}\), C=C stretching), H (1520 cm\(^{-1}\), C=C stretching), I (1470 cm\(^{-1}\), C=C stretching) and K (840 cm\(^{-1}\), sign of a para-disubstituted benzene).
Thus, the FT–IR analysis clearly shows the existence of an amide with both alkyl and aryl groups, suggesting that the condensation reaction has led to the expected polymeric material.

However, Maldi–Tof analysis (Figure 4.10) only suggests the existence of short chain oligomers bearing at maximum two acid units and three amine units (713 amu). It is not clear whether the the low molecular masses observed by Maldi–Tof arise because only oligomers have been formed or because only the lower molecular mass compounds fly in the Maldi experiment. It seems the method used for preparing the sample is not the most adequate. However, even if the polymer was not obtained, the product shows interesting properties, which seems very promising for the polymer once it is synthesised. The samples obtained do not melt at 170°C and seem stable under air, as no colour change is observed. This suggests that the polymer may have a very high melting point.

Moreover, the reaction was stopping at an early stage so it may provide only short oligomers. Indeed, the monomers react together only by means of diffusion in the liquid phase, as they are melted. This way, once the oligomers are formed, they solidify again and the diffusion stops, preventing the different oligomers to enter in contact and eventually react together for giving higher molecular weight species.
4.3 Preparation of aromatic polyamides

Thermogravimetric analysis (TGA) has been done on the sample. The analysis shows that under air the material is perfectly stable until 300°C. From 300°C to 350°C a light loss of mass is observed, while a total loss is observed over 350°C. The material, after the TGA experiment, has completely vanished. These results show that this new material is able to hold very high temperature (up to 300°C) being stable under air, which makes this polymer a potential material usable for very demanding conditions.

4.3.5 The Revont with a longer alkyl chain

Following the success of the synthesis of the Revont with a C\textsubscript{12} chain, we attempted to produce a similar polyamide with a longer carbon chain. It was shown in Chapter 3 that tall oil fatty acids can be employed for preparing dimethyl 1,19–nonadecanedioate (Dino) in an inexpensive and rapid manner. Therefore, the condensation reaction between Dino and benzene–1,4–diamine was attempted under the same reaction conditions as for dodecanedioic acid (170°C under nitrogen). Even if the ester function has a lower reactivity than the acid function towards the condensation reaction with amines, we reasoned that the high temperature employed might enhance the reactivity by the favoured and irreversible elimination of methanol. Indeed, the condensation reaction occurred as expected but seems to take a much longer time than when it was done using dodecanedioic acid.

Therefore, the corresponding C\textsubscript{19} dicarboxylic acid was synthesised and used for the condensation reaction and after a few minutes water drops start to appear on the neck of the flask, showing the reaction to be fast using the dicarboxylic acid. The resulting
material, slightly brownish, is solid at 170°C and is stable under air until 300°C according to the TGA analysis.

4.3.6 Further work on these aromatic polyamides

The Revont polymer is an interesting material that could have potential applications similar to Nyon 6T or 12T. The way to prepare the monomer 12-(4-aminophenylamino)-12-oxododecanoate involves the aminocarboxylation of methyl 10-undecenoate with benzene-1,4-diamine. The synthesis has proven to be extremely difficult. Obtaining a high GC yield was very challenging and reaching completion was never achieved. Moreover, the isolation of the product is extremely difficult and no useful material was obtained on work up. However, an easier way of synthesising the Revont was found, involving the same starting materials, methyl 10-undecenoate and benzene-1,4-diamine. The condensation reaction between dodecanedioic acid and benzene-1,4-diamine should in theory lead to the expected polymer. The synthesis of the polymer was thus greatly simplified. However, it may be that only short chain oligoesters were obtained in our brief study. Further work will consist in synthesising long chain oligoesters for obtaining adequate samples of the polymers. The polyamides need studies to determine their properties, such as tensile strength and glass transition temperature to determine if they have any potential for industrial use. In conclusion, a new material of potential high interest for technological applications has been synthesised using a natural-derived monomer, prepared by a more eco-friendly way than the one employed in industry.

4.4 General Conclusion

Linear amides can be produced with high selectivity from the aminocarbonylation of unsaturated acids. Aniline is the preferred base, and diethyl ether the preferred solvent. Significant advantages in terms of catalyst activity and stability are obtained if the reactions are carried out in the presence of 2-naphthol and potassium iodide. The amides obtained were supposed to be employed in the synthesis of polyamides, however a synthetic path involving carboxylic acid was shown to be more efficient. In conclusion, some amides and polyamides (with very high temperature resistance) are synthesised from a starting material derived from a natural resource, castor oil, which is non-competing with food crops.
Chapter 5

NHC–Metal complexes in catalysis

5.1 The Suzuki-Miyaura reaction in aqueous medium

The work presented in the following section was achieved in close collaboration with Thibault Schmid, PhD Student in the Dr Cazin Group at the University of St Andrews. Some of his results are presented here for a better comprehension of my work. The full work has been published in Dalton Transactions in 2013.

5.1.1 Introduction

Green Chemistry is a burgeoning field and the amount of research activity in this area is growing. In the previous chapters, the focus was on using renewable materials (such as rapeseed and sunflower oil overproductions), side-products from the paper industry (tall oil fatty acids) and derivatives of castor oil for producing a new range of polyesters and polyamides precursors.

Herein, the topic will be focused on the solvent: water. The utilisation of water for replacing other solvents is at first sight to be considered as a “green” possibility. However, the main disadvantage of water for industrial applications is the potential high cost and the tremendous energy consumption for cleaning operations in case of water contamination. Our particular focus is the Suzuki-Miyaura cross-coupling reaction involving chlorinated reagents, as the very common use of this reaction makes it a suitable target for developing in aqueous media. Indeed, the interest of developing the Suzuki-Miyaura reaction in water resides in the potential to generate novel bioactive
molecules.\textsuperscript{247} These two criteria – the use of chlorinated reagents, the use of water as a solvent – have been targeted in the recent years using various strategies. For instance, the development of phosphine ligands permitting the solubility of the palladium complex in water has been considered. This approach was successful for Plenio and co-workers by using cationic phosphine ligands with tetrafluoroborate or sulfonate as an anion.\textsuperscript{248,249} In the same way, this group designed phosphines bearing sulfonates group,\textsuperscript{250,251} and Buchwald and co-workers developed a similar system.\textsuperscript{252} In both approaches, the catalytic system was formed \textit{in situ} and the use of a well-defined catalyst is not mentioned. However, not only water-soluble phosphine ligands have been considered. A very original approach from Zhang and co-workers on developing a guanidine-derived ligand was carried out.\textsuperscript{253} The catalyst is then soluble in water, but permits also the Suzuki-Miyaura coupling of aryle chlorides at very low catalyst loading at ambient temperature.

In the field of NHC-based systems, numerous complexes have been developed that enable the solubility of the pre-catalyst in water, \textit{e.g.} Buchwald and co-workers designed a sulfonated phosphine, the Plenio\textsuperscript{254} and Peris\textsuperscript{255} groups who developed a sulfonated NHC. Other systems where the NHC contains a carboxylic acid function were developed by Hong and co-workers,\textsuperscript{256} or the NHC having a sugar group was developed by Peng and co-workers.\textsuperscript{257} However, the main drawback of the NHC-based systems is the need for a high catalyst loading. Moreover, a very interesting way to optimise the activity of a NHC-based system would be to use a synergistic effect: the high activity of the phosphine-based systems combined with the high stability of the NHC-based systems.\textsuperscript{258} A straightforward route for synthesising such mixed phosphine/NHC palladium (0) complexes has been developed by Fantasia and Nolan.\textsuperscript{259} This method is used for preparing the Pd(0) complexes presented below. Some catalytic activities in the Suzuki-Miyaura coupling reaction in aqueous media are reported.

### 5.1.2 Selection of an adequate complex

\textit{Results of section 5.1.2 are courtesy of Thibault Schmid.}

The synthesised complexes differ in their coordinated phosphine ligand. As the IPr-based complexes (IPr = N,N′–bis–(2,6–diisopropylphenyl)imidazol–2–ylidene) display the highest activities for the Suzuki-Miyaura coupling reaction,\textsuperscript{260–262} they were selected as the common NHC for all complexes. A series of [PdCl\textit{2}(IPr)(PR\textit{2}R′)] complexes were synthesised by cleavage of the dimer [Pd(µ–Cl)(Cl)(IPr)]\textit{2} by the addition of two equivalents of phosphine. A range of phosphine ligands was selected for their disparity in terms of steric and electronic properties (Figure 5.1). As a benchmark reaction, the coupling of 4–chlorotoluene with phenylboronic acid with a catalyst loading of 0.5 mol % and sodium hydroxide as a base was investigated. Sodium hydroxide presents the
advantages of being soluble in water, economical and of benign environmental impact. Moreover, this base was found to be the most efficient one in a previous study on NHC-phosphite Pd(II) pre-catalysts for the Suzuki-Miyaura coupling reaction. Therefore, sodium hydroxide was selected for this study.

Complexes 5a and 5b were tested in the benchmark reaction for 14 h at 80°C in water. However, a rapid formation of palladium black was observed in the reaction medium, which resulted in limited conversions. It was then decided to look for an additive that would improve the solubility of our complexes and thus limit the deactivation of the formed catalysts. The Suzuki-Miyaura coupling under mild conditions was successfully performed by Nolan and co-workers using isopropanol as a solvent. The same group later developed a methodology for the reduction/trapping of Pd(II) complexes into the carbene-phosphine mixed Pd(0) species in isopropanol, the latter playing the role of a reducing agent via the isopropoxide anion. Considering the advantages of isopropanol, it was therefore chosen as an additive. The ratio 9:1 (H₂O:iPrOH) was chosen for testing the palladium catalysts. The use of this solvent mixture resulted in an improvement of the activity of the complexes 5a and 5b, and this mixture was used for the rest of the study.

