The Design and Synthesis of Complexes for the Activation of Carbon Dioxide

A Thesis Presented by

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In Partial Fulfilment of The Requirements For The Award of The Degree of

Doctor of Philosophy

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Declaration

I, Rafael Bou Moreno confirm that the work presented in this thesis is my own. Where information has been derived from other sources, I confirm that this has been indicated in the thesis.

ACKNOWLEDGMENTS

I would like to thank the person who made possible the production of this work and this thesis, which has been my mentor, source of inspiration, enthusiasm, extremely supportive and intelligent, as well as a friend; who not only thought me how to look at chemistry in a different way, but also valuables lessons in life: Professor James C. Anderson.

I would also like to thank all the past and present members of the Anderson group who have been a source of inspiration, learning and very good friends: Warren, Helen C., Helen G., Liz, Greg, Michelle, Matt, Lisa, Adam, György, Rob, Jon, Paul and Andreas. Specially those who shared the “London Adventure”.

Throughout my studies we have got financial support from BPF, The University of Nottingham and University College London, to whom we are very grateful. In the same way I would like to thank the technical staff at both universities for their constant help.

Finally I would like to thank my parents and my sister who have been so far away, yet so supportive and always believed in me. I couldn’t have done it without their constant moral support.

ABBREVIATIONS

Å	Angstrom
app	Apparent
Ar	Aromatic
Bn	Benzyl
br	Broad
°C	Degree centigrade
calcd.	Calculated
Cy	Cyclohexyl
d	Doublet
DME	1,2-Dimethoxyethane
DMAP	4-*N*,*N*-Dimethylaminopyridine
Et_2O	Diethyl ether
EI	Electron impact
ES	Electrospray
Et_3N	Triethylamine
E^+	Electrophile
g	Gram
h	Hours
Hz	Hertz
HOMO	Highest occupied molecular orbital
IR	Infra-red
J	Coupling constant
Lut	2,6-Lutidine
LUMO	Lowest unoccupied molecular orbital
Lit.	Literature
m	Multiplet
m	Meta
m/z	Mass to charge ratio
M	Molar
mg	Milligram

mL	Millilitre
min	Minutes
m.p.	Melting point
NMR	Nuclear magnetic resonance
Nu	Nucleophile
n-BuLi	Normal butyllithium
o	Ortho
p	Para
Ph	Phenyl
ppm	Parts per million
ppmv	Part per million in volume
^{i}Pr	Isopropyl
Py	Pyridine
Pyr	Pyrrole
q	Quartet
r.t.	Room temperature
Rf	Retardation factor
s	Singlet
sept	Septet
^{t}	Tertiary
t	Triplet
tlc	Thin layer chromatography
THF	Tetrahydrofuran
TMSCl	Chlorotrimethylsilane
δ	Chemical shift

All yields reported in Chapter 1 correspond to those in the literature and they are linked to the corresponding references. Yields reported in Chapters 2, 3, 4 and 5 correspond to experiments performed in the work on this thesis, except those described in scheme 2.4 and 2.5.

ABSTRACT

This thesis describes developments in the studies of the activation and use of carbon dioxide as a building block in synthesis by early transition metal complexes. The proposed route required the reaction of carbon dioxide with a metal-imido complex *via* a heterocumulene metathesis to produce an isocyanate. An attempt at the use of molybdenum-imido complexes for the process generated a novel low valent molybdenum bisimido complex with no success in the activation of carbon dioxide.

Generation of simple 12-electron titanium-imido complexes showed successful heterocumulene metathesis with isocyanates to develop a novel methodology for the synthesis of carbodiimides and ureas. The studies of this methodology proved a four-membered ring metallocycle was an intermediate and suggested the mechanism of the process as plausible, as well as showing the activation of carbon dioxide.

Our studies were concluded by the generation and modification of titanium-imido complexes to synthesise families of complexes containing aromatic imido ligands, which showed no reactivity with carbon dioxide with the exception of the 2,6-diisopropylphenylimido ligand. Unsuccessful isolation of alkylimido titanium complexes impeded the generation of families of complexes. *In situ* generation of alkylimido titanium complexes showed activation of carbon dioxide to generate ureas, proposing two consecutive heterocumulene metatheses first with carbon dioxide and a second with the generated isocyanate. Studies with intermediates and comparisons with the generation of carbodiimides support this mechanism.

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CHAPTER 1:

INTRODUCTION

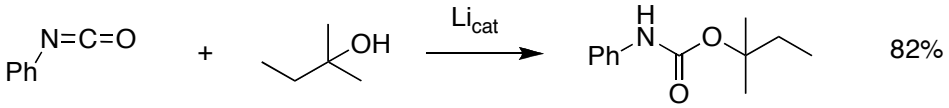
CHAPTER 1: INTRODUCTION

1.1 Isocyanates and Their Chemistry

1.1.1 Polyurethanes

Humans throughout history have used a variety of different materials for tools and weapons. The use of tools started in the Stone Age, going to the Bronze Age and finally to the Iron Age. From the first stones used for hunting and fishing, more than 2 million years ago, to the most sophisticated war machine in World War II, and everything in between. However, since the 1950's a complete range of new synthetic materials called polymers have been developed. Most of the old materials that we could find in the market were replaced by cheaper, lighter and stronger pieces of these innovative products. We can consider that we have changed from the Iron Age to the Polymer Age.

Nowadays a large number of polymers exist which have been introduced into the daily life of humans, becoming necessities. Polyurethanes are a very important category among all the types of polymers. The basic unit of the polyurethanes is the urethane or carbamate (**3**) and it is formed by the reaction of an alcohol and an isocyanate in the presence of a catalyst (Scheme 1.1).[1] Applying the same reactivity to diisocyanates and diols or polyols, polyurethanes are obtained.



1 **2** **3**

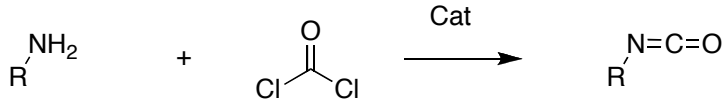
Scheme 1.1: Formation of carbamates.

Although the study was developed by Bayer and co-workers in 1937, it wasn't until 1952 that polyurethanes became commercially available.[2] According to the American Chemistry Council,™ in 2007 approximately 115.8 million tonnes of polyurethanes

were produced in America, converting isocyanates to a very valuable and commercially attractive material.

1.1.2 Industrial Production of Isocyanates

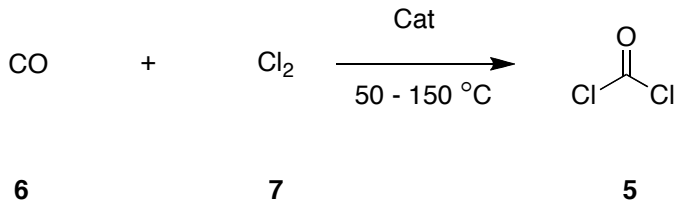
In the year 2000 the global consumption of diisocynanates was 4.4 million tonnes, which was broken down as methylene diphenyl diisocyanate 61.3%, toluene diisocyanate 34.1%, hexamethylene diisocyanate 3.4% and 1.2% for the rest of the isocyanates.[3] The vast majority of the isocyanate production was to feed the polyurethanes market. Isocyanates are industrially produced worldwide on large scale by a standard method consisting of the reaction of an amine (**4**) and phosgene (**5**) in the presence of a base (Scheme 1.2).[4] The use of toxic materials such as phosgene increase the toxicity and the danger of the process. But the presence of these two compounds are not the only dangerous side of the process.



4 **5** **1**

Scheme 1.2: Generation of isocyanates.

Due to the fact that phosgene is toxic and a gas, among other characteristics, it has to be produced in the same plant that it is used. Its production proceeds by the reaction of carbon monoxide and chlorine gas when they are passed through a bed of activated carbon as catalyst (Scheme 1.3).[5] It is an exothermic process (ΔH_{rxn} = -107.6 kJ/mol) that needs the reaction temperature moderating to 50 - 150 °C to avoid decomposition into starting material. The presence of toxic gases such as carbon monoxide and chlorine, in addition to phosgene, increases the danger and risk in the process of manufacturing isocyanates.



Scheme 1.3: Generation of phosgene.

1.1.3 Synthesis of Isocyanates

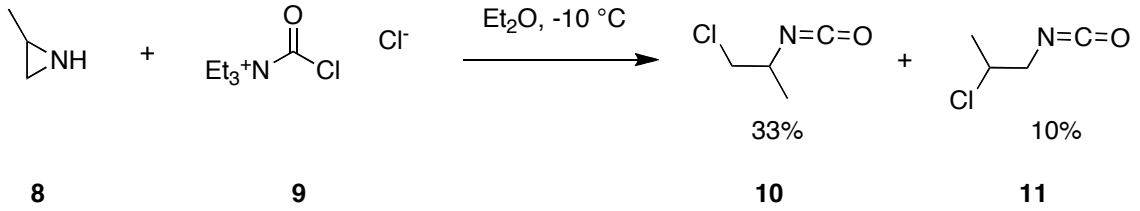
Academic chemical research also requires the generation of isocyanates. Although they are not commonly found in final products, they are versatile intermediates that can be converted into different functionalities present in published natural products, non-natural products such as drug candidates and other organic compounds for research.

For the academic synthesis of isocyanates there exists two basic strategies: amide derivative rearrangements and amines reacting with carbonyl carriers.

1.1.3.1 Carbonyl Carriers

I. Phosgene and Derivatives.

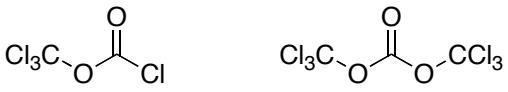
The easiest and most common reaction for the synthesis of isocyanates is the reaction between phosgene and the desired primary amine in the presence of a base, as was seen for the industrial generation (Scheme 1.2).[6] The overall reaction leads to carbonylation on the amine and two equivalents of the hydrochloric salt of the base as a by-product. Generally, only primary isocyanates can be obtained. In 1966, Johnson *et al*. showed that some cyclic secondary amines (such as aziridines) could be transformed with poor regioselectivity into the corresponding primary isocyanate by the same method (Scheme 1.4).[7] Despite the unusual reactivity due to the strained ring system, secondary amines generally react with phosgene to generate carbamoyl chloride or ureas.



8 **9** **10** **11**

Scheme 1.4: Isocyanates from secondary amines.

Although phosgene is still the most commonly used reagent for the industrial and academic synthesis of isocyanates, some other reagents have been developed with similar reactivity but less toxicity and are easier to handle. This family of alternative reagents contains trichloromethyl chloroformate (diphosgene)[8] (**12**) and bis-(trichloromethyl)carbonate (triphosgene) (**13**) (Figure 1.1).[9] The advantages of theses two phosgene alternatives is that at ambient temperature they are liquid and solid respectively and only generate phosgene *in situ* once activated.

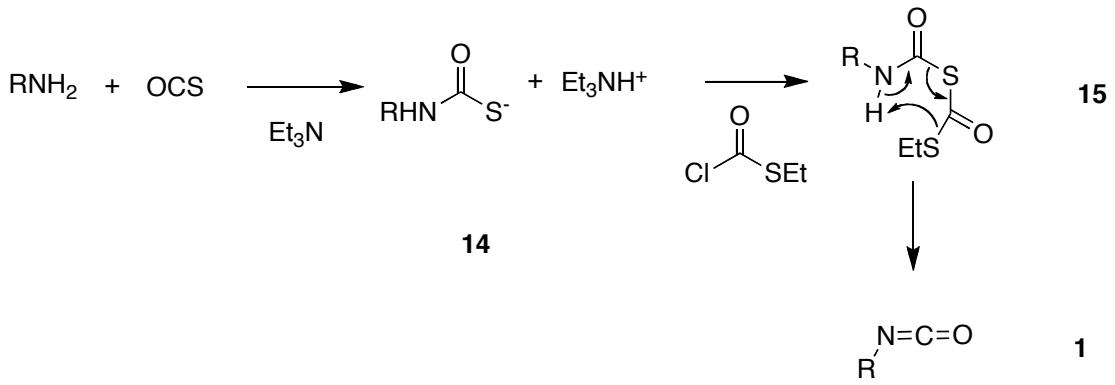


12 **13**

Figure 1.1: Phosgene derivatives.

II. Elimination of Amide Derivatives.

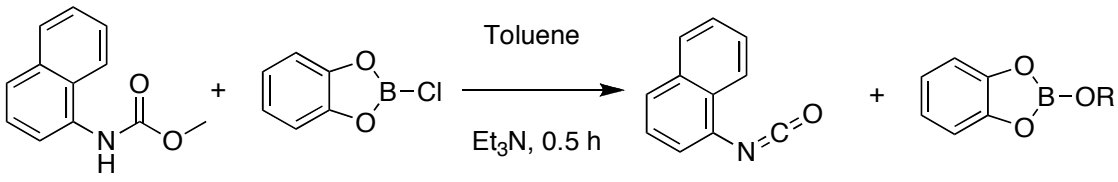
In the use of phosgene for the synthesis of isocyanates, the reaction proceeds *via* an elimination from a carbamoyl chloride intermediate. However, other derivatives such as carbamate anhydrides (**15**) have also been used.[10] The formation of the carbamate anhydride requires the use of carbonyl sulfide and monothiocarbamate to avoid side reactions between by-products and isocyanates. Thermal decomposition yields isocyanate in moderate yield after distillation (Scheme 1.5).



14 15 1

Scheme 1.5: Isocyanates by amide derivatives elimination.

In more recent years, another method was developed for the removal of alcohols from carbamates to yield isocyanates.[11] By using chlorocatecholborane (**17**) the formation of the isocyanate was promoted and the alcohol was trapped as the alkoxide catecholborate (**19**) (Scheme 1.6). It represented a methodology which allowed the reverse process to the formation of carbamate from isocyanates and alcohols. In a similar fashion, Knölker and co-workers developed the synthesis of isocyanates by the reaction between amines and $(Boc)_2O$ using catalytic DMAP.[12]



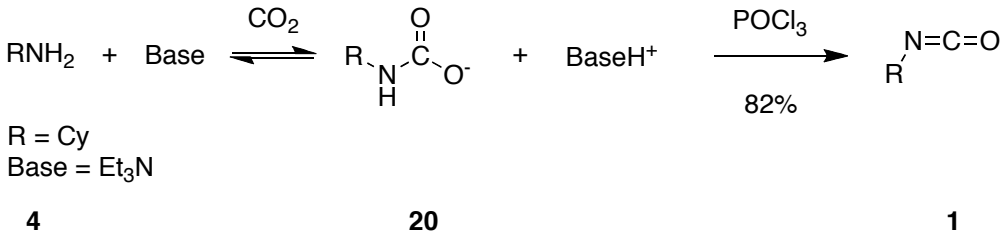
16 17 18 19

Scheme 1.6: Dealcoholysis of carbamates.

III. Carbamic Acid Dehydration.

Under an atmosphere of carbon dioxide, amines are known to be in equilibrium with carbamate salts. McGhee and co-workers used this knowledge together with a dehydration reaction to generate isocyanates from amines and carbon dioxide.[13] The requirement of at least one equivalent of dehydrating agent and the production of large amounts of waste prevents it from being an effective and alternative process for the

industrial synthesis of isocyanates. The choice of the correct conditions and $POCl_3$ as dehydrating agent played a key role in the process (Scheme 1.7).

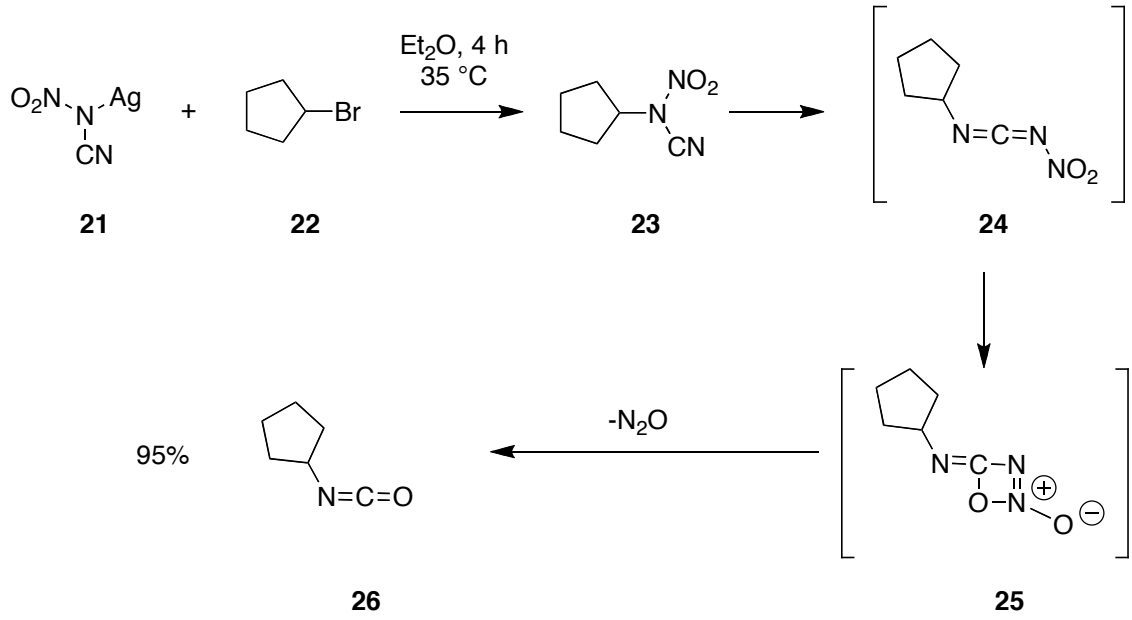


Scheme 1.7: Dehydration of carbamic acid.

In addition to the successful synthesis of isocyanates (Scheme 1.7), the use of P_4O_{10} as dehydrating agent achieved a 49 : 1 ratio of symmetrical urea to isocyanate with complete conversion of the amine starting material.

IV. Rearrangements of Nitrocyanamides.

Alkylation of silver nitrocyanamides was developed in 1988 as a novel synthesis for the generation of isocyanantes. It has not been further developed or used as a standard method presumably due to the poor availability of the organo-silver starting material.[14] Alkylation of silver nitrocyanamides (**21**) with an alkyl halide (**22**) produced a nitrocarbodiimide (**23**) which was rapidly thermolysed quantitatively to isocyanate (**26**) and N_2O (Scheme 1.8).

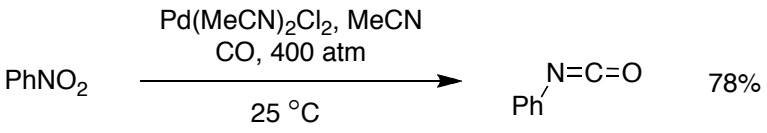


21 **22** **23** **24** **26** **25**

Scheme 1.8: Nitrocyanamide rearrangement to synthesise isocyanates.

V. Transition Metals and Carbon Monoxide.

Despite being a toxic gas, many groups have attempted and achieved the use of carbon monoxide as a source of carbonyl for the generation of isocyanates. In 1973 the development of the one-pot procedure for the transformation of nitro aryls into aryl isocyanates using palladium catalysis was published.[15] This two-step process was composed by first transforming the nitro group into an azide, followed by reaction with carbon monoxide to generate isocyanate (Scheme 1.9). It was believed that a nitrene species was involved in the mechanism, with the formation of minor by-products. Parallel experiments with azides supported this hypothesis.

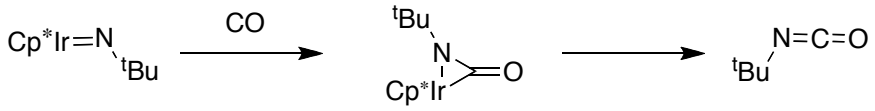


27 **1**

Scheme 1.9: Generation of isocyanates from nitro groups.

More in depth studies were developed when in 1989 Bergman *et al*. reacted an iridium-imido complex with carbon monoxide forming a three-membered ring which slowly

decomposed to the corresponding isocyanate and iridium complex by-product (Scheme 1.10).[16] More recent studies by different groups, have shown that nickel imido complexes can react with carbon monoxide *via* a three membered ring metallocycle to generate isocyanates.[17] Although the reaction was stoichiometric, a faster process was developed using nickel compared to iridium, and no isolation of the metallocycle intermediate was necessary. Cobalt complexes have also shown the same reactivity with no detection of the intermediate, using harsh temperatures and high pressures of carbon monoxide.[18] The most recent of the developments has been by using iron as the transition metal, with the same advantages and disadvantages mentioned above.[19] The lack of a catalytic process and the fact that it was a very slow process means that the reaction is of little use for industry or academia.



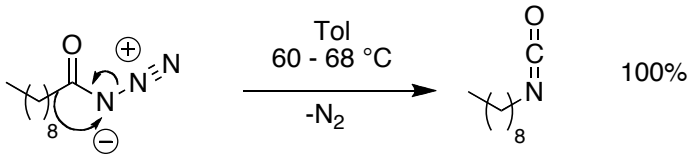
28 **29** **1**

Scheme 1.10: Stoichiometric [2+1] cycloadditions to get isocyanates.

1.1.3.2 Rearrangements of Amide Derivatives

I. Curtius Rearrangement.

The Curtius Rearrangement is the thermal decomposition of acyl azides **30** to yield isocyanates **31** (Scheme 1.11). It is suggested that the azides react *via* a concerted process as no nitrene intermediate has been isolated.[20] Subsequent reaction with water yields the amine, with one carbon less than the original acyl azide, and proceeds *via* decarboxylation of the carbamic acid.

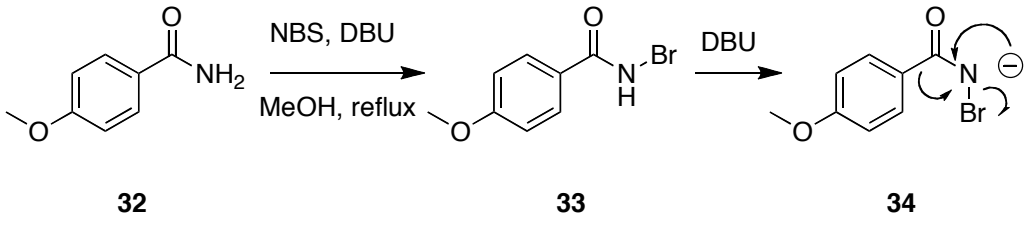


30 **31**

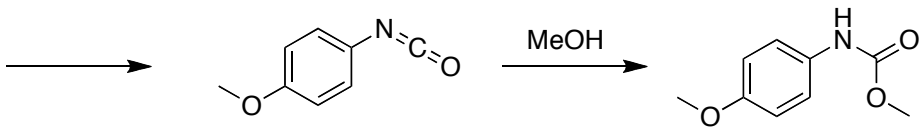
Scheme 1.11: Curtius rearrangement.

II. Hofmann Rearrangement.

Another original rearrangement of amide derivatives was discovered by Hofmann who obtained primary amines, with one carbon less than the starting material *via* hydrolysis of the isocyanate, after treating an *N*-unsubstituted amide with sodium hypobromite.[21] Monobromination of the primary amide creates a very acidic proton. This was deprotonated by the base and subsequent rearrangement generated the isocyanate. Hydrolysis and decarboxylation produced the amine with one carbon less. This is proposed to be a concerted mechanism and there is no evidence for the formation of nitrene.[22] Keillor and co-workers showed that other source of Br^+ such as NBS could be used, and when the reaction was performed in an alcohol as solvent, carbamate was isolated (Scheme 1.12).[23]



32 **33** **34**

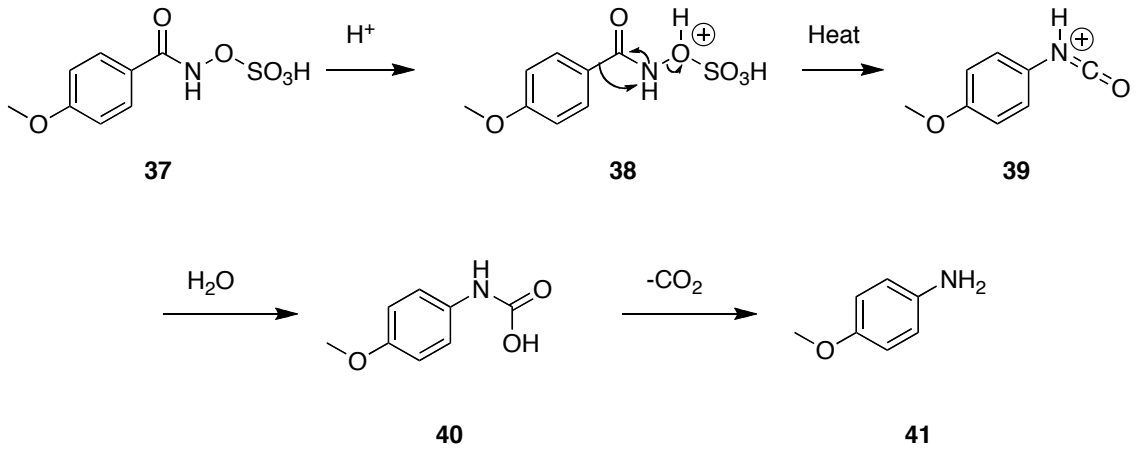


35 **36**

Scheme 1.12: Hoffman rearrangement.

III. Lossen Rearrangement.

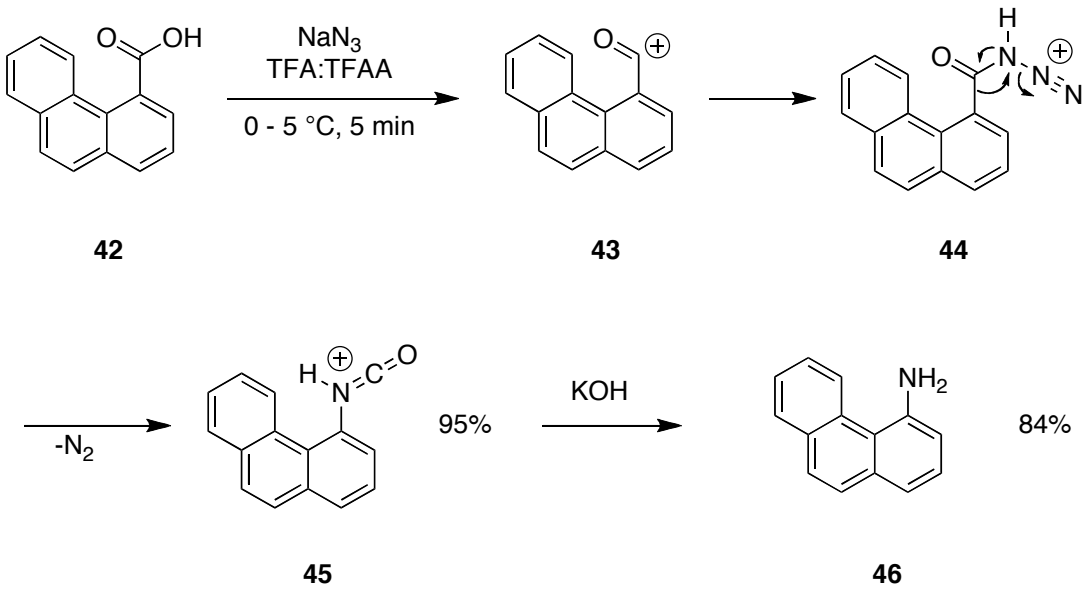
The first rearrangement of amide derivatives was discovered by Lossen, obtaining amines with one carbon less from derivatives of hydroxamic acids (Scheme 1.13).[24] The reaction was proved to work for *O*-acyl and *O*-sulphonic derivatives.[25] This reaction proceeds *via* a similar mechanism as the above mentioned rearrangements, with the difference being that the reaction was carried out under acidic conditions.



Scheme 1.13: Lossen rearrangement.

IV. Schmidt Reaction.

The latest of the amide derivative rearrangements was developed by Schmidt in the 1920's and it occurs when a carboxylic acid is treated with an acid azide in the presence of a catalyst.[26] The Schmidt reaction does not follow the same mechanism as the Curtius rearrangement. The Curtius rearrangement is a thermal decomposition of an acyl azide, whereas the Schmidt reaction is performed in acidic media and forms the cation of the acyl azide, which promotes the decomposition and rearrangement (Scheme 1.14).



Scheme 1.14: Schmidt rearrangement.

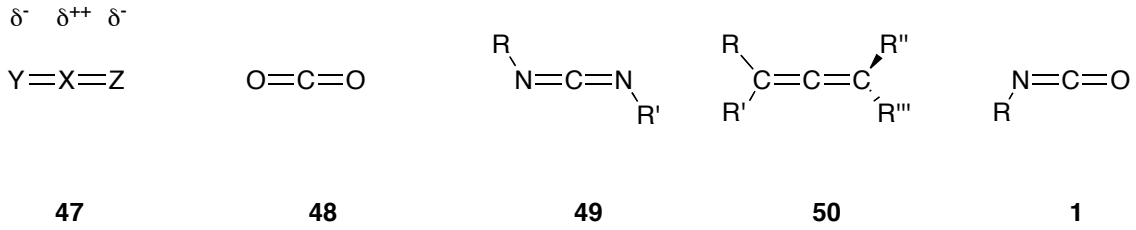
The four mentioned reactions are successful at laboratory scale, each having their own limitations. Despite all these reactions being well known for many years, they are not commonly applied at industrial scale. This is because all of the rearrangements use expensive materials compared to the phosgene reaction and none of them would represent an advantage to the production of isocyanates. It has also to be considered that azides are toxic and explosive, and rearrangements could cause dangerous processes at large scale.