The test reaction was therefore extended to the whole series of complexes and compared to commercially available complexes [Pd(µ–Cl)(Cl)(IPr)]₂, [Pd(η⁻³–allyl)(Cl)(IPr)]₂ and [PdCl₂(IPr)(3–chloropyridine)] (PEPPSI–IPr). In order to assess the synergy resulting from the presence of the mixed NHC/Phosphine ligand, the dimer [Pd(µ–Cl)(Cl)(SPhos)]₂ (SPhos = 2–dicyclohexylphosphino–2′,6′–dimethoxybiphenyl) was synthesised. The results of these catalysts screening are reported in Table 5.1.
Table 5.1: Catalyst screening: selection of the most active species

<table>
<thead>
<tr>
<th>Entry</th>
<th>Catalyst</th>
<th>Loading (mol%)</th>
<th>Conversion (GC)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td><a href="5a">PdCl₂(IPr)(PPh₃)</a></td>
<td>0.5</td>
<td>37%*</td>
</tr>
<tr>
<td>2</td>
<td><a href="5a">PdCl₂(IPr)(PPh₃)</a></td>
<td>0.5</td>
<td>42%</td>
</tr>
<tr>
<td>3</td>
<td><a href="5b">PdCl₂(IPr)(PCy₃)</a></td>
<td>0.5</td>
<td>6%*</td>
</tr>
<tr>
<td>4</td>
<td><a href="5b">PdCl₂(IPr)(PCy₃)</a></td>
<td>0.5</td>
<td>19%</td>
</tr>
<tr>
<td>5</td>
<td><a href="5c">PdCl₂(IPr)(P(o-tolyl)₃)</a></td>
<td>0.5</td>
<td>43%</td>
</tr>
<tr>
<td>6</td>
<td><a href="5d">PdCl₂(IPr)(P(1–Ad)(nBu))</a></td>
<td>0.5</td>
<td>22%</td>
</tr>
<tr>
<td>7</td>
<td><a href="5e">PdCl₂(IPr)(PCy₂(o-biphenyl))</a></td>
<td>0.1</td>
<td>&gt;99%</td>
</tr>
<tr>
<td>8</td>
<td><a href="5f">PdCl₂(IPr)(XPhos)</a></td>
<td>0.1</td>
<td>&gt;99%</td>
</tr>
<tr>
<td>9</td>
<td><a href="5g">PdCl₂(IPr)(SPhos)</a></td>
<td>0.1</td>
<td>&gt;99%</td>
</tr>
<tr>
<td>10</td>
<td>[Pd(µ–Cl)(Cl)(IPr)]₂</td>
<td>0.5</td>
<td>37%</td>
</tr>
<tr>
<td>11</td>
<td>[Pd(η₃–allyl)(Cl)(IPr)]</td>
<td>0.5</td>
<td>42%</td>
</tr>
<tr>
<td>12</td>
<td>[PdCl₂(IPr)(3–chloropyridine)]</td>
<td>0.5</td>
<td>57%</td>
</tr>
<tr>
<td>13</td>
<td>[Pd(µ–Cl)(Cl)(SPhos)]₂</td>
<td>0.5</td>
<td>&gt;99%</td>
</tr>
</tbody>
</table>

Reaction conditions: 4–chlorotoluene (1 mmol), PhB(OH)₂ (1.05 mmol), NaOH (1.5 mmol), catalyst 0.5–0.1 mol% Pd, H₂O:iPrOH (9:1) (0.5 mL), 80°C, 14 h
*Reaction performed in water only

5.1.3 Synthesis of [Pd(IPr)(SPhos)] and reaction profiling

As Pd(0) species are believed to be the active species in the Suzuki-Miyaura coupling reaction, the complex 5g showing the best activity for the coupling of 4–chlorotoluene with phenylboronic acid, it was selected for the preparation of its Pd(0)

Figure 5.2: Synthesis of the [Pd(IPr)(SPhos)] complex

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78 NHC–Metal complexes in catalysis
5.1 The Suzuki-Miyaura reaction in aqueous medium

The one-pot synthesis consists of a reduction of $[\text{Pd}(\eta^3\text{allyl})(\text{Cl})(\text{IPr})]$ with potassium tert-butoxide followed by addition of the SPhos ligand (Figure 5.2), in a mixture of toluene and isopropanol (1:1), at room temperature during five days. $[\text{Pd}(\text{IPr})(\text{SPhos})]$ presents similar NMR features as its Pd(II) analogue: the backbone carbons $C^4$ and $C^5$ appear as a doublet ($\delta$ 125.1 ppm, $^4J_{CP} = 17.2$ Hz), the carbene carbon atom was shifted downfield when compared to the Pd(II) compounds and presented a much smaller coupling constant with the phosphorus atom ($\delta$ 199.5 ppm, $^2J_{CP} = 84.5$ Hz). Finally, the $^{31}\text{P}--^1\text{H}$ NMR spectrum exhibits a sharp singlet at $\delta$ 66.9 ppm. $[\text{PdCl}_2(\text{IPr})(\text{SPhos})]$ and $[\text{Pd}(\text{IPr})(\text{SPhos})]$ led to similar conversions for the coupling of 4-chlorotoluene with phenylboronic acid: at a catalyst loading of 0.1 mol%, while the Pd(II) species gives a 99% conversion, the Pd(0) homologue provides a 96% conversion. These similar results support the existence of the same active species in the catalytic cycle. In order to study this case in more details, a comparative reaction profiling was performed (Figure 5.3). An induction period of about ten minutes was observed for $[\text{PdCl}_2(\text{IPr})(\text{SPhos})]$ whereas $[\text{Pd}(\text{IPr})(\text{SPhos})]$ reacted immediately. Indeed, the Pd(0) species might deactivate rapidly, whereas the Pd(II), which needs an activation period, would act as a “reservoir” for the active species. Therefore, the reaction can reach completion with the Pd(II) species, having a lifetime artificially much longer than its Pd(0) homologue.

Considering the air-sensitivity of the $[\text{Pd}(\text{IPr})(\text{SPhos})]$ complex and the difficulty of its synthesis leading to a poor isolated yield, the remainder of this study (scope of substrates) was carried out by Thibault Schmid with the Pd(II) precursors.
5.1.4 Conclusion

The complex [Pd(IPr)(SPhos)] was synthesised and characterised. It has been used for the Suzuki-Miyaura coupling reaction in comparison to its Pd(II) homologue. However, it has shown to be less active than expected. For this reason, and due to the difficulties for synthesising [Pd(IPr)(SPhos)], it has been abandoned and the remaining studies were carried out with the Pd(II) species.

5.2 Copper–NHC complexes as carbene transfer reagents

The work presented in the following section was partially published in Chemical Communication in 2010.\(^{269}\)

5.2.1 A path for assembling NHC–Transition Metal Complexes

Transition metal catalysed reactions are efficient synthetic tools. Cross-coupling reactions permitting the creation of carbon-carbon bonds using palladium as catalyst are amongst the most important and have found numerous applications in the pharmaceutical industry\(^{270}\) and the synthesis of natural products and liquid crystals.\(^{271}\) A more recent burgeoning area of transition metal mediated transformations has focus on the use of gold in catalysis.\(^{272,273}\) In this context the use of numerous gold–phosphine and gold–NHC complexes have proven to be very useful in the assembly of simple and complex architectures.\(^{274–276}\) The development of catalysts and their final usefulness is often associated with the cost of their synthesis. The assembly of NHC–Transition metal complexes can be problematic\(^{277,278}\) and is most often accomplished by generating the free NHC followed by binding to a metal centre either in a ligand substitution or in dimer scission reactions. The direct NHC transfer from one metal centre to another, in one reaction, appears most practical and straightforward. As an example of this transmetallation approach, the silver-mediated reaction is the most common method for NHC transfer,\(^{279,280}\) and in this manner, transmetallation can be achieved successfully with numerous metals.\(^{281,282}\) However, the NHC transfer from silver does not always proceed correctly.\(^{283,284}\) An alternative reported route makes use of a gold(I)–NHC complex as transfer agent to palladium(II).\(^{285}\) However, both these NHC transfer reagents (Au and Ag) have important drawbacks: the transfer from silver (I) must be conducted in the dark whilst the transfer from gold requires PPh\(_3\) and an oxygen-free atmosphere. Moreover, both approaches have obvious cost disadvantages. Therefore, a more effective, practical and cost effective method is highly desirable. In this context, we considered that the least expensive metal of group 11, copper, might represent a viable alternative
to gold and silver complexes. Recently, Albrecht and co-workers showed that transfer from copper to ruthenium was possible. However, the main drawback to the copper approach is the presently used synthetic routes to Cu(I)–NHC complexes based on the addition of free NHC (in situ or preformed) to copper halide, as such preparations involve the use of strong and expensive bases, an inert atmosphere and generate inorganic salts. These problems were finally overcome by using a pioneering methodology that uses Cu$_2$O and an imidazolium salt. Cazin and co-workers concurrently reported a similar synthetic protocol.

Thus, a facile and versatile synthetic route leading to Cu(I)–NHC complexes now exists (Figure 5.4). The potential use of these copper complexes in transmetallation reactions can be considered.

### 5.2.2 Transmetallation from Cu(I) to Au(I) and Pd(II)

Herein, we report a study dealing with reactions involving the transfer of NHC from copper(I) to gold(I) and palladium(II) to support our original hypothesis that Cu(I)–NHC complexes could be used in this fashion. Four copper(I) complexes were selected for this study (Figure 5.5). This choice was motivated by the fact that they would lead to gold(I) and palladium(II) complexes frequently used in catalytic applications. The transmetallation from copper(I) to gold(I) and palladium(II) was performed in dichloromethane. This solvent choice was judicious because of the solubility of the used gold and palladium precursors: [AuCl(SMe$_2$)] and [PdCl$_2$(NCPh)$_2$]. Moreover, the organometallic complexes formed are very soluble in...
dichloromethane, where the copper chloride salt is not. We therefore predicted the reaction to proceed with efficient kinetics as all starting materials are soluble and one of the products is insoluble, which should drive the reaction towards completion. Furthermore, a very simple filtration should allow the separation of the desired product from CuCl. Reactions of [CuCl(IMes)] ($\text{IMes} = \text{N,N'-bis-}(\text{dimesityl})\text{imidazol-2-ylidene}$) and [CuCl(SIMes)] ($\text{SIMes} = \text{N,N'-bis-}(\text{dimesityl})\text{imidazol-4,5-dihydro-2-ylidene}$) with [AuCl(SMe$_2$)] lead, within one hour at 40°C, to the complete transfer of the mesityl-derived NHC from copper to gold. In this manner, [AuCl(IMes)] and [AuCl(SIMes)] were obtained in high isolated yields. When [CuCl(IPr)] ($\text{IPr} = \text{N,N'-bis-}(2,6\text{-diisopropylphenyl})\text{imidazol-2-ylidene}$) was used, a slightly longer reaction time of two hours was required for complete transfer of the NHC leading to the formation of [AuCl(IPr)] which was isolated in an 84% yield. Following the same synthetic strategy, copper complexes were reacted with [PdCl$_2$(NCPh)$_2$], leading to the formation of the chloro-bridged dimeric species [Pd($\mu$-Cl)Cl(NHC)]$_2$ after carbene transfer reaction (Fig. 5.6). Interestingly, the reaction times necessary to reach complete transfer of the NHC to the palladium centre match those needed for the gold reactions. Indeed, whilst IMes and SIMes are transferred within a hour, IPr requires nearly two hours. This might be due to the slightly higher steric hindrance of the latter compared to the mesityl derivatives. Finally, when using the even more hindered SIPr ligand, decomposition of the gold and palladium salts was observed, even when the reaction was carried out at low temperature (0°C). This degradation of the starting salts to metallic Au and Pd impeded the isolation of the desired complexes. In order to find if the problem of transferring the SIPr ligand was due to the reaction itself or to any effect of the SIPr ligand, a similar reaction was carried out using the “classical” silver complex as the NHC transfer agent. When [AgCl(SIPr)] was employed for transferring the ligand to [AuCl(SMe$_2$)], only a 66% conversion to the desired complex was observed on $^1$H NMR after two hours at room temperature. Further studies were not carried out for attempting to transfer the SIPr ligand. Although the method developed with the copper complexes is efficient for the SIMes, IMes and IPr ligands, it seems obvious that it is inadequate for the SIPr ligand.

The NHC transfer from copper to gold(I) and to palladium(II) has proven to be efficient and rapid for three of the most frequently encountered NHC ligands (Figure 5.6). This represents, to the best of our knowledge, the first example of the transfer of a NHC ligand from [CuCl(NHC)] to another metal centre. Furthermore the use of Cu(I)–NHC complexes as carbene transfer reagents has been shown viable for the synthesis of Au(I) and Pd(II) complexes, systems that are frequently used in transition metal-mediated catalysis. This new method possesses obvious economic and practical advantages over the common silver-based and over the less frequently encountered gold-based approaches.
5.2.3 Attempts for extending the process to other metals

The success of the transmetallation from copper to gold and palladium with the most common NHC ligands led to several attempts for preparing a various range of NHC–Metal species. The aim was to have an overview of the feasibility of synthesising existing complexes or preparing new species using the transmetallation method. As the IPrCuCl species was the most easily available in the laboratory at the time of these studies, the NHC transfer from the copper centre to another metal centre was employed as a model reaction. The NHC transfer reaction was attempted on some transition metal (Cr, Fe, Ru, Co, Rh, Ir and Ni) and post-transition metals (Al, In and Sn). Most of the tests were totally unsuccessful, but some were promising and would deserve further study. Only a very brief description of some applications of the NHC–Metal species will be given, and only in the field of catalysis. All the reactions described above were carried out in an atmosphere of argon.