After considering all the available routes for the synthesis of isocyanates, a standard, safe, easy, and environmentally friendly method for the generation of isocyanates at both industrial scale as well as at laboratory scale is required.

1.1.4 Applications of Isocyanates in Organic Synthesis

An isocyanate (**1**) is a functional group with cumulated double bonds, containing a central carbon atom double bonded to oxygen and also double bonded to nitrogen. Like in other cumulated double bonds such as carbon dioxide (**48**), carbodiimides (**49**) or allenes (**50**), a quadrupolar moment exists (Figure 1.2). However, due to its unsymmetrical structure there is a dipole, whereas in carbon dioxide the dipole is non

existent. In the case of carbodiimides and allenes, only symmetrical structures will generate zero dipole.



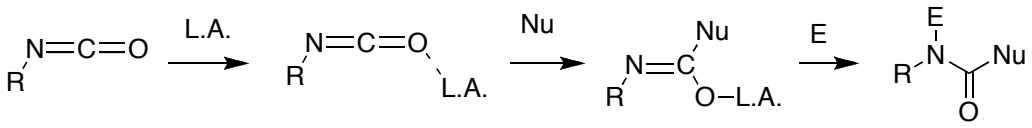
47 **48** **49** **50** **1**

Figure 1.2: Heterocumulated double bonds.

Isocyanates are very reactive functional groups. In addition to the fact that their major use relies on their reaction with nucleophiles to generate urea derivatives, the reactivity of isocyanates has been widely explored in their use as building blocks in synthesis. This has generated important subunits which are present in many natural product syntheses and for the generation of drug candidates.

1.1.4.1 Reactions with Nucleophiles

The nucleophilicity and basicity of isocyanates is very poor. However, the carbon centre is very electrophilic and reacts very easily with nucleophiles (Scheme 1.15). Subsequently, the intermediate formed can react with electrophiles *via* the electron-rich nitrogen atom. This reactivity is enhanced by the use of Lewis acids.

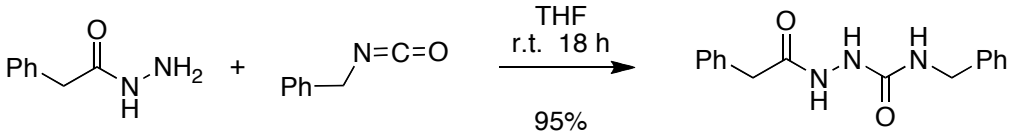


1 **51** **52** **53**

Scheme 1.15: Nucleophilic addition to isocyanates.

The two most commonly used reactions of isocyanates have been the conversion to carbamates (Scheme 1.1) by reaction with alcohols, and the generation of ureas by the reaction with amines (Scheme 1.16).[27] Ammonia, primary amines and secondary amines

can be used as nucleophiles to form a variety of ureas.[28] In the same fashion thioureas can be generated from the reaction between thioisocyanates and amines. Amides can be synthesised by the reaction of isocyanates and Grignard reagents.[29]

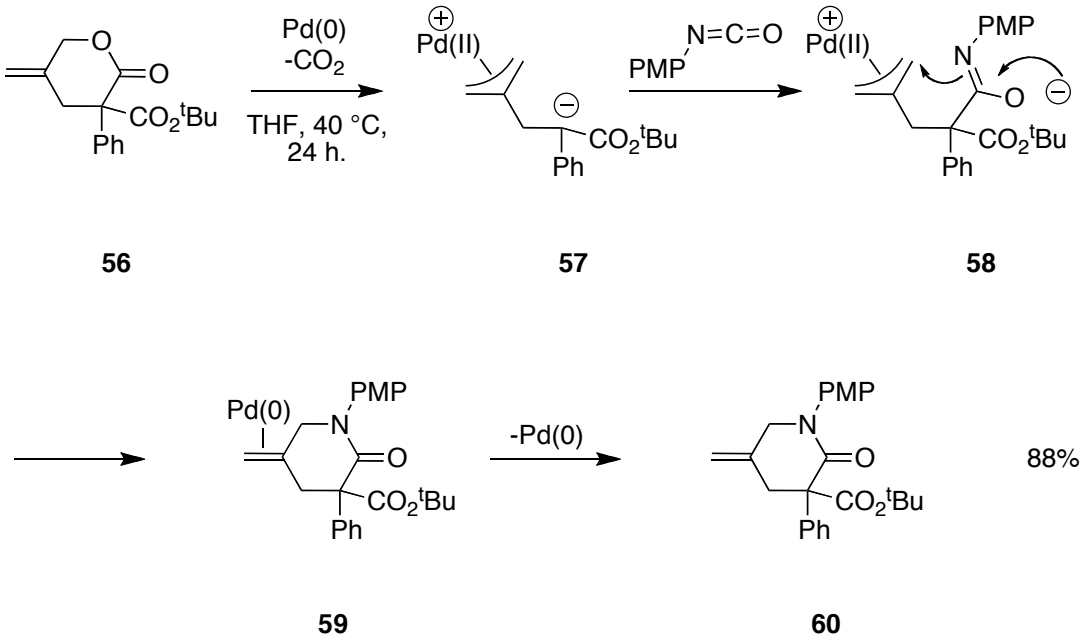


54 **1** **55**

Scheme 1.16: Formation of ureas from isocyanates.

1.1.4.2 Cascade Nucleophilic Addition-Palladium Coupling Reactions

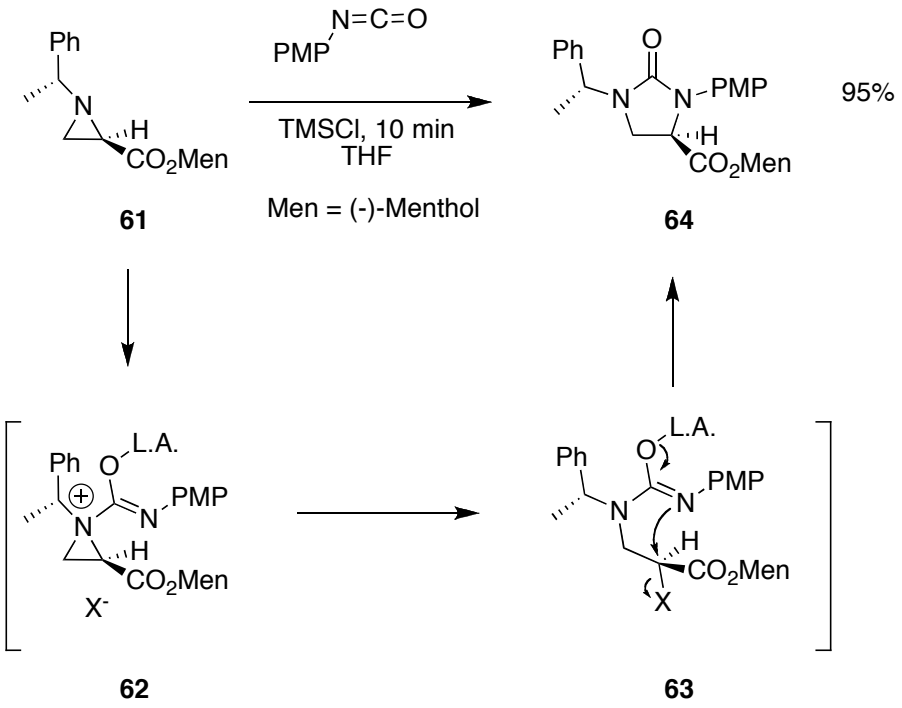
The above mentioned examples use only a proton as the electrophile, however, in more recent years new reactions have been developed which use other kind of electrophiles. The most interesting of these examples is the cascade nucleophilic addition-palladium coupling reaction, mostly developed for π-allyl reactions.[30] A three-step process starts by the coordination of a palladium species to the alkene followed by decarboxylation forming palladium-π-allyl intermediate **57** containing an enolate. This enolate adds to the isocyanate to form intermediate **58**. Final palladium-π-allyl coupling generates the product (**60**) after β-hydride elimination (Scheme 1.17). The overall process generates the formation of a C-C and a C-N bond.



Scheme 1.17: Cascade nucleophilic addition - palladium coupling reaction.

1.1.4.3 Formation of Oxazolidinones and Cyclic Ureas

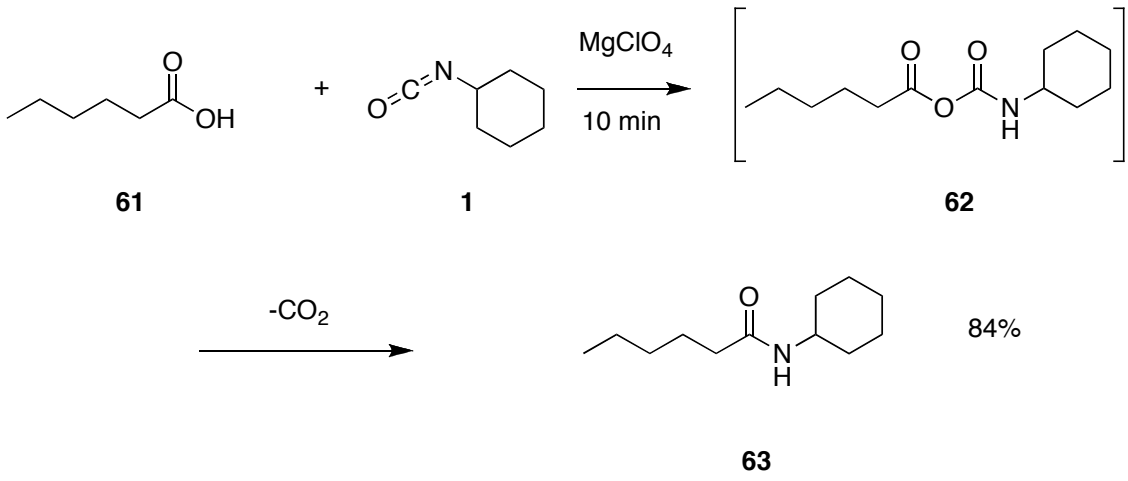
Shibata and co-workers showed that the synthesis of oxazolidinones can be achieved by a 1,3-dipolar cycloaddition between an epoxide and an isocyanate in the presence of a Lewis acid.[31] In more recent studies with aziridines, it has been proposed that a nucleophilic addition of the aziridine to the isocyanate occurs, which is promoted by the Lewis acid. As the carbon - nitrogen bond weakens, aziridinium opening promoted by S_N2 attack of the counter ion occurs, and finally nitrogen ring-closing *via* another S_N2 reaction to produce cyclic ureas (Scheme 1.18).[32] The fact that the stereochemistry is maintained supports the mechanism, in preference to the dipolar cycloaddition. Variants of this reaction have been studied by thermal ring opening and show similar reactivity to reactions involving Lewis acids. In those cases the stereochemistry is lost, suggesting a similar mechanism to that of epoxides.[33]



Scheme 1.18: Synthesis of cyclic ureas from aziridines and isocyanates.

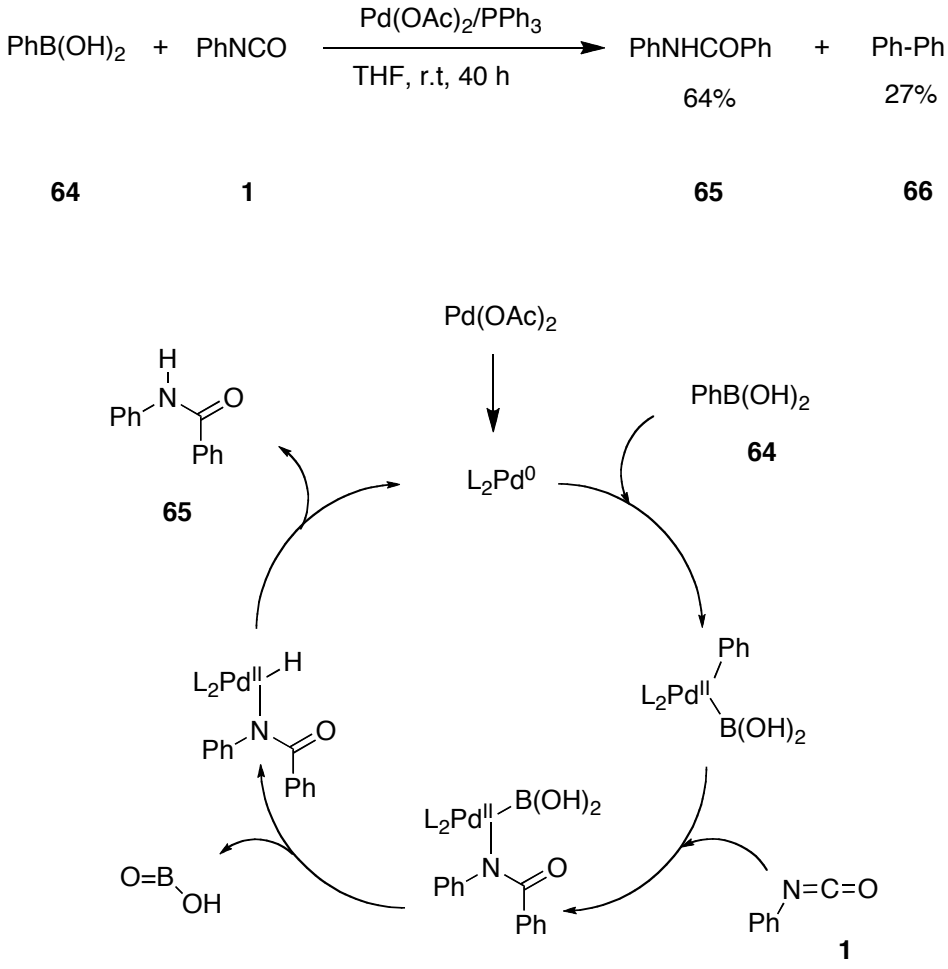
1.1.4.4 Amide Formation Under Mild Conditions

The reaction between an isocyanate (**1**) and a carboxylic acid (**61**) forms amides *via* the *o*-acylcarbamate intermediate compounds (**62**). Although the decarboxylation of carbamic acids is known, the decarboxylation of α-amino mixed anhydride compounds, to yield amides in the presence of a catalyst, has also been developed.[34] This reactivity represents an unusual and novel formation of amides from isocyanates and carboxylic acids using mild conditions (Scheme 1.19).



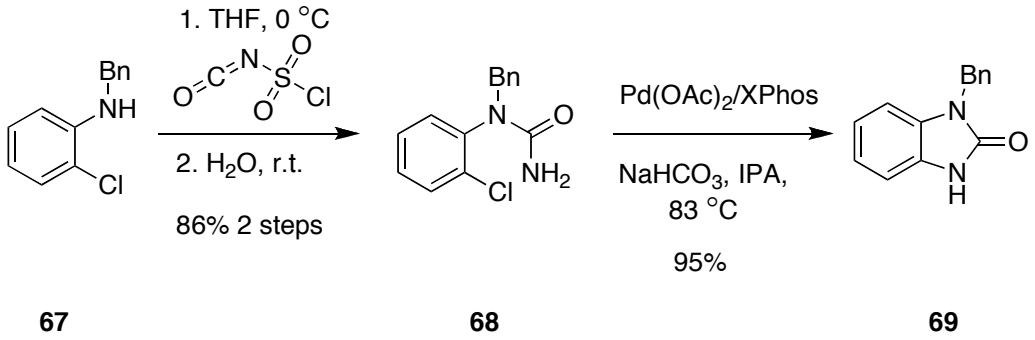
Scheme 1.19: Formation of amides under mild conditions.

Another strategy for the mild formation of amides from isocyanates has been recently developed using a Suzuki type reaction with boronic acids and palladium as a catalyst.[35] It is proposed that follows an initial oxidative addition of the palladium into the C-B bond, the palladium intermediate reacts with the isocyanate forming a C-C bond, with the palladium-boronic acid species attached to the amine. Reductive elimination of boronic acid produces a hydride transfer to the palladium, and a final reductive elimination generates the amide and palladium(0) as the catalyst (Scheme 1.20).



Scheme 1.20: Formation of amides under mild conditions.

Other amide derivatives which can be obtained from isocyanates are unsymmetrical ureas, which are formed when isocyanates react with amines. In a two-step process, McLaughlin and co-workers joined the formation of urea with a palladium coupling to form a cyclic urea (Scheme 1.21).[36]



Scheme 1.21: Generation of urea by addition - palladium coupling.

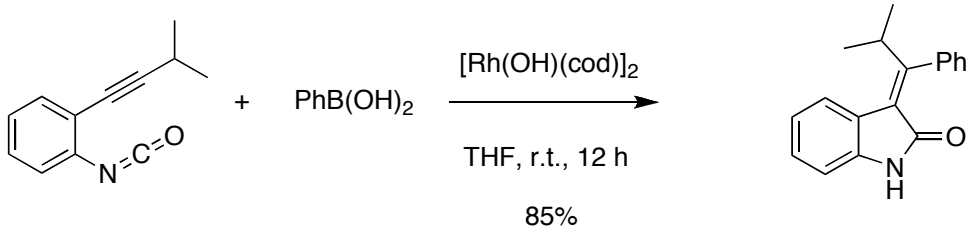
1.1.4.5 Cycloadditions

The presence of cumulated double bonds in isocyanates provides the molecule with a functional group with 4π-electrons, which gives them the ability to undergo cycloaddition processess. These cycloadditions are generally catalysed by transition metals and provide efficient routes to aromatic and non-aromatic heterocyclic compounds. Although isocyanates posses 4π-electrons available to react, only 2π-electrons react in most of the cases. These cycloadditions also introduce nitrogen functionality into the heterocycle, which is beneficial for natural product synthesis and drug development.

I. Oxindole Synthesis

In the same way that much of organic chemistry is evolving towards greener processes, isocyanates have been involved in transition metal catalysed cascade reactions.[37] Once again, their particular 2π - 2π system allows interaction with transition metals. The use of transition metal catalysed cascade alkyne alkylation - isocyanate insertion reactions to generate oxindoles have been studied. Both alkynes and isocyanates are known to be acceptors of organorhodium (I) species. In this particular case, versatile intermediates such as oxindoles (**72**) are generated from 2-alkynylaryl isocyanates (**70**) reacting with an organoboron species (**71**) in the presence of a Rh(I) species as a catalyst in very good yield and under mild conditions (Scheme 1.22). This methodology not only allows the

operator to obtain valuable intermediates, but also regioselectively forms a carbon - carbon bond in an alkyne and builds indole moieties *via* another C-C bond formation.



70 **71** **72**

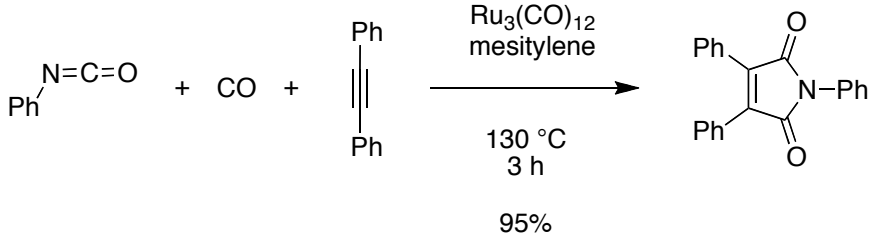
Scheme 1.22: Oxindole synthesis from isocyanates.

II. [2π + 2π]

Among all the types of cycloadditions that isocyanates can undergo, [2π + 2π] is the most important, as well as the one which has been studied the most over the years. One type of [2π + 2π] cycloaddition is dimerisation which will be explained in section 1.1.4.5.V. Another type is [2π + 2π] cycloadditions involving transition metals and [2π + 2π] cycloaddition - [2π + 2π] retro-cycloaddition (heterocumulene metathesis); these two types of reaction will be explored in more detail in section 1.4.

III. [2π + 2π + 1π]

The formal [2π + 2π + 1π] cycloaddition of alkenes, alkynes and carbon monoxide is known as the Pauson-Khand reaction, and represents a powerful route to cyclopentenones. By using isocyanates as a partner instead of alkenes, a variation of the Pauson-Khand reaction takes place which leads to the construction of maleimides, with ruthenium acting as a catalyst in the reaction (Scheme 1.23).[38] In the overall process two C-C bonds are formed and two more carbon-nitrogen bonds are also formed. It represents a very versatile catalytic multicomponent reaction for the synthesis of heterocycles, capable of being used in industry and academia.

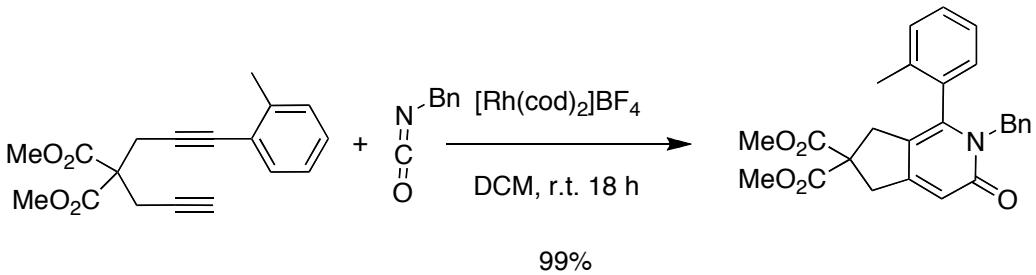


1 **73** **74**

Scheme 1.23: Synthesis of maleimides from isocyanates.

IV. [2π + 2π + 2π]

In the catalysed 6π-electron process involving two alkynes and an isocyanate, other types of important heterocycles can be obtained in very good yield. Pyridones were first obtained *via* catalysed [2π + 2π + 2π] cycloadditions in 1982 using a nickel catalyst, and since then different variations and different transition metals have been used.[39] All of these reactions follow the same basic mechanism, and have evolved from multicomponent reactions using two equivalents of alkyne and cobalt as catalyst, to partially intramolecular variants with two different alkynes and a ruthenium catalyst and finally to the use of diynes and isocyanates engaging rhodium as catalyst.[40] However, the most interesting of the reported examples is the regio- and chemoselective cycloaddition of Tanaka and co-workers (Scheme 1.24). In this example unsymmetrical diynes react with isocyanates to generate 2-pyridones in high yield, under mild conditions and with complete regioselectivity.[41]

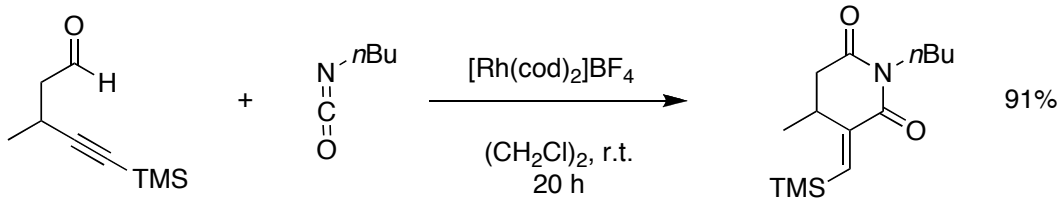


75 **1** **76**

Scheme 1.24: Synthesis of pyridones from isocyanates.

V. Catalytic Cyclisation

The first catalysed [4π + 2π] cyclisation using isocyanates was reported in 2006.[42] The use of rhodium as catalyst promotes the reaction between an aldehyde **77**, an alkyne and an isocyanate **1** to yield glutaramide derivative **78** (Scheme 1.25). This single step process represents a very good approach to a full family of important units in the world of natural product synthesis and drug discovery.



77 **1** **78**

Scheme 1.25: Generation of glutaramide from isocyanates.

VI. Dimerisations and Trimerisations

In addition to transition metals catalysing reactions of isocyanates, organophosphorus compounds have also been found to be very effective.[43] This reactivity has only been studied in the formation of dimers **80** and trimers **79**, it is another possibility to expand the self reaction of isocyanates to form heterocycles (Figure 1.3).

79 **80**

Figure 1.3: Heterocycles from dimerisation and trimrisation of isocyanates.

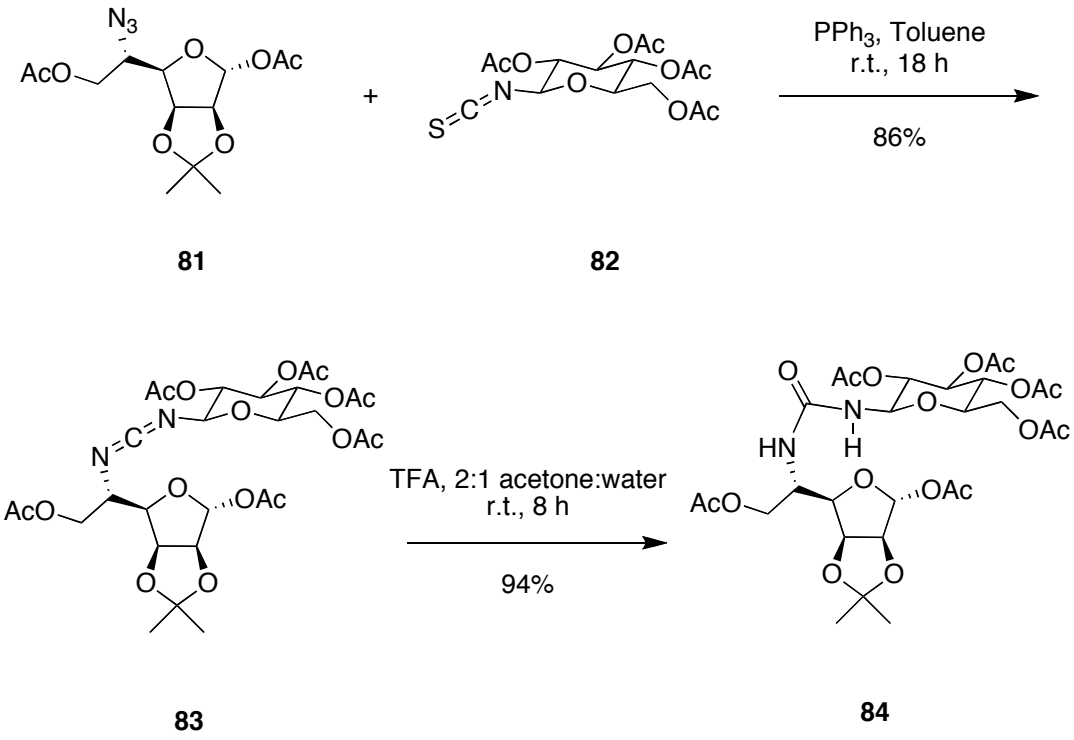
1.1.5 Applications of Carbodiimides in Organic Synthesis

Carbodiimides belong to the family of heterocumulenes and are directly related to isocyanates. There have been several methods reported for their synthesis from isocyanates (section 1.5.2). In academia, carbodiimides are used in three main different ways: oxo-imido exchange, formation of heterocycles and polymer chemistry.

1.1.5.1 Oxo-Imido Exchange

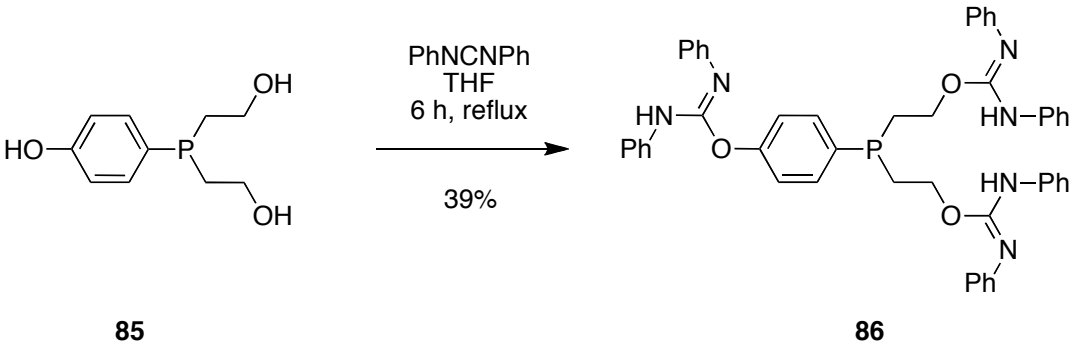
Medicinal chemistry and organic chemistry requires the formation of a huge range of functional groups in a short number of steps. Some common functionalities are those derived by the exchange of a carboxyl group to an imido group. Literature precedent has shown the ability of carbodiimides to synthesise particular functionalities which can be difficult to access by other routes.

Urea is the simplest motif which can be derived by simple hydrolysis of carbodiimide. Some molecules require the formation of ureas under mild conditions due to the functionalities present. Mellet and co-workers showed the coupling of two carbohydrates *via* an aza-Wittig reaction to form carbodiimide **83** (explained in detail in section 1.5.2.6) followed by hydrolysis to give urea **84** (Scheme 1.26).[44]



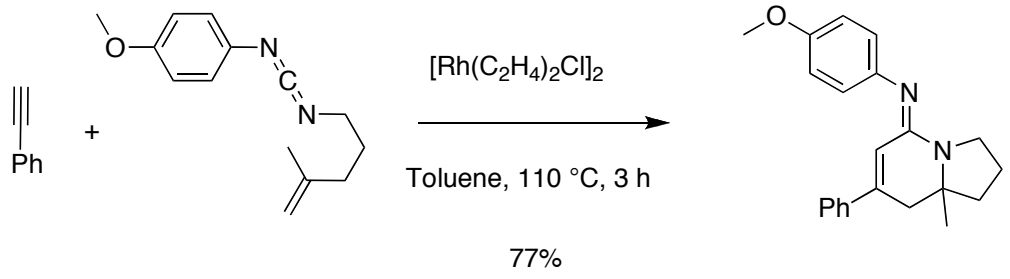
Scheme 1.26: Aza-wittig to generate carbodiimides.