5.2.3.1 Transition metals

**Group 6** The only studied metal was chromium.

Chromium(III)–NHC complexes show a high activity towards the polymerisation of ethylene.\(^{299}\) We attempted to transfer the IPr ligand from IPrCuCl to CrCl\(_3\). At first sight, the reaction performed well, a deposit of CuCl being observed. However, a \(^1\)H NMR study of the obtained species revealed that the IPr ligand was protonated.
**Group 8**  In this group, the interest was focused on iron and ruthenium.

The reason for selecting iron was the lack of studies describing well-defined NHC–Fe complexes, at least for applications as catalysts. The very first use of NHC–Fe species for homogeneous catalysis was reported by Grubbs and co-workers. Moreover, the Kumada cross-coupling reaction has been reported by using NHC–Fe catalysts. Finally, the arylmagnesiation of aryl(alkyl)acetylenes was reported to be catalysed by NHC–Fe catalysts. It was attempted to synthesise the complex $\text{[Fe(IPr)(CO)₂Cp]}$ in dichloroethane at 80°C (Figure 5.7), but it has been unsuccessful. No further tests have been done for iron.

Figure 5.7: Attempted transmetallation from Cu to Fe

The other studied metal in Group 8 was ruthenium. Ruthenium has its widest applications in the very large field of metathesis but also in the isomerisation of olefins or transfer hydrogenation. In the latter area, the complex $\text{[Ru(IPr)₂(CO)(H)(Cl)]}$ has shown excellent activity in the hydrogenation of ketones. Originally this complex was synthesised by thermolysis of $\text{[Ru(AsPh₃)₃(CO)H₂]}$ in toluene containing a excess of the free IPr, followed by an addition of dichloromethane. It has been attempted to synthesise this complex in toluene at 110°C (Figure 5.8). Some new species were observed but no confirmation that the desired complex was formed has been obtained.

Figure 5.8: Attempted transmetallation from Cu to Ru

**Group 9**  The interest is now focused on Cobalt, Rhodium and Iridium.

Catalytic reactions involving cobalt bearing NHC ligands are rare, and the first catalyst was only synthesised in 2003 as a NHC–dicobalt complex. The major applications of NHC–Co complexes are for the catalysis of cyclisation reactions. It has been attempted to synthesise this complex in toluene at 110°C (Figure 5.9). However, this attempt gave no conversion to the desired species.
5.2 Copper–NHC complexes as carbene transfer reagents

Another metal in Group 9, of greater interest than cobalt, is rhodium. The main catalytic applications of NHC–Rh species are for transfer hydrogenation\(^ {310,311} \) and hydroformylation\(^ {312} \). For the purpose of transmetallation, the complex \([\text{RhCl(COD)}]_2\) has been employed, as it is a source of the versatile electrophile species “\([\text{Rh(COD)}]^+\)”. The goal was to synthesise either the species \([\text{Rh(IPr)}_2\text{Cl}]\), or the complex \([\text{Rh(IPr)(COD)}]^+,\text{Cl}^-\) (Figure 5.10). Nevertheless, neither the first complex nor the second one has been obtained by the transmetallation path.

Finally, the last metal from this group, iridium, deserved some studies dealing with the NHC transfer, considering its general Chemistry is very similar to the one of rhodium. As for rhodium, the NHC transfer to the \([\text{IrCl(COD)}]_2\) has been attempted, and failed.

**Group 10** In Group 10, we focused on Nickel.

The reason for selecting Nickel was the NHC–Ni complexes find promising numerous applications in the field of catalysis. For instance, the formation of C–C bonds through the Suzuki-Miayaura\(^ {313–317} \), Kumada\(^ {318,319} \) or Negishi\(^ {320} \) cross-coupling reactions start to be feasible using NHC–Ni catalysts. Moreover, the formation of a carbon–heteroatom bond has been reported: C–S\(^ {321} \) and C–N\(^ {322–324} \) bond formations both operate in moderate to excellent yields. The NHC transfer form IPrCuCl to NiCl\(_2\) has been attempted. However, \(^1\)H NMR studies show that the reaction did not occur (Figure 5.11)

![Diagram](image-url)
5.2.3.2 Post-transition metals

Non-transition metals NHC complexes have been developed in the recent years. Our selection of aluminium, indium and tin was due to the easy availability of the chloride species in the laboratory. Nevertheless, if the NHC transfer from IPrCuCl to SnCl₂ (Figure 5.12), InCl₃ (Figure 5.13) and AlCl₃ (Figure 5.14) occurred, ¹H NMR undoubtedly showed that the desired complexes were not formed.

\[
\text{IPrCuCl} + \text{SnCl}_2 \underset{100^\circ C}{\xrightarrow{\text{1-propanol}}} [\text{Sn(IPr)Cl}_2] - \text{CuCl}
\]

**Figure 5.12:** Attempted transmetallation from Cu to Sn

\[
\text{IPrCuCl} + \text{InCl}_3 \underset{65^\circ C}{\xrightarrow{\text{THF}}} [\text{In(IPr)Cl}_3] - \text{CuCl}
\]

**Figure 5.13:** Attempted transmetallation from Cu to In

\[
\text{IPrCuCl} + \text{AlCl}_3 \underset{100^\circ C}{\xrightarrow{\text{1-propanol}}} [\text{Al(IPr)Cl}_3] - \text{CuCl}
\]

**Figure 5.14:** Attempted transmetallation from Cu to Al

5.2.4 Conclusion

The new method for transferring a NHC ligand from copper to another metallic centre possesses obvious economic and practical advantages over the common silver-based approach. The method is very efficient for transferring the IPr, IMes and SIMes ligand to gold and palladium centres. Nevertheless, this method is inefficient for the transfer of the SIPr ligand. Moreover, it seems that this method is not very general for other metals. In conclusion, the methodology needs much improvements to be reliable for the transfer to metals other than gold and palladium. However, with such improvements, a great methodology involving cheap and easily-prepared starting materials would emerge.
Appendix A

Experimental Data

A.1 Chapter 2

All reactions were performed using standard Schlenk line and glovebox techniques. Solvents were degassed with nitrogen. $^1$H and $^{13}$C nuclear magnetic resonance (NMR) spectra were recorded at 298 K on a Bruker 300 MHz or 400 MHz spectrometer for $^1$H NMR and 75 MHz or 100 MHz for $^{13}$C NMR, using the residual solvent peak to reference the spectra to tetramethylsilane at $\delta$ 0 ppm. IR spectra were recorded on a Perkin Elmer Spectrum GX FT–IR spectrometer using KBr discs. Matrix assisted laser desorption time of ight mass spectrometry. MALDI–MS was acquired using a 4800 MALDI–TOF/TOF Analyser (ABSciex, Foster City, CA) equipped with a Nd:YAG 355 nm laser and calibrated using a mixture of peptides. The sample (0.5 mL), dissolved in the appropriate solvent, was applied to the MALDI target along with $\alpha$–cyano–4–hydroxycinnamic acid matrix (0.5 mL, 10 mg/mL in 50 : 50 acetonitrile : 0.1% aq. TFA) and allowed to dry. The spot was analysed in positive MS mode over the appropriate mass range, by averaging 1000 laser spots. Elemental analyses were performed by the University of St Andrews Microanalytical Service and Elemental Analysis Service of the London Metropolitan University.

$[\text{Pd}_2(\text{dba})_3]$, $[\text{Ru(acac)}_3]$, 1,1,1–tris–(diphenylphosphinemethyl)ethane, zinc, linoleic acid, dimethyl maleate (Sigma Aldrich), 1,2–bis(ditertbutylphosphinomethyl)benzene (Lucite International) and methane sulfonic acid (Alfa Aesar) were used as supplied. Natural oils (Rapeseed, Sunflower, Olive) were obtained from a local supermarket and used as supplied. They were analysed for their different carboxylic acid contents by a literature method.
Dimethyl 1,19–nonadecanedioate

In a glovebox, \([\text{Pd}_2(\text{dba})_3]\) (549 mg, 0.6 mmol) and 1,2–bis(ditertbutylphosphinomethyl)benzene (2367 mg, 6 mmol) were introduced into a steel autoclave and sealed. Degassed methanol (30 mL), natural oil (10 mL) and methane sulfonic acid (0.78 mL, 12 mmol) were added to the autoclave by cannula. The autoclave was purged with CO and the CO pressure was set to 30 bar. The autoclave was heated to 80°C for 22 h. After cooling, venting and opening, the yellow powder was dissolved by adding dichloromethane (20 mL) and the yellow solution was filtered through a plug of cotton wool. The solvent was removed on a rotary evaporator until a white precipitate appeared. Ice cold methanol was added and the mixture was stirred in an ice bath for 20 min before filtration. The remaining deep orange solvent was again evaporated on a rotary evaporator until precipitate appeared, which was cooled in an ice bath for 20 min, and filtered. The desired diester was obtained as a white powder in different isolated yields, depending on the starting natural oil; from olive oil: 6.93 g (74.7%); from sunflower oil: 3.36 g (36.8%); from rapeseed oil: 6.44 g (69.3%). Yields are based on the amount of unsaturated esters contained in the oil. Elemental analysis: found C 71.10, H 11.21%; \(\text{C}_{21}\text{H}_{40}\text{O}_4\) requires C 70.74, H 11.31%.

\[\text{1H NMR (400 MHz; CDCl}_3\text{): } \delta 3.66 (s, 6H, –O–C}_3\text{H}_3\text{), 2.29 (t, J = 7.6 Hz, 4H, –C}_2\text{H}_2–C\text{O–O–CH}_3\text{), 1.61 (quintet, J = 7.3Hz, 4H, –C}_2\text{H}_2–C\text{O–O–CH}_3\text{), 1.24 (s, 26H, alkyl chain).} \]

\[\text{13C NMR (100 MHz; CDCl}_3\text{): } \delta 174.49 (s, C_{\text{carbonyl}}), 51.58 (s, C_{\text{methoxy}}), 34.26 (s, –C}_2\text{H}_2–C_{\text{carbonyl}}, 29.81 (s), 29.78 (s), 29.74 (s), 29.60 (s), 29.40 (s), 29.30 (s), 25.11 (s, –C}_2\text{H}_2–C_{\text{carbonyl}}). \] These data are consistent with those described in the literature.

1,19–nonadecanedioic acid

Dimethyl 1,19–nonadecanedioate (400 mg, 1.12 mmol) was introduced into a round bottom flask. Dioxane (30 mL), distilled water (20 mL) and hydrochloric acid (36% in water, 1 drop, 10 mg, 0.28 mmol) were added and the mixture was left to reflux overnight. After cooling, the solvent was removed on a rotary evaporator. Distilled water (100 mL) was added and the heterogeneous mixture stirred fast before being filtered through a Büchner funnel. The white solid was washed with water (50 mL) and dried under vacuum. The desired diacid was obtained as a white powder (230 mg, 62%). Elemental analysis: found C 69.62, H 10.91%; \(\text{C}_{19}\text{H}_{36}\text{O}_4\) requires C 69.47, H 11.05%.

\[\text{1H NMR (300 MHz; THF): } \delta 10.54 (broad s, 2H, –CO}_2\text{H}, 2.21 (t, J = 7.4 Hz, 4H, –C}_2\text{H}_2–C\text{O}_2\text{H}, 1.57 (quintet, J = 7.2 Hz, 4H, –C}_2\text{H}_2–C\text{O}_2\text{H})\text{, 1.30 (s, 30H, alkyl chain).} \]

\[\text{13C NMR (75 MHz; THF): } \delta 174.41 (s, –CO}_2\text{H}, 34.23 (s, –C}_2\text{H}_2–C\text{O}_2\text{H}, 30.62–30.12 (m, alkyl chain).} \]
1,19–nonadecanediol

First method. [Ru(acac)$_3$] (4.5 mg, 0.011 mmol), 1,1,1–tris–(diphenylphosphinemethyl)ethane (14 mg, 0.022 mmol) and dimethyl nonadecanedioate (393 mg, 1.103 mmol) were introduced into an autoclave and sealed. The autoclave was purged three times with nitrogen. Dioxane (10 mL) and water (1 mL) were introduced by cannula. The autoclave was purged with H$_2$ and the H$_2$ pressure was set to 40 bar before heating to 220°C for 16 h. After cooling, depressurising and opening, the crude mixture was transferred to a round bottom flask (50 mL). The solvent was removed on a rotary evaporator. Dichloromethane (10 mL) was added and the yellow solution containing white crystals was stirred for 20 min before filtration. The desired diol was obtained as a white powder (265 mg, 80%). Elemental analysis: found C 75.93, H 13.36%; C$_{19}$H$_{40}$O$_2$ requires C 75.94, H 13.42%.

$^1$H NMR (300 MHz; THF): δ 3.45 (t, J = 6.4 Hz, 4H, –C$_{19}$H$_{20}$–OH), 1.45 (quintet, J = 6.1 Hz, 4H, –C$_{19}$H$_{20}$–CH$_2$–OH), 1.28 (s, 30H, alkyl chain).

$^{13}$C NMR (75 MHz; THF): δ 62.53 (s, –C$_{19}$H$_{20}$–OH), 34.11 (s, –C$_{19}$H$_{20}$–CH$_2$–OH), 30.68 (s), 30.62 (s), 30.55 (s), 26.93 (s, –C$_{19}$H$_{20}$–CH$_2$–CH$_2$–OH). These data are consistent with those described in the literature.

Second method. [Ru(acac)$_3$] (4.5 mg, 0.011 mmol), 1,1,1–tris–(diphenylphosphine-methyl)ethane (14 mg, 0.022 mmol), dimethyl nonadecanedioate (393 mg, 1.103 mmol) and zinc powder (8.6 mg, 0.132 mmol), were introduced into an autoclave and sealed. The autoclave was purged three times with nitrogen. Methanol (10 mL) was introduced via cannula. The autoclave was purged with H$_2$ and the H$_2$ pressure was set to 70 bar. The autoclave was heated to 140°C for 16 h. After cooling, venting and opening, dichloromethane (10 mL) was added and the mixture transferred to a round bottom flask (50 mL). The solvent was removed on a rotary evaporator. Dichloromethane (10 mL) was added and the yellow solution containing white crystals was stirred for 20 min. The two phases mixture was allowed to settle for 20 min (the product stays in the upper phase, the metallic zinc stays at the bottom). The upper phase was decanted and filtered. The desired diol was obtained as a white powder (270 mg, 81%). Elemental analysis: found C 76.03, H 13.17%; C$_{19}$H$_{40}$O$_2$ requires C 75.94, H 13.42%. $^1$H NMR (400 MHz; THF): δ 3.45 (t, J = 6.5 Hz, 4H, –CH$_2$–OH), 1.47 (quintet, J = 6.7 Hz, 4H, –CH$_2$–CH$_2$–OH), 1.30 (s, 30H, alkyl chain).

$^{13}$C NMR (100 MHz; THF): δ 62.54 (s, –CH$_2$–OH), 34.11 (s, –CH$_2$–CH$_2$–OH), 30.69 (s), 30.63 (s), 30.55 (s), 26.93 (s, –CH$_2$–CH$_2$–CH$_2$–OH).

Oligoesters were prepared using the first method described above for the diol, starting from nonadecanedioic acid, in anhydrous dioxane. The oligomers were obtained as white solids. Elemental analysis: found C 75.83, H 11.64%; C$_{57}$H$_{112}$O$_6$ (i.e. oligomers with 3 units terminated by –OH groups) requires C 76.62, H 12.63%. Typical NMR data: $^1$H NMR (400 MHz; CDCl$_3$): δ 4.05 (t, J = 6.8 Hz, 1H, –CO–O–CH$_2$–), 3.64 (t, J =
6.6 Hz, 1H, –CH₂–OH), 2.28 (t, J = 7.6 Hz, 1H, –CH₂–CO–O–CH₂–), 1.64–1.53 (m, 3H), 1.25 (s, 22H, alkyl chain), 0.88 (t, J = 6.9 Hz, saturated end group). \(^{13}\)C NMR (100 MHz; CDCl₃): \(\delta\) 64.56 (s, –CH₂–CO–O–), 63.26 (s, –CH₂–OH), 34.58 (s), 32.98 (s), 29.83–28.82 (m, alkyl chain), 26.10 (s), 25.90 (s), 25.19 (s). IR: 3450 cm\(^{-1}\) (\(\nu\)(OH)), 2918 cm\(^{-1}\) and 2850 cm\(^{-1}\) (\(\nu\)(CH)), 1735 cm\(^{-1}\) (\(\nu\)(C=O)), 1630 cm\(^{-1}\), 1470 cm\(^{-1}\) (CH₂), 1180 cm\(^{-1}\), 1060 cm\(^{-1}\), 720 cm\(^{-1}\) (CH₂).
All reactions were performed using standard Schlenk techniques. All solvents were degassed with nitrogen. Unless otherwise stated, solvents were used as supplied and were not previously dried. $^1$H and $^{13}$C nuclear magnetic resonance (NMR) spectra were recorded at 298K on a Bruker 300 MHz for $^1$H NMR and 75 MHz for $^{13}$C NMR spectrometer, using the residual solvent peak to reference the spectra to tetramethylsilane at $\delta = 0$ ppm. Elemental analyses were performed by the Elemental Analysis Service of the London Metropolitan University.

$[\text{Pd}_2(\text{dba})_3]$, linoleic acid, dimethyl maleate (Sigma Aldrich), 1,2–bis(diterbutylphosphinomethyl)benzene (Lucite International), methyl 10–undecenoate, 2–undecenoic acid, 2–hexadecenoic acid (Tokyo Chemical Industry), Tall oil fatty acids (Mistral Lab Chemicals) and methane sulfonic acid (Alfa Aesar) were used as supplied.

**Dimethyl 1,19–nonadecanediolate from Tofa**

**Method 1:** Under air, $[\text{Pd}_2(\text{dba})_3]$ (37 mg, 0.04 mmol, (0.08 mmol Pd)) and 1,2–bis(diterbutylphosphinomethyl)benzene (158 mg, 0.4 mmol) were introduced into a hastelloy autoclave, sealed and purged with nitrogen. Methanol (10 mL), Tofa (2.5 mL) and methane sulfonic acid (MSA) (0.05 mL, 0.8 mmol) were added to the autoclave by cannula. The autoclave was purged three times with CO and the pressure was set to 30 bar. The autoclave was heated to 90°C for 48 h. It was then cooled to room temperature and degassed. A sample was taken for GC analysis.

**Method 2:** An esterification of Tofa (2.5 mL) was carried out over 3 h in dry refluxing methanol (10 mL) in the presence of MSA (0.05 mL) and magnesium sulfate (200 mg) under an atmosphere of dry nitrogen. The solution was cooled and introduced into the degassed autoclave containing $[\text{Pd}_2(\text{dba})_3]$ (37 mg, 0.04 mmol, (0.08 mmol Pd)) and 1,2–bis(diterbutylphosphinomethyl)benzene (158 mg, 0.4 mmol) by cannula bearing a filter. The autoclave was heated to 90°C for 10 h, then cooled to room temperature, degassed and a sample was taken for GC analysis. For both Methods 1 and 2, a suspension of 170 mg Pd/C 5% (8.5 mg Pd (0.08 mmol Pd)) in methanol (10 mL) was added by cannula. The autoclave was purged three times with H$_2$ and the H$_2$ pressure was set to 30 bar. The temperature was set to 90°C for 20 h. After cooling, venting and opening, the remaining yellow powder was dissolved by addition of dichloromethane (20 mL) and the yellow solution was filtered through paper. The solvent was removed on a rotary evaporator. Methanol was added and the mixture was warmed until the products dissolved. The mixture was placed in the freezer for 30 min and filtered using a Büchner funnel. The desired product was obtained as a white powder (Method 1:
Experimental Data

0.92 g, 32%; Method 2: 1.33 g, 49%). Elemental analysis: found C 70.81, H 11.35%; 
C_{21}H_{40}O_{4} requires C 70.74, H 11.31%. $^1$H NMR (300 MHz; CDCl$_3$): $\delta$ = 3.65 (s, 6H, O–C$_H$$_3$), 2.28 (t, J = 7.5 Hz, 4H, –CH$_2$–CO–O–CH$_3$), 1.60 (quintet, J = 7.3 Hz, 4H, CH$_2$–CH$_2$–CO–O–CH$_3$), 1.23 (s, 26H, alky chain). $^{13}$C NMR (300 MHz; CDCl$_3$): $\delta$ = 174.51 (s, CO), 51.60 (s, CH$_3$O–), 34.28 (s, CH$_3$O–CO–CH$_2$–), 29.84-29.32 (s, alky chain), 25.13 (s, –CH$_2$–CH$_2$–CO–O–CH$_3$). These data are consistent with those from the literature.

**Trimethyl heptadecane–1,n,17–tricarboxylate from linoleic acid**

**Method 1:** The carboxylation was carried out as described in Method 1 above but using methyl linoleate in place of Tofa, the reaction time being 64 h. After depressurisation of carbon monoxide, dichloromethane was added and the crude mixture was introduced into a round bottom flask. The solvent was removed on a rotary evaporator. The crude product was passed through a silica chromatography column (Hexane / Ethyl acetate : 92 / 8). The desired product was obtained as a transparent oil (635 mg, 19%).