Although not as common as ureas, the imido carbamate is one interesting subunit found in natural products and is interesting for medicinal chemistry. One method of generating them is by addition of an alcohol or alkoxide into a carbodiimide.[45]



Scheme 1.27: Generation of carbamates from isocyanates.

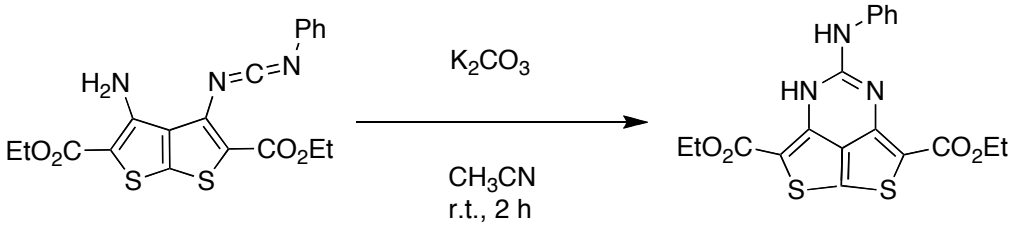
Following the same pattern, amidines have been generated by a rhodium catalysed [2+2+2] cycloaddition reaction with acceptable yields and excellent enantioselectivity.[46] In this particular example, Rovis *et al*. developed the formation of bicyclic amidines **89** by reaction of alkene-carbodiimide **88** with alkynes **87** (Scheme 1.28). In general alkyl addition to carbodiimides can also be achieved.[47]



87 **88** **89**

Scheme 1.28: Synthesis of imidines.

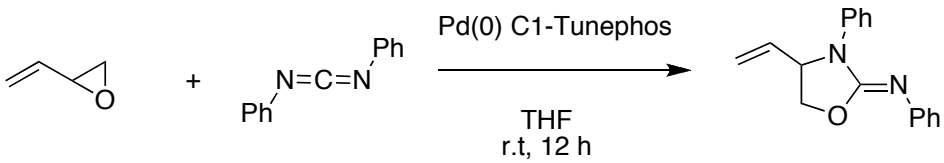
A very important subunit in biological processes is the guanidine group, due to its abundance in every living entity, which is the imine derivative of a urea. Its generation can be mediated by the addition of an amine to a carbodiimide in the presence of a base.[48] Ding and co-workers transformed amines into guanidines **91** by formation of carbodiimide **90** *via* an aza-Wittig reaction and intramolecular addition of an amine using potassium carbonate (Scheme 1.29).



90 **91**

Scheme 1.29: Synthesis of guanidines.

Finally, another group of compounds that can be synthesised as imido derivatives of carbonyl compounds are imido oxazolidinones. They belong to the cyclic family of imido carbamates.[49] Ring opening of an allylic epoxide **92** in the presence of carbodiimide **93** promoted the addition of the oxygen to the carbodiimide followed by ring closure to generate the product in high yield (Scheme 1.30).



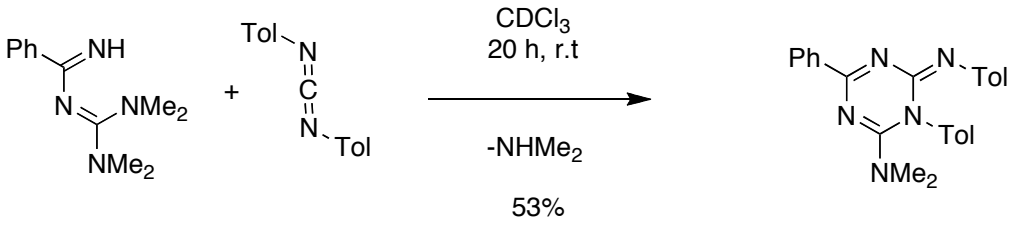
92 **93** **94**

Scheme 1.30: Formation of imido oxazolidinones.

1.1.5.2 Formation of Heterocycles

The use of heterocumulenes for the generation of heterocycles has also been reported as a general method with very successful results. Different approaches have been developed, yielding different heterocyclic structures.

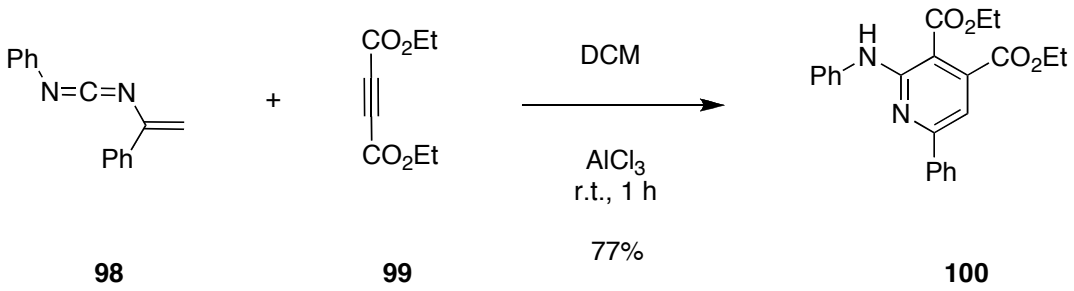
The easiest process has been the use of carbodiimides in formal Diels-Alder type reactions. By using the carbodiimide (**94**) moiety as the dienophile and diimines **95** as dienes, 1,3,5-triazines **97** can be generated in high yield and excellent regiochemistry (Scheme 1.31).[50]



95 **96** **97**

Scheme 1.31: Formation of heterocycles using carbodiimides.

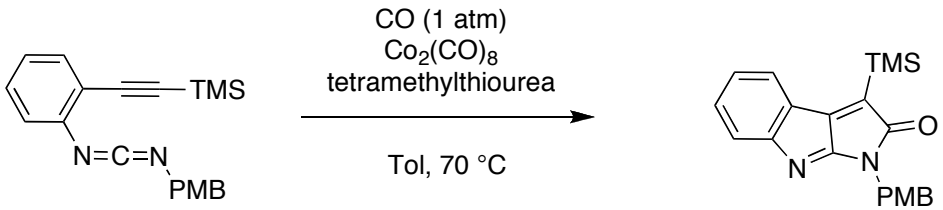
Conversely, carbodiimides have also been part of the dienophile partner in the Diels-Alder reaction.[51] Saito *et al*. generated pyridines (**100**) by the reaction between vinyl carbodiimides **98** and alkynes **99** promoted by a Lewis acid in moderate yield (Scheme 1.32).



98 **99** **100**

Scheme 1.32: Synthesis of pyridines using carbodiimides.

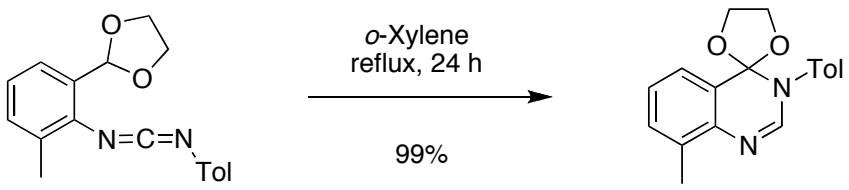
Cyclisation of 1-carbodiimido-2-alkynyl benzenes represents a powerful route to the generation of indoles.[52] Mukai and co-workers developed an aza-Pauson-Khand reaction involving these type of substrates in high yield and under mild reaction conditions (Scheme 1.33). Indoles and quinolines have also been synthesised in a similar manner *via* a radical mechanism.[53]



101 **102**

Scheme 1.33: Generation of indoles from carbodiimides.

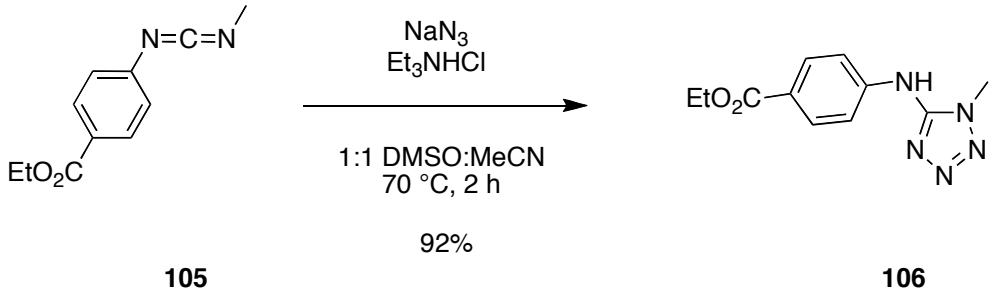
Heterocycles containing two nitrogen atoms in the same cyclic structure which have been provided by the carbodiimide have also been generated *via* a [1,5]-H shift.[54] Acetal protected *o*-carbodiimido benzaldehyde **103**, after refluxing in *o*-xylene, rearranged and cyclised to heterocycle **104** in high yield (Scheme 1.34).



103 **104**

Scheme 1.34: Synthesis of dihydroquinolines from carbodiimides.

Tetrazoles have also been synthesised by the reaction of carbodiimides **105** and sodium azide.[55] The reaction worked by addition of the azide onto the carbodiimide followed by cyclisation, with the only requirement being the addition of a quaternary ammonium salt to promote the addition of the azide (Scheme 1.35).

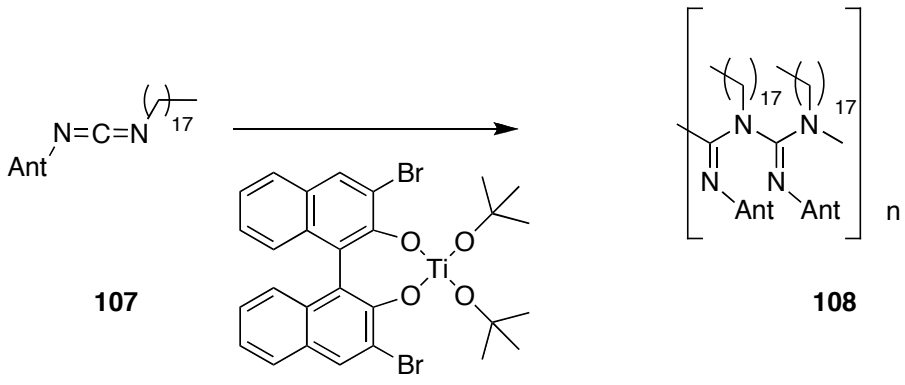


105 **106**

Scheme 1.35: Generation of tetrazoles from carbodiimides.

1.1.5.3 Formation of Polymers

Although polymerisation of carbodiimides has not been extensively studied, some examples have been reported of titanium alkoxides catalysing the polymerisation of carbodiimides.[56] Self-polymerisation to generate polyguanidine structures led to a new generation of polymers (Scheme 1.36).



107 **108**

Scheme 1.36: Carbodiimide as polymer source.

1.2 Proposed Research

After considering the lack of a clean and safe route for the synthesis of isocyanates, it was decided to study a new catalytic cycle which would allow the generation of isocyanates at industrial and academic research scale, using cheap, non-toxic and abundant raw materials. Moreover, the by-products of the process should be environmentally friendly, and kept to a minimum, to increase the atom economy of the process.

The design and synthesis of the catalyst for the proposed cycle is the key step for the process to succeed. Our interest was focused on transition metal complexes which can undergo heterocumulene metathesis as seen in Figure 1.4. The starting point of the cycle would be the reaction of a metal-imido complex (**109**) with carbon dioxide *via* a [2+2] cycloaddition reaction to produce a four membered ring metallocycle intermediate (**110**). This would be an unstable compound which should decompose *via* a [2+2] retro-cycloaddition reaction to a metal-oxo complex (**111**) and an isocyanate (**1**). The last sequence of the cycle would be the reaction of the metal-oxo complex (**111**) with an amine (**4**) or amine derivative, to generate the metal-imido complex (**109**) and a by-product. This last process might need an extra step for the activation of the metal-oxo complex to react with amines and some means of sequestering the water by-product or equivalent.

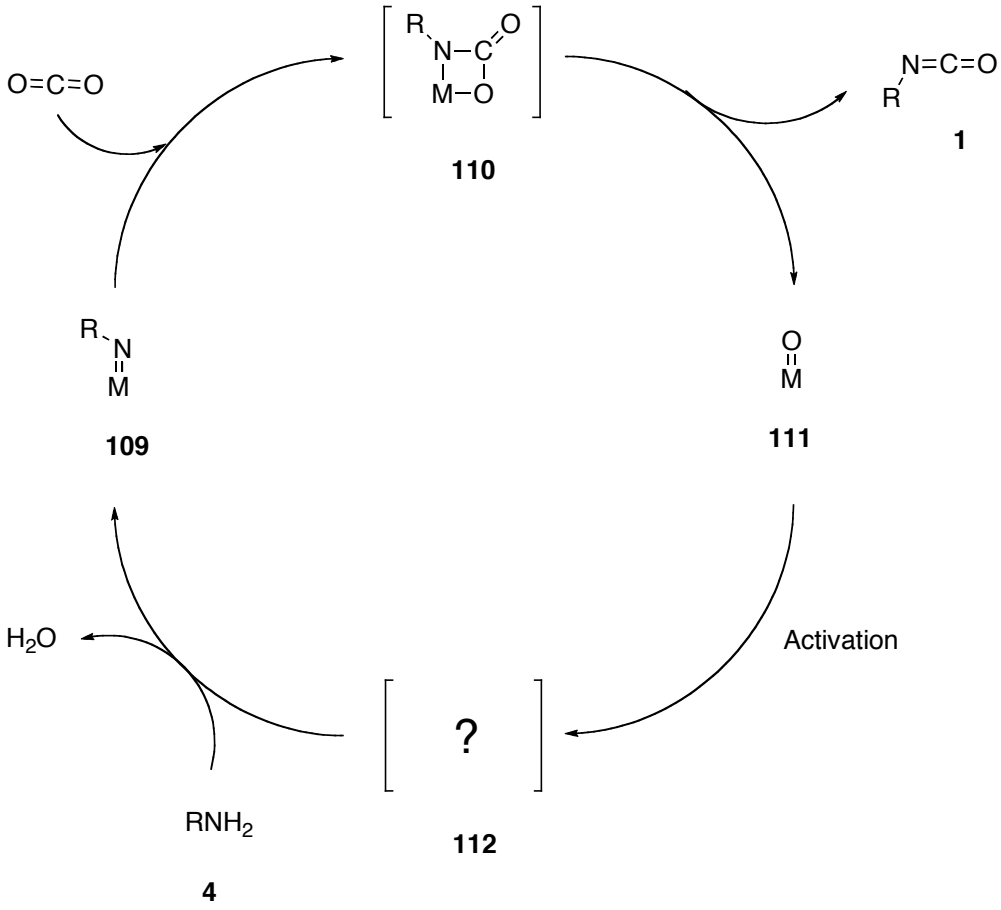
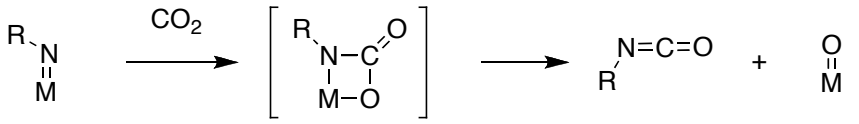


Figure 1.4: Proposed catalytic cycle.