**Method 2:** In a Schlenk flask containing [Pd$_2$(dba)$_3$] (37 mg, 0.04 mmol, 0.08 mmol Pd), 1,2–bis(di tert butylphosphinomethyl)benzene (158 mg, 0.4 mmol) and magnesium sulfate (200 mg), dry methanol (10 mL) and Tofa (2.5 mL) were introduced via cannula. The solution was stirred under nitrogen for 10 min and introduced in the autoclave by cannula. The autoclave was closed and pressurised with CO (30 bar) and heated to 90°C with magnetic stirring for 64 h. After cooling and depressurisation of CO, dichloromethane was added and the crude mixture was introduced into a round bottom flask. The solvent was removed on a rotary evaporator. The crude product was passed through a silica chromatography column (Hexane / Ethyl acetate : 92 / 8). The desired product was obtained as a transparent oil, 1.38 g, 44%). Elemental analysis: found C 66.52, H 10.07%; C$_{23}$H$_{42}$O$_6$ requires C 66.63, H 10.21%. $^1$H NMR (300 MHz; CDCl$_3$): (mixture of isomers) $\delta$ = 3.67 (s, 3H, CH$_3$O– (branched)), 3.66 (s, 6H, CH$_3$–O–), 2.29 (t, J = 7.5 Hz, CH$_3$O–CO–CH$_2$– ), 1.62 (s, CH$_3$–O–CO–CH$_2$–CH$_2$–), 1.44 (m), 1.23 (s, alky chain). $^{13}$C NMR (75 MHz; CDCl$_3$): (mixture of isomers) $\delta$ = 51.63 (s, CH$_3$O–), 45.68 – 45.53 (s, CH$_3$O–CO–CH–(CH$_2$–CH$_2$–)$_2$–), 34.29–34.05 (s, CH–(CH$_2$–CH$_2$–)$_2$), 32.70 (s, CH$_3$OOCO–CH$_2$–), 31.93 (s, CH–(CH$_2$–CH$_2$–)$_2$), 29.79–25.13 (alkyl chain), 23.01 (s, CH$_3$ O–CO–CH$_2$–CH$_2$–).
Methyl \(n\)-\( \text{o xo} \)octadecanoate from linoleic acid

**Method 1:** The carbonylation was carried out as described in Method 1 for Tofa above but using linoleic acid in place of Tofa. After depressurisation of carbon monoxide, dichloromethane was added and the crude mixture was introduced into a round bottom flask. The solvent was removed on a rotary evaporator. The crude product was passed through a silica chromatography column (Hexane / Ethyl acetate : 92 / 8). The desired product was obtained as a white solid (654 mg, 25%, mixture of isomers). This fraction was then passed down a silica chromatography column using hexane / ethyl acetate (90 / 10) and fractions containing only methyl 17-oxooctadecanoate were collected and evaporated to dryness (Yield 3%). Elemental analysis: found C 72.90, H 11.60%; \( \text{C}_{19}\text{H}_{36}\text{O}_{3} \) requires C 73.03, H 11.61%.

\(^1\)H NMR (300 MHz; CDCl\(_3\)): \( \delta = 3.66 \) (s, 3H, \( \text{CH}_3\text{O}– \)), 2.41 (t, \( J = 7.5 \) Hz, 2H, \( \text{CH}_3\text{–CO–CH}_2– \)), 2.29 (t, \( J = 7.5 \), 2H, \( \text{CH}_3\text{O–CO–CH}_2– \)), 1.65-1.51 (m, 4H, –CO–\( \text{CH}_2– \)), 1.24 (s, 22H, alkyl chain). \(^{13}\)C NMR (75 MHz; CDCl\(_3\)): \( \delta = 209.53 \) (s, \( \text{CO} \) (ketone)), 174.48 (s, \( \text{CO} \) (ester)), 51.57 (s, \( \text{CH}_3\text{O}– \)), 43.97 (s, \( \text{CH}_3\text{–CO–CH}_2– \)), 34.26 (s, \( \text{CH}_3\text{O–CO–CH}_2– \)), 29.98 (s, \( \text{CH}_3\text{–CO–CH}_2– \)), 29.77–29.29 (s, alkyl chain), 25.10 (s, \( \text{CH}_3\text{O–CO–CH}_2– \)), 24.02 (s, \( \text{CH}_3\text{–CO–CH}_2– \)). These data are consistent with those in the literature.

**Method 2:** The reaction was carried out as described in Method 1 for Tofa above but using methyl linoleate in place of Tofa, and nitrogen (40 bar) instead of carbon monoxide. After depressurisation of nitrogen, dichloromethane was added and the crude mixture was introduced into a round bottom flask. The solvent was removed on a rotary evaporator. The crude product was passed through a silica chromatography column (Hexane / Ethyl acetate : 92 / 8). The desired product was obtained as a white solid (1004 mg, 42%, isomers without methyl 17-oxooctadecanoate). Elemental analysis: found C 73.13, H 11.70%; \( \text{C}_{19}\text{H}_{36}\text{O}_{3} \) requires C 73.03, H 11.61%.

\(^1\)H NMR (300 MHz; CDCl\(_3\)): \( \delta = 3.61 \) (s, 3H, \( \text{CH}_3\text{O}– \)), 2.33 (tt, \( J = 7.5 \) Hz, 4J = 2.6 Hz, 4H, \( \text{CH}_2\text{–CO–CH}_2– \)), 2.27 (t, \( J = 7.5 \), 2H, \( \text{CH}_3\text{O–CO–CH}_2– \)), 1.60–1.44 (m, 6H, –CO–\( \text{CH}_2– \text{CH}_2– \)), 1.21 (s, 18H, alkyl chain), 0.88-0.80 (m, 3H, \( –\text{CH}_2–\text{CH}_3 \)). \(^{13}\)C NMR (75 MHz; CDCl\(_3\)): \( \delta = 211.54 \) (s, \( \text{CO} \) (ketone)), 174.24 (s, \( \text{CO} \) (ester)), 51.38 (s, \( \text{CH}_3\text{O}– \)), 42.79–42.49 \( \text{CH}_2\text{–CO–CH}_2– \)), 34.07 \( \text{CH}_3\text{O–CO–CH}_2– \), 31.82–31.44 (s, \( \text{CH}_3\text{–CH}_2– \text{CH}_2– \)), 29.77–29.29 (s, alkyl chain), 24.94 (s, \( \text{CH}_3\text{O–CO–CH}_2– \)), 23.85 (s, \( –\text{CH}_2–\text{CH}_2– \)), 22.64–22.37 (s, \( \text{CH}_3–\text{CH}_2– \)). These data are consistent with those in the literature.\(^{197}\)
Dimethyl 1,12–dodecanedioate from 2–undecenoic acid

Under air, [Pd₂(dba)₃] (25 mg, 0.027 mmol (0.054 mmol Pd)) and 1,2–bis(ditertbutylphosphinomethyl)benzene (107 mg, 0.27 mmol) were introduced into a hastelloy autoclave, sealed and purged with nitrogen. Degassed methanol (10 mL), 2–undecenoic acid (1 mL, 5.43 mmol) and MSA (0.07 mL, 1.08 mmol) were added to the autoclave by cannula. The autoclave was purged three times with CO and the pressure was set to 30 bar. The autoclave was heated to 90°C for 44 h. After cooling, venting and opening, the yellow solution was filtered through paper and the solvent was removed on a rotary evaporator. Methanol was added and the mixture was then stirred at -78°C for 10 min and filtered using a Büchner funnel. The desired product was obtained as a white powder. Isolated yield (0.6 g, 43%) Elemental analysis: found C 65.15, H 10.19%; C₁₄H₂₆O₄ requires C 65.09, H 10.14%. ¹H NMR (300 MHz; CDCl₃): δ 3.66 (s, 6H, CH₃–), 2.29 (t, J = 7.5 Hz, 4H, CH₃–CO–C₂H₅–), 1.60 (quintet, J = 7.3 Hz, 4H, 3–O–CO–CH₂–CH₂–), 1.26 (broad s, 12H, alkyl chain). ¹³C NMR (75 MHz; CDCl₃): δ 51.90 (s, C₃–), 29.78–29.55 (s, alkyl chain), 25.37 (s, CH₃O–CO–CH₂–CH₂–) These data are consistent with the literature.

Dimethyl 1,12–dodecanedioate from 11–undecenoic acid

Under air, [Pd(dba)₂] (127 mg, 0.022 mmol) and 1,2–bis(ditertbutylphosphinomethyl)benzene (439 mg, 1.10 mmol) were introduced into a hastelloy autoclave, sealed and purged with nitrogen. Degassed methanol (20 mL), 11–undecenoic acid (5 mL, 22.2 mmol) and MSA (0.3 mL, 4.6 mmol) were added to the autoclave by cannula. The autoclave was purged three times with CO and the pressure was set to 30 bar. The autoclave was heated to 90°C for 20 h. After cooling, venting and opening, the yellow solution was filtered through paper and the solvent was removed on a rotary evaporator. Methanol was added and the mixture was then stirred at -78°C for 10 min and filtered using a Büchner funnel. The desired product was obtained as a white powder. Isolated yield (3.36 g; 58%). Elemental analysis: found C 65.14, H 10.18%; C₁₄H₂₆O₄ requires C 65.09, H 10.14%. ¹H NMR (300 MHz; CDCl₃): δ 3.66 (s, 6H, CH₃–), 2.29 (t, J = 7.5 Hz, 4H, CH₃–CO–C₂H₅–), 1.60 (quintet, J = 7.2 Hz, 4H, 3–O–CO–CH₂–CH₂–), 1.26 (broad s, 12H, alkyl chain). ¹³C NMR (75 MHz; CDCl₃): δ 51.90 (s, C₃–), 34.53 (s, CH₃O–CO–CH₂–), 29.78–29.55 (s, alkyl chain), 25.37 (s, CH₃O–CO–CH₂–CH₂–) These data are consistent with these from the literature.
**Dimethyl 1,1,7-heptadecanedioate from 2-hexadecenoic acid**

Under air, \([\text{Pd}_2(\text{dba})_3] (18 \text{ mg, 0.0197 mmol, 0.0394 mmol Pd})\) and 1,2-bis(ditertbutyl-phosphinomethyl)benzene (78 mg, 0.197 mmol) were introduced into a hastelloy autoclave, sealed and purged with nitrogen. Degassed methanol (8 mL), 2-hexadecenoic acid (1.0 g, 3.93 mmol) and MSA (0.05 mL, 0.8 mmol) were added to the autoclave by cannula. The autoclave was purged three times with CO and the pressure was set to 30 bar. The autoclave was heated to 90°C for 20 h. After cooling, venting and opening, the yellow solution was filtered through paper and the solvent was removed on a rotary evaporator. Methanol was added, the mixture was put in the freezer for 20 min and filtered using a Büchner funnel. The desired product was obtained as a white powder (0.75 g, 58%) Elemental analysis: found C 69.56, H 10.09%; \(\text{C}_{14}\text{H}_{26}\text{O}_4\) requires C 69.47, H 11.05%. 

\(^1\)H NMR (300 MHz; CDCl\(_3\)): \(\delta\) 3.66 (s, 6H, \(\text{CH}_3\–\)), 2.30 (t, \(J = 7.5 \text{ Hz}, 4\text{H}, \text{CH}_3\–\text{CO}–\text{C}_2\text{H}_2–\)), 1.61 (quintet, \(J = 7.4 \text{ Hz}, 4\text{H}, 3\text{–O}–\text{CO}–\text{CH}_2–\text{CH}_2–\)), 1.24 (broad s, 22H, alkyl chain). \(^{13}\)C NMR (75 MHz; CDCl\(_3\)): \(\delta\) 174.64 (s, \(\text{CO}\)), 51.73 (s, \(\text{C}_3–\)), 34.40 (s, \(\text{CH}_3\–\text{O}–\text{CO}–\text{C}_2\text{H}_2–\)), 29.92–29.44 (s, alkyl chain), 25.24 (s, \(\text{CH}_3\–\text{O}–\text{CO}–\text{CH}_2–\text{CH}_2–\)).

**Trimethyl ethane–1,1,2-trioate**

Under air, \([\text{Pd}_2(\text{dba})_3] (37 \text{ mg, 0.04 mmol, 0.08 mmol Pd})\) and 1,2-bis(ditertbutyl-phosphinomethyl)benzene (158 mg, 0.4 mmol) were introduced into a hastelloy autoclave, sealed and purged with nitrogen. Degassed methanol (10 mL), dimethyl maleate (1 mL, 8 mmol) and MSA (0.05 mL, 0.8 mmol) were added to the autoclave by cannula. The autoclave was purged three times with CO and the pressure was set to 30 bar. The autoclave was heated to 90°C for 24 h. After cooling, venting and opening, the yellow solution was filtered through paper and the solvent was removed on a rotary evaporator. The crude mixture was passed through a silica chromatography column (Hexane / Ethyl acetate : 85 / 15). The desired product was obtained as a white solid. Isolated yield (1.2 g, 73%). Elemental analysis: found C 47.13, H 5.98%; \(\text{C}_8\text{H}_{12}\text{O}_6\) requires C 47.06, H 5.92%. 

\(^1\)H NMR (300 MHz; CDCl\(_3\)): \(\delta\) 3.87 (t, \(J = 7.4 \text{ Hz}, 1\text{H}, \text{CH}_3\–\text{O}–\text{CO}–\text{CH}_2–\text{CH}_2–\)), 3.77 (s, 6H, \((\text{CH}_3–\text{O}–\text{CO})_2–\text{CH}–\)), 3.71 (s, 3H, \(\text{CH}_3\–\text{O}–\text{CO}–\text{CH}_2–\)), 2.95 (d, \(J = 7.4 \text{ Hz}, 2\text{H}, \text{CH}_3\–\text{O}–\text{CO}–\text{CH}_2–\)). \(^{13}\)C NMR (75 MHz; CDCl\(_3\)): \(\delta\) 171.39 (s, \(\text{CO}\)), 168.90 (s, \(\text{CH}_3\–\text{O}–\text{CO}–\text{CH}_2–\)), 168.90 (s, \(\text{CH}_3\–\text{O}–\text{CO}–\text{CH}_2–\)), 53.06 (s, \(\text{CH}_3\–\text{O}–\text{CO}–\text{CH}–\)), 52.31 (s, \(\text{CH}_3\–\text{O}–\text{CO}–\text{CH}_2–\)), 47.56 (s, \((\text{CH}_3\–\text{O}–\text{CO})_2\)), 33.06 (s, \(\text{CH}_3\–\text{O}–\text{CO}–\text{CH}_2–\)). These data are consistent with those in the literature.\(^{327}\)
A.3 Chapter 4

All reactions were performed using standard Schlenk techniques. All solvents were degassed with nitrogen. Unless otherwise stated, solvents were used as supplied and were not previously dried. $^1$H and $^{13}$C nuclear magnetic resonance (NMR) spectra were recorded at 298K on a Bruker 300 MHz for $^1$H NMR and 75 MHz for $^{13}$C NMR spectrometer, using the residual solvent peak to reference the spectra to tetramethylsilane at $\delta = 0$ ppm. Elemental analyses were performed by the Elemental Analysis Service of the London Metropolitan University. IR spectra were recorded on a Perkin Elmer Spectrum GX FT–IR spectrometer using KBr discs. TGA were performed on a Stanton Redcroft STA–780 supplied by Thorn Scientific Services. Matrix assisted laser desorption time of ight mass spectrometry. MALDI–MS was acquired using a 4800 MALDI–TOF/TOF Analyser (ABSciex, Foster City, CA) equipped with a Nd:YAG 355 nm laser and cali-brated using a mixture of peptides. The sample (0.5 mL), dissolved in the appropriate solvent, was applied to the MALDI target along with $\alpha$–cyano–4–hydroxycinnamic acid matrix (0.5 mL, 10 mg/mL in 50 : 50 acetonitrile : 0.1% aq. TFA) and allowed to dry. The spot was analysed in positive MS mode over the appropriate mass range, by averaging 1000 laser spots.

$[\text{Pd}_2(\text{dba})_3]$, aniline (Sigma Aldrich), 1,2–bis(ditertiarybutylphosphinomethyl) benzene (Lucite International), methyl 10–undecenoate (Tokyo Chemical Industry) and methane sulfonic acid (Alfa Aesar) were used as supplied. Paraphenylenediamine (Sigma Aldrich) was recrystallised twice out of hot toluene and stored in darkness.

Aminocarbonylation of methyl 10–undecenoate

Under air, $[\text{Pd}_2(\text{dba})_3]$ (92 mg, 0.1 mmol), 1,2–bis(ditertiarybutylphosphinomethyl) benzene (395 mg, 1 mmol), 2–naphthol (1368 mg, 9.5 mmol) and KI (32 mg, 0.2 mmol) were introduced into a hastelloy autoclave, sealed and purged with nitrogen. Diethylether (10 mL), methyl 10–undecenoate (1.42 mL, 6.35 mmol) and aniline (1.16 mL, 12.7 mmol) were degassed for 10 minutes with nitrogen in an ice-cold Schlenck flask and introduced in the autoclave by cannula. Methane sulfonic acid (0.1 mL, 1.5 mmol) was added separately to the autoclave by cannula. The autoclave was purged three times with CO and the pressure was set to 30 bar. The autoclave was heated to 110°C for 16 h. After cooling, venting and opening, the remaining black mixture was solubi-lised in dichloromethane and the mixture filtered through paper. A sample was taken for GC analysis (conversion 99%). The solvent was removed on a rotary evaporator. The remaining solid was passed through a first silica chromatography column (ethyl
acetate:hexane / 1:3) and the obtained solid was passed through a second silica chromato-
graphy column (ethyl acetate:hexane / 1:9). The solid was recrystalised from ethyl
acetate/hexane. Isolated yields: from 49% to 60%. Elemental analysis: found C 71.45,
H 9.09, N 4.29%; C_{19}H_{29}O_{3}N requires C 71.44, H 9.15, N 4.38%. Melting point 79–80
° (average of three measurements). \(^1\)H NMR (400 MHz; CDCl_3): δ = 7.51 (d, J = 8.1
Hz, 2H, Ph–H), 7.31 (t, J = 7.8 Hz, 2H, Ph–H), 7.16 (s, 1H, N–H), 7.09 (t, J = 7.3 Hz,
1H, Ph–H), 3.66 (s, 3H, –OC\(_3\)H\(_3\)), 2.35 (t, J = 7.6 Hz, 2H, –CH\(_2\)–CO–NH–Ph), 2.30 (t,
J = 7.5 Hz, 2H, –CH\(_2\)–CO–OMe), 1.72 (quintet, J = 7.4 Hz, 2H, –CH\(_2\)–CH\(_2\)–CO–NH–
Ph), 1.61 (quintet, J = 7.5 Hz, 2H, –CH\(_2\)–CH\(_2\)–CO–OMe), 1.28 (s, alkyl chain). \(^{13}\)C NMR
(100 MHz; CDCl_3): δ = 174.72 (s, –CH\(_2\)–CO–NH–Ph), 171.68 (s, –CH\(_2\)–CO–
OMe), 129.33 (s, C\(_\text{Ph}\)), 124.48 (s, C\(_\text{Ph}\)), 120.04 (s, C\(_\text{Ph}\)), 51.81 (s, –CO–O\(_3\)C\(_3\)), 38.19
(s, –CH\(_2\)–CO–NH–Ph), 34.45 (s, –CH\(_2\)–CO–OMe), 29.66–29.43 (alkyl chain), 25.92 (s,
–CH\(_2\)–CH\(_2\)–CO–OMe)–. These data are consistent with the literature.

**Dimethyl 1,12–dodecanedioate**

Under air, [Pd\(_2\)(dba)_3] (101 mg, 0.22 mmol) and 1,2–bis(di-tert-butylphosphino-
methyl)-benzene (439 mg, 1.11 mmol) were introduced into a hastelloy autoclave, sealed
and purged with nitrogen. Degassed methanol (20 mL), methyl 10–undecenoate (5 mL, 22.4
mmol) and MSA (0.3 mL, 4.6 mmol) were added to the autoclave by cannula. The
autoclave was purged three times with CO and the pressure was set to 30 bar. The
autoclave was heated to 90°C for 16 h. After cooling, venting and opening, the yellow
solution was filtered through paper and the solvent was removed on a rotary evaporator.
Methanol was added and the mixture was then stirred at -78°C for 20 min and filtered
using a Büchner funnel. The desired product was obtained as a white powder. Isolated
yield (5.336 g, 92%). \(^1\)H NMR (300 MHz; CDCl_3): δ = 3.66 (s, 6H, CH\(_3\)–), 2.29 (t, J =
7.5 Hz, 4H, CH\(_3\)–CO–CH\(_2\)–), 1.60 (quintet, J = 7.3 Hz, 4H, 3–O–CO–CH\(_2\)–CH\(_2\)–),
1.26 (broad s, 12H, alkyl chain). \(^{13}\)C NMR (75 MHz; CDCl_3): δ = 51.90 (s, C\(_3\)–), 34.53
(s, CH\(_3\)–O–CO–CH\(_2\)–), 29.78–29.55 (s, alkyl chain), 25.37 (s, CH\(_3\)O–CO–CH\(_2\)–CH\(_2\)–)
These data are consistent with the literature.\(^{326}\)

**Dodecanedioic acid**

The previously synthesised dimethyl 1,12–dodecanedioate was used for this reaction
(5.536 g, 20.65 mmol). In a 250 mL round bottom flask, water (100 mL) was added.
Sodium hydroxide (2 g) was slowly added to the heterogeneous mixture. The flask
was heated to 100°C until the solution turned homogeneous, and was left for one hour more
at 100°C. HCl (8 mL, 37% aqueous solution) was added drop-wise to the mixture. The
resulting white powder was filtered using a Büchner funnel and washed with slightly acidic water (2×10 mL) and distilled water (2×10 mL), and dried overnight in an oven (80°C). The desired product was obtained as a white powder. Isolated yield (4.535 g, 85%). \(^1\)H NMR (400 MHz; THF): \(\delta = 2.19\) (t, J = 7.4 Hz, 4H, \(-\text{CH}_2\text{CO}_2\text{H}\)), 1.55 (quintet, J = 7.4 Hz, 4H, \(\text{CH}_2\text{CH}_2\text{CO}_2\text{H}\)), 1.29 (s, 12H, alkyl chain). \(^{13}\)C NMR (100 MHz; THF): \(\delta = 174.65\) (s, \(\text{HO}-\text{CO}-\text{CH}_2\text{H}^-\)), 34.33 (s, \(\text{HO}-\text{CO}-\text{CH}_2\text{H}^-\)), 30.43-30.11 (s, alkyl chain), 25.85 (s, \(\text{HO}-\text{CO}-\text{CH}_2\text{H}^-\))

**Dodecanedioyl dichloride**

Dodecanedioic acid (2 g, 8.68 mmol) was introduced in a 100 mL round bottom flask. The distillation setup was purged three times with nitrogen. Degassed and dry dichloromethane (20 mL) was introduced by cannula. Thionyle chloride (1.32 mL, 18.23 mmol) was introduced via cannula. The heterogeneous mixture was heated to 40°C until it turned homogeneous, and left for one hour more under nitrogen. The resulting dodecanedioyl dichloride was not isolated and was stored in the solvent at 0°C. The product is used directly for synthesising the Revont.