As can be seen, this two-step process can be considered as an equilibrium which could be displaced in one or the other direction. However, by changing the conditions such as the pressure of carbon dioxide, eliminating one of the products by reacting with other compounds or changing the reactivity by tuning the catalyst, the overall equilibrium might be driven towards the desired product. Another potential problem involves the formation of water as by-product. It is well known that most transition metal complexes are not compatible with the presence of water as it causes degradation of the complex and it can react with isocyanate. For the process, different complexes with different metal centres will be studied according with the literature. Different amines will also be tested.

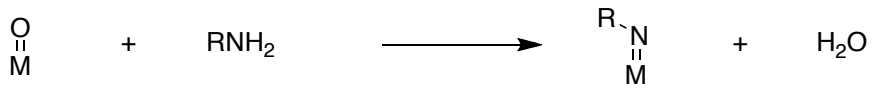
The proposed catalytic cycle will be separated into the different reactions, and each one will be studied individually, before combining them to give a one-pot process. The first part of the cycle being studied will be the heterocumulene metathesis step, which will be preceded by the successful generation of titanium-imido complexes (Scheme 1.37).



109 **110** **1** **111**

Scheme 1.37: Heterocumulene metathesis.

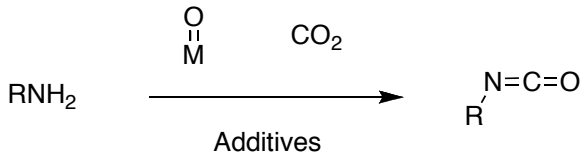
The heterocumulene metathesis studies will be followed by the application of methodologies for transformation of the metal-oxo complex (**111**) into a metal-imido complex (**109**) (Scheme 1.38). This second process has been more developed in the literature (section 1.4.1).



111 **4** **109**

Scheme 1.38: Metal-imido formation.

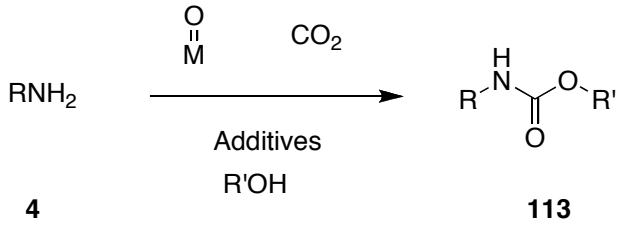
After the development of the stoichiometric process, the study will be focused on the catalytic process to generate isocyanates (Scheme 1.39).



4 **1**

Scheme 1.39: One pot catalytic process to synthesise isocyanates.

Once the process is fully developed, it will be expanded to the use of alcohols as solvents, co-solvents or reagents to generate carbamates (Scheme 1.40). The methodology will finally be applied to diamines and diols for the generation of polyurethanes by the same process.



Scheme 1.40: One pot catalytic process to synthesise carbamates.

If successful, the process could be applied on an industrial scale for the production of polyurethanes, where carbon dioxide, a cheap and abundant raw material, will be one of the starting materials. Indirectly, the amount of carbon dioxide released into the atmosphere will be reduced, helping the fight against global warming.

1.3 Carbon Dioxide

1.3.1 Threat to the Environment

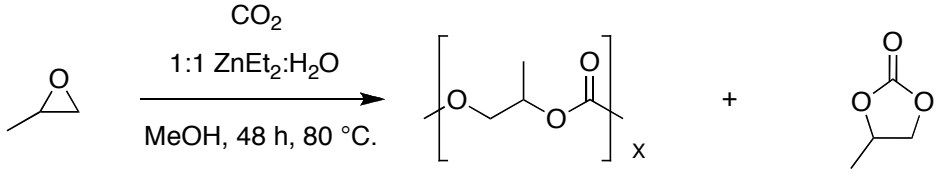
Greenhouse gases are those which can be found in the atmosphere that absorb radiation in the visible or infrared wavelength. Carbon dioxide is one of the greenhouse gases, among others, that contribute to global warming with the greenhouse effect. Since the starting of the industrial revolution, human activity has increased the levels of all greenhouse gases, specially of carbon dioxide. Data extracted from ice core and atmospheric data collected at the Manua Loa Observatory in Hawaii show that carbon dioxide levels in preindustrial times were 270 ppmv, compared to 315 ppmv in 1958 (when modern measurements were taken) and 383 in 2004.[57] According to studies, global temperatures have increased following the normal cycles of temperatures.[58] However, from 1979, land temperatures have increased about 0.25 °C per decade and sea temperatures by 0.13 °C.[59] It has been observed that there is a correlation between the increased concentration of carbon dioxide in the atmosphere and the increase of temperatures.

1.3.2 Carbon Dioxide as a Reagent

On the other hand, carbon dioxide is an inexpensive reagent as it is a by-product in many industrial processes, is very abundant, non flammable, and possesses very low toxicity. All these, together with the fact that it is a waste in industrial processes, makes it a very attractive reagent for organic synthesis and industrial production. Carbon dioxide is a thermodynamically stable compound, so it is an ideal reagent for chemical processes. Despite its stability, reactions and industrial processes employing highly reactive reagents have been explored and developed over the years.[60] There exist many different processes at laboratory and industrial level where carbon dioxide is utilised as a reagent or starting material, however, we are only going to focus on a few processes which are directly related to the chemistry reported in this thesis.

1.3.2.1 Generation of Carbonates and Polycarbonates

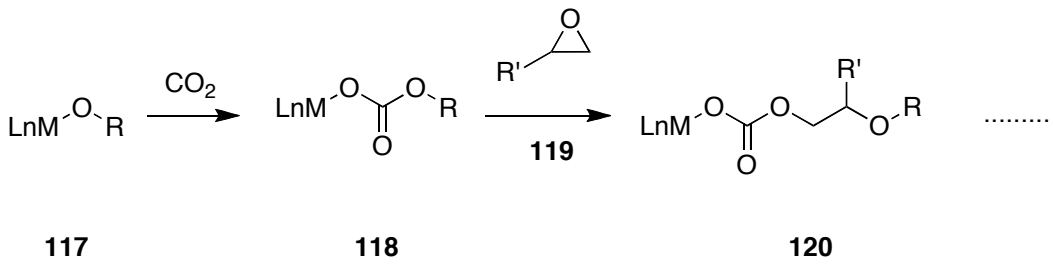
Organic carbonates are industrially important compounds either as cyclic, and linear compounds or polymers, and are also present in natural products. Dehydration is the most powerful methodology for their generation and can be compatible with alcohols,[61] ketals,[62] orthoesters[63] and oxiranes,[64] which have been employed for industrial synthesis. Evidence of their utilisation is the generation of polycarbonates in the copolymerisation process of ethylene oxide derivatives (Scheme 1.41). Inoue and co-workers were the first to report that a 1:1 mixture of $ZnEt_2$ and H_2O catalysed the copolymerisation of propylene oxide (**114**) and carbon dioxide at 20 - 50 atm.[65] In the years after the first publication, many groups explored the field and it became popular in polymer science.



114 **115** **116**

Scheme 1.41: Carbon dioxide as precursor for polymers.

The process expanded to include a full range of different catalysts, substrates and conditions. Propylene carbonate (**116**) was the usual by-product in the reaction, however, the reactivity can be driven towards only polypropylene carbonate by using ligands with more than one source of protons, whereas the use of monoprotic ligands (one alcohol or secondary amine) generates exclusively propylene carbonates.[66] Not only were variations around the metal center in the zinc catalyst were made, but it was also found that other metals were able to mediate the process. Once again, Inoue and co-workers published, in 1978, the development of the first aluminum catalyst.[67] This was followed by reactions using cobalt by Soga and co-workers in 1979, chromium by Kruper and Dellar, and lanthanide based complexes by Chen and co-workers.[68] The mechanism of the polymerisation is accepted to proceed by a two step process; first carbon dioxide inserts into the metal complex (**117**), followed by insertion of the epoxide into the metal carbonate (**118**) (Scheme 1.42). Epoxide ring opening is typically favored at the least hindered C-O bond. As a general rule, C-O cleavage occurs with inversion of configuration at the site of attack, which suggests a S_N2-type mechanism.



117 **118** **120**

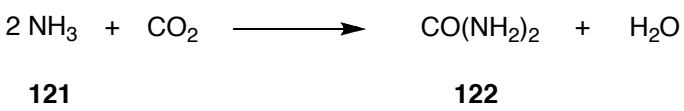
Scheme 1.42: Polymerisation using carbon dioxide.

The presence of ether linkages as a result of consecutive epoxide reactions can be observed, but this reactivity can be tuned to generate polycarbonates. The consecutive insertion of molecules of carbon dioxide has not been reported.[69]

1.3.2.2 Generation of Ureas

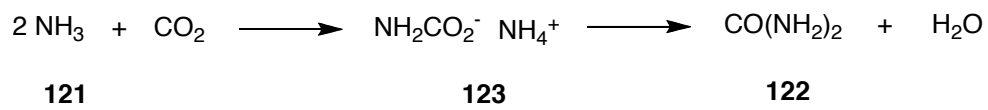
Because of the chemical characteristics of ureas, they have become very important materials since the beginning of the industrial revolution. At the end of the 19th century

urea was used to stabilise explosives, was a constituent of varnishes, was used in photographic films, was used in organic synthesis, in medicinal preparations, and as a valuable nitrogen fertiliser. It was believed that it could be generated from carbon dioxide and ammonia (Scheme 1.43). Both materials are produced in the Haber process, which is a very important industrial proces and responsible for sustaining one third of the Earth's population through the production of fertiliser.



Scheme 1.43: Generation of urea.

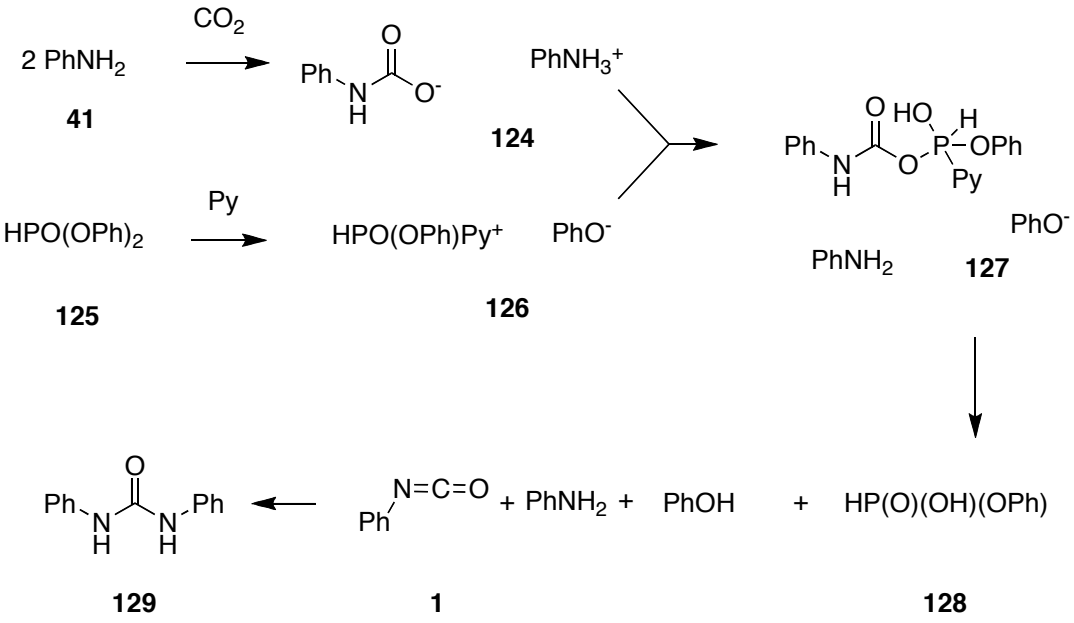
From 1870 several researchers tried to achieve the generation of urea (an organic compound) from carbon dioxide and ammonia (inorganic materials). It was in 1922 that Bosch and Meiser developed the industrial process.[70] This process was composed of two parts (Scheme 1.44); exothermic reaction of liquid ammonia with dry ice to form ammonium carbamate, and its endothermic decomposition into urea and water.



Scheme 1.44: Industrial production of urea.

The industrial synthesis of urea is another good example of the utility of carbon dioxide as a reagent.[71] This novel idea of synthesising ureas from carbon dioxide was extended to the use of primary and secondary amines instead of ammonia. The process has been studied for many years and different solutions have been found to obtain new routes. The first route developed was the use of phosphorus derivatives as Lewis acids and dehydrating agents.[72] Diphenyl and triphenylphosphites in pyridine produced acyloxy *N*-phosphonium salts **126** which promote the reaction, acting as a Lewis acid (Scheme 1.45). Amine and carbon dioxide exist in equilibrium with the carbamate salt. This carbamate salt **124** reacts with acyloxy *N*-phosphonium salt **126** to generate carbamoyl *N*-phosphonium salt **127**, which, either *via* heat or in the presence of a base (phenolate,

amine or pyridine present in the mixture) decomposes to generate isocyanates. The excess of amine in the mixture led to the formation of symmetrical ureas. This route represented the use of carbon dioxide at atmospheric pressure, with the use of stoichiometric quantities of phosphite to give isocyanates in a yield of 93%. In more recent research, this process has been used for the synthesis of symmetrical ureas under mild conditions using carbon dioxide and generating good yields.[73]

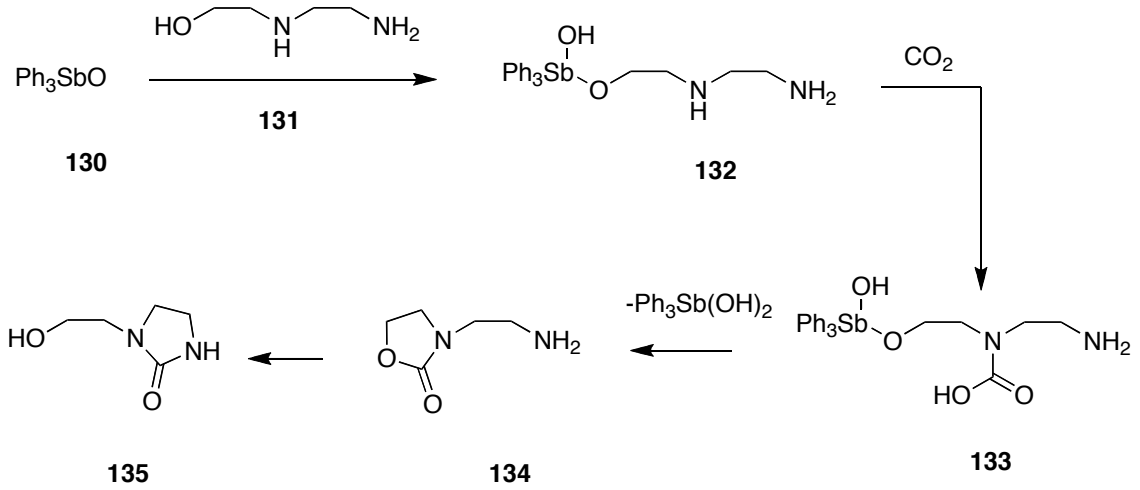


Scheme 1.45: Generation of symmetrical ureas from amines and carbon dioxide.