**Nonadecanedioic acid**

Dimethyl 1,19–nonadecanedioate synthesised from olive oil (see Appendix A.1) was used for this reaction (5 g, 14 mmol). In a 250 mL round bottom flask, water (100 mL) was added. Sodium hydroxide (2 g) was slowly added to the heterogeneous mixture. The flask was heated to 100°C until the solution turned homogeneous, and was left for one hour more at 100°C. HCl (8 mL, 37% aqueous solution) was added drop-wise to the mixture. The resulting white powder was filtered using a Büchner funnel and washed with slightly acidic water (2×10 mL) and distilled water (2×10 mL), and dried overnight in an oven (80°C). The desired product was obtained as a white powder. Isolated yield (4.100 g, 89%). \(^1\)H NMR (400 MHz; THF): \(\delta = 10.54\) (broad s, 2H, \(-\text{CO}_2\text{H}\)), 2.19 (t, J = 7.4 Hz, 4H, \(-\text{CH}_2\text{CO}_2\text{H}\)), 1.56 (quintet, J = 7.3 Hz, 4H, \(\text{CH}_2\text{CH}_2\text{CO}_2\text{H}\)), 1.29 (s, 26H, alkyl chain). \(^{13}\)C NMR (100 MHz; THF): \(\delta = 174.42\) (s, \(\text{CO}\)), 34.24 (s, \(\text{HO}_2\text{C}^-\text{CH}_2\text{H}^-\)), 30.61-30.12 (s, alkyl chain). These data are consistent with those from the literature.\(^{65}\)
Revent 12 oligomers

Via dodecanoyl dichloride

Paraphenylenediamine (500 mg, 4.64 mmol) was dissolved in hot water (20 mL). This solution was slowly added to a solution of dodecanedioyl dichloride in dichloromethane. Some precipitate forms at the interface water/dichloromethane. The precipitate is extracted from the biphasic system by filtration. Once dry, the solid collapses into a powder. No analyses were done and this method was rapidly abandoned.

Via dodecanedioic acid

Dodecanedioic acid (500 mg, 2.17 mmol) and paraphenylenediamine (234 mg, 2.17 mmol) are crushed together and added to a 50 mL round bottom flask trapped in an aluminium foil. The flask is purged three times with nitrogen and introduced in an oil bath pre-heated at 170°C. The flask is heated for one hour under nitrogen in the absence of light, and left to cool down. Once cool, the hard material (slightly brownish to purple) is analysed with FT–IR, Thermogravimetric analysis and Maldi–Tof. IR:3300 cm\(^{-1}\) (\(\nu\)C=O), 1560 cm\(^{-1}\) (N–H), 2920 cm\(^{-1}\) 2850 cm\(^{-1}\) 1400 cm\(^{-1}\) 720 cm\(^{-1}\) (\(\nu\)C–H\(_2\)), 3030 cm\(^{-1}\) (\(\nu\)CH), 1610 cm\(^{-1}\)1520 cm\(^{-1}\) 1470 cm\(^{-1}\) (\(\nu\)C=C), 840 cm\(^{-1}\) (para-disubstitued benzene). Thermogravimetric analysis results: melting point unknown; stable under air until 300°C; decomposes at T>350°C.

Revent 19 oligomers

Via nonadecanedioic acid

Nonadecanedioic acid (712 mg, 2.17 mmol) and paraphenylenediamine (234 mg, 2.17 mmol) are crushed together and added to a 50 mL round bottom flask trapped in an aluminium foil. The flask is purged three times with nitrogen and introduced in an oil bath pre-heated at 170°C. The flask is heated for one hour under nitrogen in the absence of light, and left to cool down. Once cool, the hard material (slightly brownish to purple) is analysed with FT–IR, Thermogravimetric analysis and Maldi–Tof IR:3300 cm\(^{-1}\) 1660 cm\(^{-1}\) (\(\nu\)C=O), 1560 cm\(^{-1}\) (N–H), 2920 cm\(^{-1}\) 2850 cm\(^{-1}\) 1400 cm\(^{-1}\) 720 cm\(^{-1}\) (\(\nu\)C–H\(_2\)), 3030 cm\(^{-1}\) (\(\nu\)CH), 1610 cm\(^{-1}\)1520 cm\(^{-1}\) 1470 cm\(^{-1}\) (\(\nu\)C=C), 840 cm\(^{-1}\) (para-disubstitued benzene). Thermogravimetric analysis results: melting point unknown; stable under air until 300°C; decomposes at T>340°C.
A.4 Chapter 5

A.4.1 The Suzuki-Miyaura reaction in aqueous media

All reactions were performed under an inert atmosphere of argon or nitrogen using standard Schlenk line and glovebox techniques. Solvents were dispensed from a solvent purification system. All other reagents were used without further purification. $^1$H and $^{13}$C nuclear magnetic resonance (NMR) spectra were recorded at 298 K on a Bruker 400 MHz spectrometer for $^1$H NMR, 100 MHz for $^{13}$C NMR and 121 MHz for $^{31}$P NMR. Elemental analyses were performed by the University of St Andrews Analytical Service.

$[\text{PdCl}_2(\text{IPr})(\text{SPhos})]$ 

In a glovebox, a Schlenk flask was charged with $[\text{Pd}(-\text{Cl})(\text{Cl})(\text{IPr})]_2$ (283 mg, 0.25 mmol) and SPhos (205.3 mg, 0.5 mmol). THF (3mL) was added and the solution was stirred for 3 hours. Addition of pentane (15 mL) led to a precipitate. The solid was collected by filtration and washed with hexane (10 mL), leading to the analytically pure $[\text{PdCl}_2(\text{IPr})(\text{SPhos})]$ as a pale yellow solid (477 mg, 98%). Elemental analysis: found C 64.84, H 7.67, N 3.18%; C$_{52}$H$_{71}$Cl$_2$N$_2$PPd requires C 65.19, H 7.33, N 2.87%.

$^1$H NMR (CD$_2$Cl$_2$, 400 MHz, 278K) $\delta$ (ppm) = 0.69–0.92 (m, 6H, Cy), 0.93–1.05 (m, 4H, Cy), 1.06 (d, $^3$J$_{H-H}$ = 6.9 Hz, 12H, CH–C$_3$H$_3$), 1.28–1.42 (br s, 6H, Cy), 1.35 (d, $^3$J$_{H-H}$ = 6.6 Hz, 12H, CH–C$_3$H$_3$), 1.43–1.54 (br s, 4H, Cy), 1.71 (m, 2H, Cy), 3.19 (sept, $^3$J$_{H-H}$ = 6.7 Hz, 4H, CH–C$_3$H$_3$), 3.52 (s, 6H, O–C$_3$H$_3$), 6.50 (d, $^3$J$_{H-H}$ = 8.4 Hz, 2H, Ar CH), 6.77–6.82 (m, 1H, Ar CH), 7.04 (m, 1H, Ar CH), 7.14 (d, 2H, $^5$J$_{H-P}$ = 1.2 Hz, H$^4$, H$^5$), 7.19–7.30 (m, 2H, Ar CH), 7.34 (d, $^3$J$_{H-H}$ = 7.7 Hz, 4H, Ar CH), 7.41–7.46 (m, 1H, Ar CH), 7.48 (t, $^3$J$_{H-H}$ = 7.7 Hz, 2H, Ar CH). $^{13}$C NMR (75 MHz; CDCl$_3$): $\delta$ (ppm) = 22.9 (s, CH–C$_3$H$_3$), 26.1 (s, Cy C$_2$H$_2$), 26.7 (s, CH–C$_3$H$_3$), 27.1 (d, $^2$J$_{C-P}$ = 11.7 Hz, C$_2$H$_2$), 27.3 (d, $^2$J$_{C-P}$ = 12.1 Hz, C$_2$H$_2$), 28.2 (s, Cy C$_2$H$_2$), 28.7 (s, CH–C$_3$H$_3$), 30.3 (s, Cy C$_2$H$_2$), 31.9 (d, $^1$J$_{C-P}$ = 21.1 Hz, Cy CH), 55.0 (s, O–C$_3$H$_3$), 103.1 (s, Ar CH), 119.4 (s, C$^{IV}$), 123.4 (s, Ar CH), 124.1 (d, $^4$J$_{C-P}$ = 5.4 Hz, C$^0$, C$^4$), 124.3 (d, J$_{C-P}$ = 14.2 Hz, Ar CH), 127.6 (d, $^1$J$_{C-P}$ = 33.2 Hz, C$^{IV}$), 128.5 (s, Ar CH), 128.9 (s, Ar CH), 129.7 (s, Ar CH), 131.8 (d, J$_{C-P}$ = 5.7 Hz, Ar CH), 135.8 (s, Ar C), 138.5 (d, J$_{C-P}$ = 2.5 Hz, C$^{IV}$), 140.0 (d, J$_{C-P}$ = 21.2 Hz, Ar CH), 147.4 (s, C$^{IV}$), 158.0 (s, C$^{IV}$), 175.0 (d, $^2$J$_{C-P}$ = 187.4 Hz, C$^2$). $^{31}$P NMR (CD$_2$Cl$_2$) $\delta$ (ppm) = 43.3.
In a glovebox, a 25mL flask was charged with [Pd(η^3-allyl)(Cl)(IPr)] (150 mg, 0.262 mmol), SPhos (107.6 mg, 0.262mmol), KO^tB (64.7 mg, 0.577 mmol). Solvents (toluene 3mL and isopropanol 3mL) were added. The reaction mixture was stirred during 5 days at room temperature. The solvent was evaporated under vacuum and the resulting solid was stirred in isopropanol (2mL), filtered and washed with isopropanol (3 × 2mL). The resulting yellow solid was dried under vacuum to afford [Pd(IPr)(SPhos)] as a yellow solid (88.5 mg, 37%).

1H NMR (C_6D_6, 400MHz, 298K) δ (ppm) = 0.94–1.64 (m, 22H, Cy), 1.23 (d, J_{H−H} = 6.8 Hz, 12H, CH–C_H_3), 1.72 (d, J_{H−H} = 6.8 Hz, 12H, CH–C_H_3), 3.11 (sept, J_{H−H} = 6.9 Hz, 4H, CH–C_H_3), 3.14 (s, 6H, O–C_H_3), 6.28 (d, J_{H−H} = 8.5 Hz, 2H, Ar-H), 6.53 (s, 2H, H_4, H_5), 7.04–7.09 (m, 2H, Ar C_H), 7.20–7.34 (m, 8H, Ar C_H), 9.00 (m, 1H, Ar C_H).

13C NMR (C_6D_6, 100 MHz, 298K) δ (ppm) = 24.0 (s, CH–C_H_3), 25.3 (s, CH–C_H_3), 26.7 (Cy CH_2), 27.4 (d, J_{C−P} = 5.7 Hz, Cy CH_2), 27.6 (d, J_{C−P} = 3.8 Hz, Cy CH_2), 29.0 (s, CH–C_H_3), 31.8 (d, J_{C−P} = 12.2 Hz, Cy CH_2), 32.7 (d, J_{C−P} = 13.1 Hz, Cy emphCH_2), 36.1 (d, J_{C−P} = 15 Hz, Cy CH), 55.1 (s, O–C_H_3), 103.6 (s, Ar CH), 120.7 (s, Ar CH), 121.7 (s, C^IV), 123.3 (s, CH), 125.1 (d, J_{C−P} = 17.2 Hz, C^4, C^5), 128.7 (s, Ar CH), 129.0 (s, Ar CH), 132.3 (s, Ar CH), 137.7 (d, J_{C−P} = 2.9 Hz, C^{IV}), 138.0 (d, J_{C−P} = 15.0 Hz, C^{IV}), 158.6 (s, C^{IV}), 199.5 (d, J_{C−P} = 84.5 Hz, C^2).

31P NMR (C_6D_6, 121MHz, 298K) δ (ppm) = 66.9.

General procedure for the monitoring experiments

In a glove-box, a Radley tube was charged with phenylboronic acid (640.8 mg, 5.25 mmol), sodium hydroxide (300 mg, 7.5 mmol), catalyst [Pd(IPr)(SPhos)] (4.5 mg, 0.005 mmol) or: [PdCl_2(IPr)(SPhos)] (4.9 mg, 0.005 mmol)) and isopropanol (5 mL). Out of the glove-box, degassed 4–chlorotoluene (591.5 µL, 5 mmol) was added to the Radley Tube and heated at 80°C. A sample is taken from the mixture, is diluted in ethyl acetate (1 mL) and then filtrated on pack of celite. The yield is monitored by GC. Compensatory is made every 5 minutes for 1 hour, every 10 minutes for 30 minutes, every 30 minutes for 2 hours.

A.4.2 Copper–NHC complexes as carbene transfer reagents

All reactions were performed under an inert atmosphere of argon or nitrogen using standard Schlenk line techniques and glovebox techniques. Solvents were dispensed from a solvent purification system. All other reagents were used without any further
purification. $^1$H and $^{13}$C nuclear magnetic resonance (NMR) spectra were recorded at 298 K on a Bruker 300 MHz spectrometer for $^1$H NMR and 75 MHz for $^{13}$C NMR, using the residual solvent peak to reference the spectra to tetramethylsilane at $\delta$ 0 ppm. Elemental analyses were performed by the University of St Andrews Analytical Service. All complexes of type [CuCl(NHC)] were prepared by reaction of Cu$_2$O with the chloride imidazolium salt as described in the literature.  

$^{[\text{AuCl(IMes)}]}$

A mixture of [AuCl(SMe$_2$)] (137.2 mg, 0.47 mmol) and [CuCl(IMes)] (187.9 mg, 0.47 mmol) in dichloromethane (5 mL) was stirred at 40°C for 1 h. The mixture was filtered through celite and the solvent was removed in vacuo. Dichloromethane (3 mL) and petroleum ether (10 mL) were added, resulting in the precipitation of an off-white solid. The product was collected by filtration, washed with petroleum ether (3 x 5 mL) and obtained as a colourless solid in 71% yield (178 mg, 0.33 mmol). Elemental analysis: found C 47.09, H 4.33, N 5.03%; C$_{21}$H$_{24}$ClN$_2$Au requires C 46.98, H 4.51, N 5.22%. $^1$H NMR (300 MHz; CDCl$_3$): $\delta$ = 7.10 (s, 2H, $H_4$ and $H_5$), 7.00 (s, 4H, CH$_{\text{mesityl}}$), 2.36 (s, 6H, CH$_3$), 2.11 (s, 12H, CH$_3$). $^{13}$C NMR (75 MHz; CDCl$_3$): $\delta$ = 173.6 (s, C$^2$carbene), 140.05 (s, CH mesityl), 135.0 (s, CH mesityl), 134.9 (s, CH mesityl), 129.8 (s, CH mesityl), 122.4 (s, C$^4$H and C$^5$H), 21.4 (s, CH$_3$), 18.0 (s, CH$_3$). These data are consistent with those in the literature.

$^{[\text{AuCl(SIMes)}]}$

A mixture of [AuCl(SMe$_2$)] (136.7 mg, 0.46 mmol) and [CuCl(SIMes)] (188.1 mg, 0.46 mmol) in dichloromethane (5 mL) was stirred at 40°C for 1 h. The mixture was filtered through celite and the solvent was removed in vacuo. Dichloromethane (3 mL) and petroleum ether (10 mL) were added, resulting in the precipitation of an off-white solid. The product was collected by filtration, washed with petroleum ether (3 x 5 mL) and obtained as a colourless solid in 90% yield (225 mg, 0.42 mmol). Elemental analysis: found C 46.32, H 4.77, N 4.89%; C$_{21}$H$_{26}$ClN$_2$Au requires C 46.81, H 4.86, N 5.20%. $^1$H NMR (300 MHz; CDCl$_3$): $\delta$ = 6.95 (s, 4H, CH$_{\text{mesityl}}$), 3.99 (s, 4H, $H_4$ and $H_5$), 2.32 (s, 12H, CH$_3$), 2.30 (s, 6H, CH$_3$). $^{13}$C NMR (75 MHz; CDCl$_3$): $\delta$ = 195.4 (s, C$^2$carbene), 139.2 (s, CH mesityl), 135.8 (s, CH mesityl), 134.85 (s, CH mesityl), 130.1 (s, CH mesityl), 51.0 (s, C$^4$H and C$^5$H), 21.35 (s, CH$_3$), 18.3 (s, CH$_3$). These data are consistent with those in the literature.
A mixture of $[\text{AuCl(SMe}_2\text{)}]$ (118.6 mg, 0.40 mmol) and $[\text{CuCl(IPr)}]$ (196.3 mg, 0.40 mmol) in dichloromethane (5 mL) was stirred at 40°C for 2 h. The mixture was filtered through celite and the solvent was removed in vacuo. Dichloromethane (3 mL) and petroleum ether (10 mL) were added, resulting in the precipitation of an off-white solid. The product was collected by filtration, washed with petroleum ether (3 x 5 mL) and obtained as a colourless solid in 84% yield (209 mg, 0.34 mmol). Elemental analysis: found C 51.76, H 5.83, N 4.23%; $\text{C}_{27}\text{H}_{36}\text{ClN}_2\text{Au}$ requires C 52.22, H 5.84, N 4.51%.

$^1$H NMR (300 MHz; CDCl$_3$): $\delta$ = 7.57 (t, 2H, CH phenyl), 7.34 (d, 4H, CH phenyl), 7.23 (s, 2H, H$_4$ and H$_5$), 2.57 (pseudo-septuplet, 4H, CH isopropyl), 1.33 (d, 12H, CH$_3$ isopropyl), 1.23 (d, 12H, CH$_3$). $^{13}$C NMR (75 MHz; CDCl$_3$): $\delta$ = 146.6 (s, CH phenyl), 131.55 (s, CH phenyl), 125.1 (s, CH phenyl), 124.2 (s, $^4$CH and $^5$H), 29.7 (s, CH isopropyl), 25.0 (s, CH$_3$ isopropyl), 24.60 (s, CH$_3$ isopropyl). These data are consistent with those in the literature.

$[\text{Pd(µ–Cl)Cl(IMes)}]_2$

A mixture of $[\text{PdCl}_2(\text{NCPh})_2]$ (199 mg, 0.52 mmol) and $[\text{CuCl(IMes)}]$ (209.4 mg, 0.52 mmol) in dichloromethane (5 mL) was stirred at 40°C for 1 h. The mixture was filtered through celite and the solvent was removed in vacuo. Dichloromethane (3 mL) and petroleum ether (10 mL) were added, resulting in the precipitation of a yellow solid. The product was collected by filtration, washed with petroleum ether (3 x 5 mL) and obtained as a yellow solid in 79% yield (196 mg, 0.20 mmol). Elemental analysis: found C 52.67, H 5.12, N 5.71%; $\text{C}_{42}\text{H}_{48}\text{Cl}_4\text{N}_4\text{Pd}_2$ requires C 52.36, H 5.02, N 5.81%. $^1$H NMR (300 MHz; CDCl$_3$): $\delta$ = 7.33 (s, broad, 8H, CH mesityl), 6.95 (s, 4H, H$_4$ and H$_5$), 2.45 (s, 12H, CH$_3$), 2.24 (s, 12H, CH$_3$), 2.09 (s, 12H, CH$_3$). $^{13}$C NMR (75 MHz; CDCl$_3$): $\delta$ = 139.5 (s, CH mesityl), 135.9 (s, CH mesityl), 134.7 (s, CH mesityl), 129.7 (s, CH mesityl), 124.8 (s, $^4$H and $^5$H), 21.6 (s, CH$_3$), 19.3 (s, CH$_3$), 19.0 (s, CH$_3$). These data are consistent with those in the literature.

$[\text{Pd(µ–Cl)Cl(SIMes)}]_2$

A mixture of $[\text{PdCl}_2(\text{NCPh})_2]$ (198.2 mg, 0.52 mmol) and $[\text{CuCl(SIMes)}]$ (209.5 mg, 0.52 mmol) in dichloromethane (5 mL) was stirred at 40°C for 1 h. The mixture was filtered through celite and the solvent was removed in vacuo. Dichloromethane (3 mL) and petroleum ether (10 mL) were added, resulting in the precipitation of a yellow solid. The product was collected by filtration, washed with petroleum ether (3 x 5 mL) and
obtained as a yellow solid in 82% yield (205 mg, 0.21 mmol). Elemental analysis: found C 52.12, H 5.49, N 5.56%; C_{42}H_{52}Cl_{4}N_{4}Pd_{2} requires C 52.14, H 5.42, N 5.79%. \textsuperscript{1}H NMR (300 MHz; CDCl\textsubscript{3}): \(\delta = 7.00\) (broad s, 8H, CH mesityl), 3.86 (broad s, 8H, \(H^4\) and \(H^5\)), 2.45 (s, 12H, CH\textsubscript{3}), 2.41 (s, 12H, CH\textsubscript{3}), 2.26 (s, 12H, CH\textsubscript{3}). \textsuperscript{13}C NMR (75 MHz; CDCl\textsubscript{3}): \(\delta = 138.7\) (s, CH mesityl), 134.6 (s, CH mesityl), 129.9 (s, CH mesityl), 51.5 (s, \(C^4\)H and \(C^5\)H), 19.4 (s, CH\textsubscript{3}). These data are consistent with those in the literature.

\textbf{[Pd(\(\mu\)-Cl)Cl(IPr)]\textsubscript{2}}

A mixture of [PdCl\textsubscript{2}(NCPh)\textsubscript{2}] (169.4 mg, 0.44 mmol) and [CuCl(IPr)] (215.4 mg, 0.44 mmol) in dichloromethane (5 mL) was stirred at 40\(^\circ\)C for 2 h. The mixture was filtered through celite and the solvent was removed in vacuo. Dichloromethane (3 mL) and petroleum ether (10 mL) were added, resulting in the precipitation of a yellow solid. The product was collected by filtration, washed with petroleum ether (3 x 5 mL) and obtained as an ochre yellow solid in 82% yield (206 mg, 0.18 mmol). Elemental analysis: found C 57.09, H 6.41, N 4.66%; C\textsubscript{54}H\textsubscript{72}Cl\textsubscript{4}N\textsubscript{4}Pd\textsubscript{2} requires C 57.30, H 6.41, N 4.95%. \textsuperscript{1}H NMR (300 MHz; CDCl\textsubscript{3}): \(\delta = 7.55\) (t, 4H, CH phenyl), 7.30 (d, 8H, CH phenyl), 6.99 (s, 4H, \(H^4\) and \(H^5\)), 2.87 (broad s, 2H, CH isopropyl), 2.61 (broad s, 2H, CH isopropyl), 1.31 (broad d, 24H, CH\textsubscript{3} isopropyl), 0.99 (broad d, 24H, CH\textsubscript{3} isopropyl). \textsuperscript{13}C NMR (75 MHz; CDCl\textsubscript{3}): \(\delta = 148.14\) (s, CH phenyl), 146.53 (s, CH phenyl), 134.54 (s, CH phenyl), 130.6 (s, CH phenyl), 125.5 (s, CH phenyl), 124.5 (s, \(C^4\)H and \(C^5\)H), 28.9 (s, CH isopropyl), 26.5 (s, CH\textsubscript{3} isopropyl), 23.5 (s, CH\textsubscript{3} isopropyl). These data are consistent with those in the literature.
Bibliography