In more recent studies, Jessop and co-workers developed a phosphine route to tetrasubstituted ureas using one bar of carbon dioxide and secondary amines, in moderate yields.[74]

In a similar manner, Nomura and co-workers made the process catalytic by the use of triphenylantimonate oxide, generating cyclic ureas.[75] The key step of the sequence was transesterification to generate the urea instead of a dehydration reaction (Scheme 1.46). Triphenylantimonate oxide (**130**) reacts with the alcohol of an *N*-2-hydroxyethyl-1,2-diamine (**131**) to give an alkyl ether hydroxyl triphenylantimonate (**132**). Reaction of the secondary amine with carbon dioxide and elimination of the antimonate species generates carbamate (**134**), followed by transesterification to yield cyclic carbamate (**135**) and bishydroxyl triphenylantimonate. The remaining free amine in the molecule is

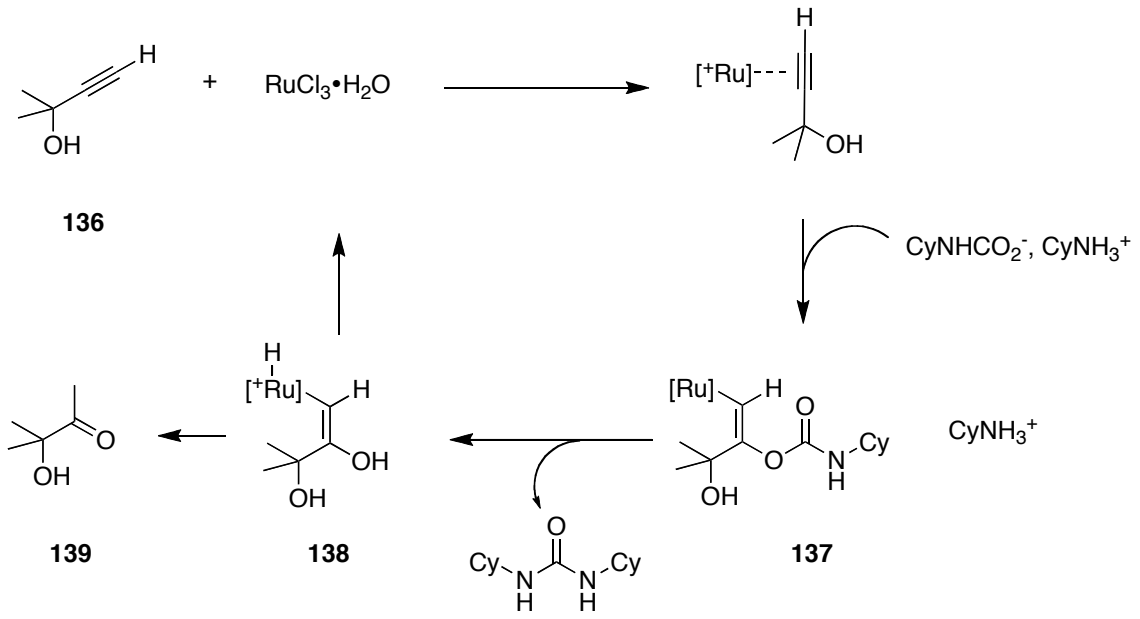
now capable of generating urea by adding to the carbonyl and ejecting the alcohol. Dehydration of the antimonate complex is spontaneous and recycles the catalyst for the reaction. Although the conditions required were 24 hours at 50 bar of carbon dioxide and 170 °C, yields were from moderate to good.



Scheme 1.46: Generation of cyclic ureas by activation with Sb.

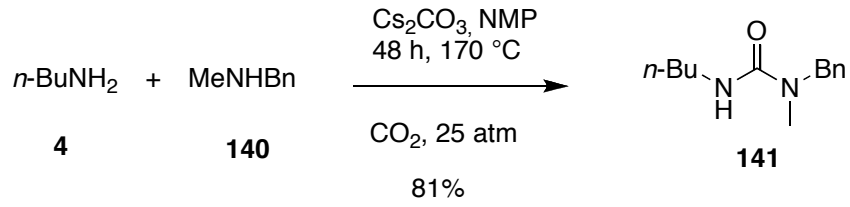
This methodology was further developed to the use of 1,2-diamines under 60 bar of carbon dioxide and 200 °C giving similar yields.[76]

An improvement to the use of Lewis acid, is the use of catalysts to promote the reaction using dehydrating agents as co-reagents. Dixneuf and co-workers developed a double reaction to synthesise ureas, and convert alkynes to ketones as the dehydrating process, by the use of transition metals (Scheme 1.47).[77] The reaction was performed using $RuCl_3 \cdot H_2O$ as a catalyst and 50 bar of carbon dioxide, yielding 61% of symmetrical ureas.



Scheme 1.47: Generation of symmetrical ureas by activation with Ru.

Base catalysis of the reaction of carbon dioxide and amines has been another route for symmetrical urea synthesis with the requirement of 25 atmospheres of pressure, 170 °C and 48 h giving ureas in moderate yield.[78] Although due to the harsh conditions used in the reaction, it is not a very efficient procedure, it allows synthesis of unsymmetrical ureas by using a primary amine and a secondary amine under the same conditions (Scheme 1.48).

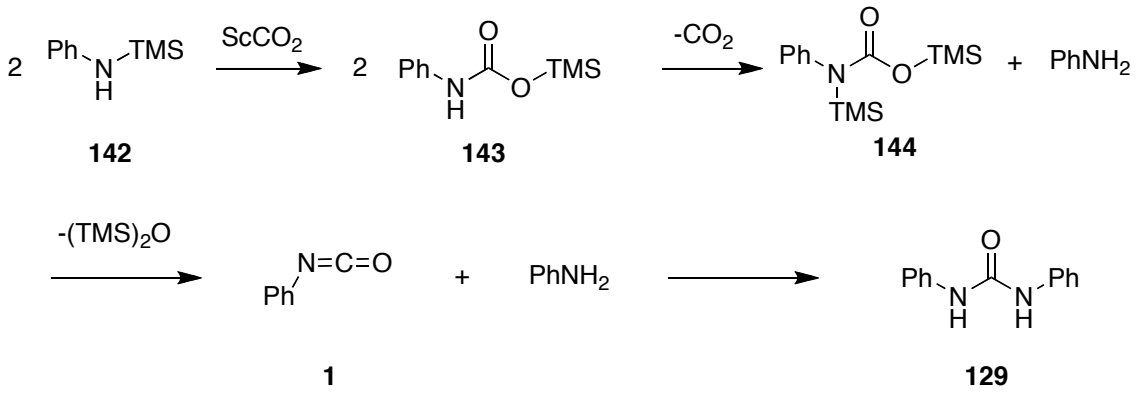


Scheme 1.48: Generation of unsymmetrical urea.

The use of room temperature ionic liquids, due to their peculiar physicochemical properties (low vapor pressure, solvent character...), has also been reported as a medium to undertake synthesis of ureas. Although the pressure required for the experiment was 60 atmospheres, moderate to high yields of symmetrical ureas were achieved without the need to add any dehydrating agent.[79] In addition to the ionic liquid, a catalytic amount of CsOH was required for the reaction to proceed in reasonable yield. The

mixtures of ionic liquid and catalyst were clean and could be reused up to three times before they lost activity.

In recent studies, supercritical carbon dioxide has been used by Holmes and co-workers to generate bis-substituted and tetra-substituted symmetrical ureas from silyl-protected amines.[80] Under the supercritical conditions, carbon dioxide is inserted between the nitrogen and the silicon atoms to form a *O*-silylcarbamate (**143**). The molecule rearranges to form isocyanate (**1**) and bis-silylether as by product. It is believed that the rearrangement occurs between an *O*-silylcarbamate and a silyl amine *via* a proton - silyl transfer - decarboxylation to yield amine and *N*-silyl-*O*-silylcarbamate (**144**). Further reaction between the isocyanate and amines yields urea (Scheme 1.49). The reaction proceeds in moderate yields under harsh conditions of 140 bar and 120 °C.



Scheme 1.49: Synthesis of symmetrical ureas using $ScCO_2$.

1.3.2.3 Generation of Carbamates

The industrial production of carbamates (polyurethanes) is based on the reaction between isocyanates and amines, as was explained in section 1.1.2, and does not require the use of carbon dioxide in any of its sequences. However, scientists have been trying to developed cleaner and safer alternative routes in spite of the existing simple phosgene strategy. Some of these routes use carbon dioxide as one of the starting materials. The simplest of the series has been a process consisting of two steps; first the formation of carbamic acid by reaction between amines and carbon dioxide, followed by reaction *in situ* with alkyl halides (Scheme 1.50).[81] The first step is an equilibrium which generally

favors the starting material; however, pressure of carbon dioxide, low temperatures and bases promote the equilibrium towards the carbamic acid.

145 **146** **147**

Scheme 1.50: Generation of carbamates.

In the same way that oxiranes are used for the generation of carbonates, aziridines can be used in a similar process to synthesise carbamates. Alkali metal salts as catalysts promote the reaction, however, they are not essential.[82]

1.4 [2π+2π] Cycloadditions

Cycloaddition reactions have been known for many years and have become a powerful tool in organic synthesis for the generation of rings, especially for the generation of aromatic and non-aromatic heterocycles.[83] According to the Woodward-Hoffmann rules, the [2nπ+2π] cycloaddition is forbidden under thermal conditions and allowed under photochemical conditions. The reason for the behavior lies in the aptitude of an unfavorable anti-bonding relationship between the LUMO of one of the double bonds with the HOMO of the other double bond (Figure 1.5). When the number of electrons changes to [4nπ+2π], cycloadditions are allowed under thermal conditions and forbidden under photochemical conditions.[84] In our case we were interested in concerted [2π+2π] cycloaddition reactions.

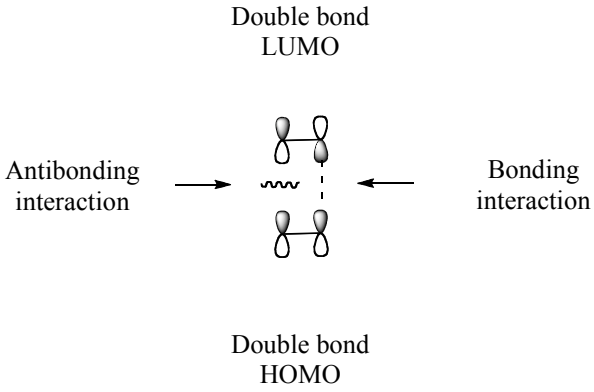
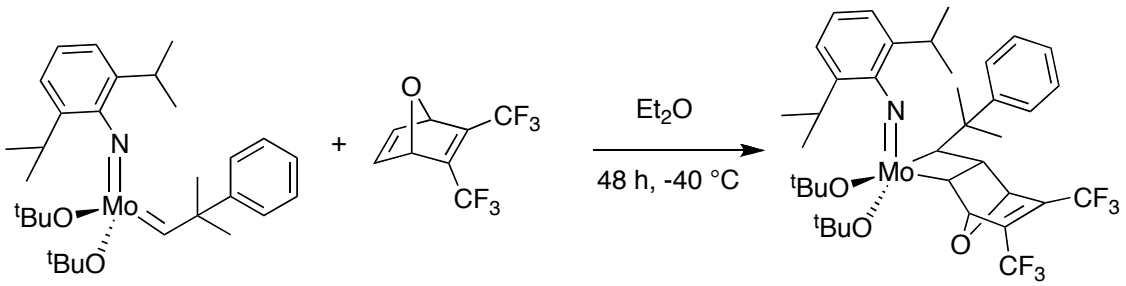


Figure 1.5: Bonding - anti-bonding interaction between HOMO and LUMO.

On the other hand, the Woodward-Hoffmann rules can only be applied when sp^2 orbitals are initially involved in the cycloaddition. When transition metal complexes are part of one of the double bonds in the cycloaddition, *d*-orbitals can be involved allowing thermal [2π+2π] cycloaddition.[85] As an example of this reactivity, Schrock and co-workers have reported the formation of metallocycles for molybdenum and tungsten which exhibited selectivity towards the electron-donating ability of the olefin (Scheme 1.51). This is an example of [2π+2π] cycloaddition process where the presence of the metal centre allows the reaction due to its *d*-orbitals.



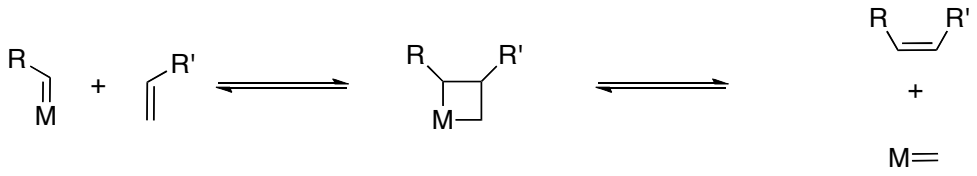
148 **149** **150**

Scheme 1.51: [2+2] Cycloaddition using Schrock's catalyst.

In some of the cases, such as the example above, it is possible to isolate and characterise the four-membered ring metallocycle. However, despite these examples, some cycloadditions are followed by a retro-cycloaddition and the metallocycle is a very unstable intermediate, never isolated. In other cases the intermediates can be isolated

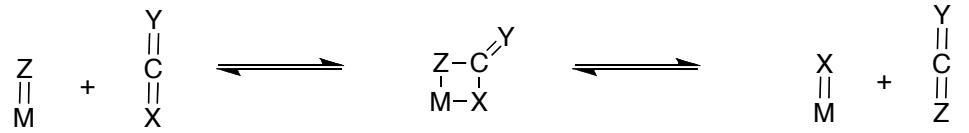
and the reaction can also be driven to completion (retro-cycloaddition) by the formation of the most thermodynamically stable of the products.

Relating these two above-mentioned processes, it is left to identify the junction of the use of transition metal complexes which allows processes with the metathesis process (cycloaddition - retro-cycloaddition). In fact, most of the cases where a transition metal is involved in a [2π+2π] cycloaddition reaction are followed by a [2π+2π] retro-cycloaddition. The most used, known and studied of these reactions has been the olefin metathesis reaction in all its variations (ring closure, ring opening, crossed and enyne metathesis), which has become a very important field in organic, organometallic and inorganic chemistry (Scheme 1.52). The importance of this field was highlighted when in 2005 the Nobel prize was awarded to Yves Chauvin, Robert H. Grubbs and Richard R. Schrock for their contribution to studies in the field.



Scheme 1.52: Equilibria cross-metathesis.

However, metathesis is not limited to C-C π bonds, other heteroatom containing systems can also undergo similar reactions. Other subunits such as cumulated double bonds instead of simple olefins can also be used following this reactivity. This includes heterocumulene metathesis, in which a cumulated double bond (**152**) reacts with a double bond (**151**) exchanging one of the atoms (Scheme 1.53). Preferably, the metal complex forms one of the atoms in the olefin. As we are interested in [2π+2π] cycloadditions, the intermediate (**153**) is a four-membered ring metallocycle in most of the cases. The product of the process is another heterocumulene (**155**) and a new metallo-olefin (**154**). The overall process is an equilibrium with an heteroatom exchange. However, it can be displaced favoring one direction according to the thermodynamic stability of the products.



151 **152** **153** **154** **155**

Scheme 1.53: Equilibria heterocumulene metathesis.

Although there exist different types of metathesis reactivity, we are only going to focus on heterocumulene metathesis, and inside this family we will be studying in more detail the equilibrium between isocyanates and carbon dioxide on one side; on the other side the synthesis of carbodiimide (or the equilibrium between carbon dioxide - isocyanate - carbodiimide).

1.4.1 Isocyanate - Carbon Dioxide Equilibria

For more than 20 years the reaction of transition metal complexes with cumulated double bonds has been known and studied. In all these investigations, isocyanates represent the most studied of the heterocumulenes, which implies reactivity with an enormous number of transition metals. Isocyanates are very reactive and unsymmetrical functional groups. There exists a delocalisation of the electron-density towards the two heteroatoms, leaving a very electron-positive carbon (Figure 1.6). There is also a dipole in the molecule where orientation depends on the substituents on the nitrogen atom. The two π-bonds are orthogonal to one another.

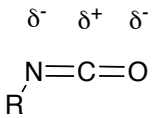
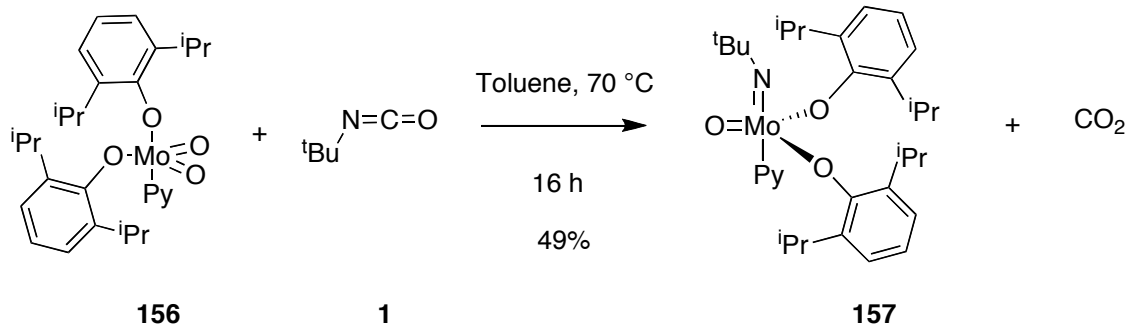


Figure 1.6: Polar moment in isocyanates.

The delocalisation of the electron-density into two different and separated atoms (nitrogen and oxygen), can be interpreted as two different reaction sites in the functional group. This characteristic gives isocyanates the ability to coordinate *via* two different places, generating completely different reactivity. On the other hand the functional

group only has one electron-deficient centre which limit its reactivity with nucleophiles. Considering dipolar cycloadditions, the regiochemistry could also be another issue due to the delocalisation of the electron-density into two different atoms, giving different possibilities of reactivity. Two key factors influence this behavior; steric hindrance in the nitrogen atom and its electronic nature which are affected by the *N*-substituents. Generally oxygen is more electronegative than the imido substituent and less hindered, therefore its electron-density and nucleophilicity will be higher.

One of the first heterocumulene metathesis reactions reported using isocyanates and metal complexes was the generation of metal-imido complexes from metal-oxo complexes.[86] It soon became an extended, reliable and well known method for the generation of the metal-imido moiety, opening the door towards the study of these new functional groups (Scheme 1.54). A wide variety of metal-oxo complexes have also been shown to undergo this reaction, such as tungsten,[87] niobium,[88] rhenium,[89] vanadium,[90] tantalum[91] and molybdenum[92] which have been the most studied.



156 **1** **157**

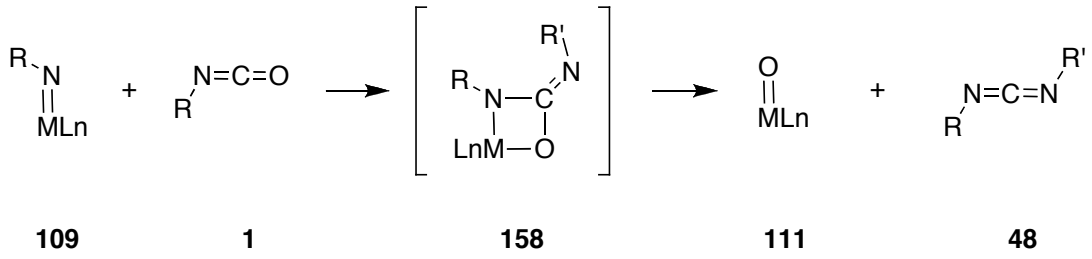
Scheme 1.54: Anderson generation of Mo=N.

This robust method for the generation of metal-imido complexes generally requires high temperatures and long periods of time to yield the product. The by-product in these metathesis reactions is assumed to be carbon dioxide. The accepted transition state or intermediate is a high energy four-membered ring metallocycle. It is not known whether the process is energetically favorable or not. However, the removal of one of the products by formation of carbon dioxide gas, displaces the equilibrium towards the products. The cases where the reactivity is reversed and carbon dioxide is used to generate isocyanates and metal-oxo complexes are very rare.

1.4.2 Isocyanate - Carbodiimide Equilibria

Carbodiimides are the bisimines of carbon dioxide. There is a quadrupolar moment in the molecule. However, depending on the substituents on the nitrogen atoms, there might be separation of the dipole.

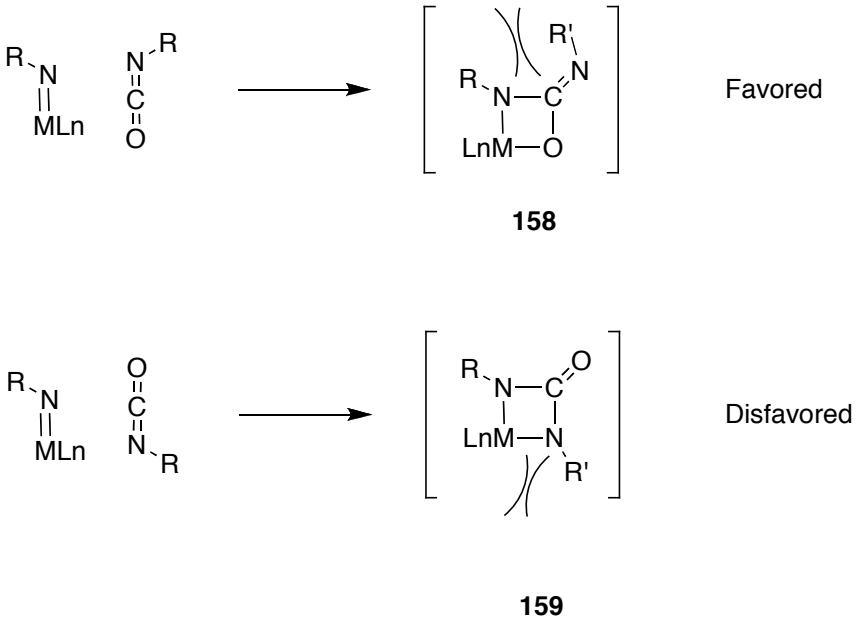
The [2+2] cycloaddition - [2+2] retro-cycloaddition equilibrium explained above can be extrapolated to isocyanates and carbodiimides as they are another example of the heterocumulene metathesis reaction (Scheme 1.55). There are big differences between the two processes: the use of a different starting material is the obvious starting point and this [2+2] process requires a metal-imido complex and an isocyanate.



109 **1** **158** **111** **48**

Scheme 1.55: Generation of carbodiimides by heterocumulene metathesis.

Despite the presence of two electron-rich centres in the molecule, the hindrance generated between the clash of the imido group and the isocyanate forces the approach of the molecules to react *via* C=O (Scheme 1.56). Either oxygen or nitrogen could approach the metal, however, when the oxygen end of the isocyanate approaches it, steric interactions are minimised generating a more stable transition state. On the other hand, the approach of the nitrogen end of the isocyanate generates higher steric interactions, leading to a higher energy transition state, leading to a faster retro-cycloaddition. This selectivity may also be affected by the choice of the metal.

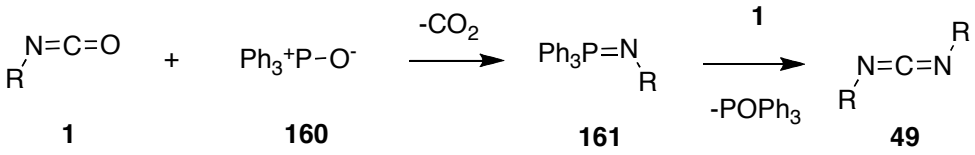


Scheme 1.56: Possible approaches in heterocumulene metathesis.

The last of the differences is the generation of a carbodiimide, which is more stable and less reactive than an isocyanate.

1.4.3 Combination of Equilibria

Obviously both equilibria are related and in some of the cases work consecutively. This is the case for the aza-Wittig reaction, the self reaction of isocyanates (**1**) to generate symmetrical carbodiimides (**49**).[93] In the first step a phosphine oxide (**160**) reacts with an isocyanate *via* the equilibrium explained above to generate an iminophosphorane (**161**). Although phosphine-oxides have a very strong phosphorus - oxygen double bond, the formation of carbon dioxide as a gas and the employment of harsh conditions allows the process to succeed. The second part of the process is the reaction of the iminophosphorane (**161**) with carbonyl compounds such as isocyanates (Scheme 1.57). In this second step the generation of a strong phosphine-oxide double bond favors the reaction, and more stable compounds such as carbon dioxide and carbodiimides are formed from isocyanates.



Scheme 1.57: Aza-Wittig for the formation of carbodiimides.

Although, according to the mechanism it is a catalytic process, a stoichiometric amount of phosphine oxide is required for the reaction to proceed, reported by the authors.[93] By ^{18}O labeling experiment it has been demonstrated that each carbon dioxide molecule is formed by an oxygen from the isocyanate and another from the phosphine oxide. Other transition metal complexes have been shown to catalyse the process.[94]

1.4.4 Spectator Ligand Effect

The spectator ligand effect is a highly studied characteristic in catalytic metathesis reactions. Previous to this research, some work had been done in our group concerning a study of the spectator ligand effect to assist the [2+2] addition of M=O bonds across the C=C bond of ketenes.[95] Transition metal oxo and imido bonds can have various bond orders; they can vary from one to three depending on the nature of the complex and the rest of the ligands. Both oxygen and nitrogen are highly electronegative compared to the transition metal, therefore can tolerate high electron-density. In the studied cases of oxo and imido ligands, the heteroatom ligand has one filled orbital of σ-symmetry and another of π-symmetry (Figure 1.7). In both cases there is a filled *p*-orbital on the heteroatom which can interact with empty *d*-orbitals in the metal centre, and depending on the nature of the complex this interaction will be stronger or weaker, producing more or less triple bond character. This effect could transform some ligands which are only 4-electron donors into 6-electron donor.

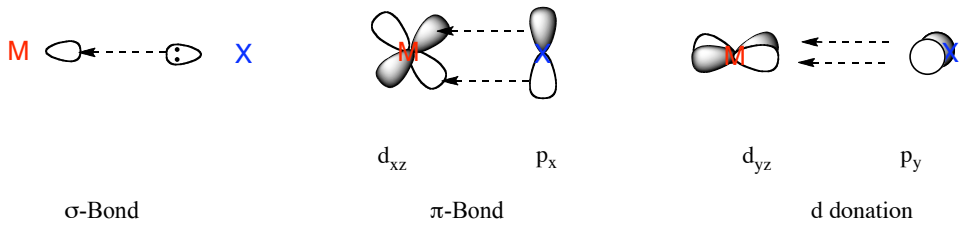


Figure 1.7: Possible overlap of orbitals ligand-metal multiple bonds.

More interesting cases are those where the presence of another multiple bond ligand may vary this donation effect. There is a limitation when there are two or more oxo or imido ligands trying to overlap with the same empty *d*-orbitals (Figure 1.8). The ligand more able to donate electrons normally has more triple bond character. This is a very interesting effect which could enhance the electronic richness and reactivity of the other ligand. Evidences for this effect can be obtained by X-ray diffraction in bond lengths and bond angles.

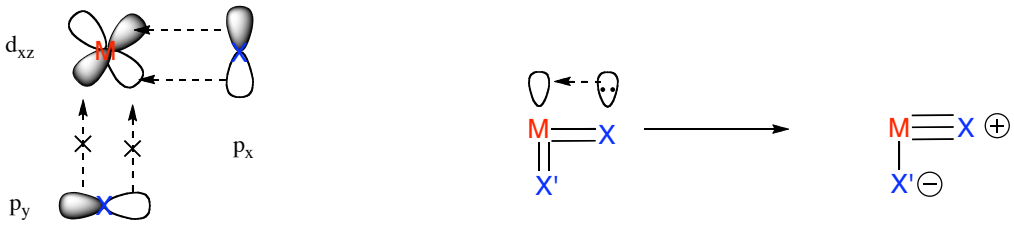
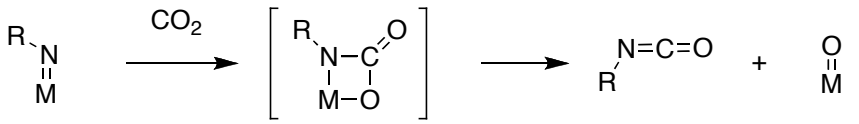


Figure 1.8: Spectator ligand effect.

1.5 Previous Work

The proposed research (section 1.2) had as the most important and key step of the process the heterocumulene metathesis reaction to transform a metal-imido complex (**109**) into a metal-oxo complex (**111**) using carbon dioxide and obtaining isocyanate (**1**) (Scheme 1.58).



109 **110** **1** **111**

Scheme 1.58: Heterocumulene metathesis to generate isocyanates.

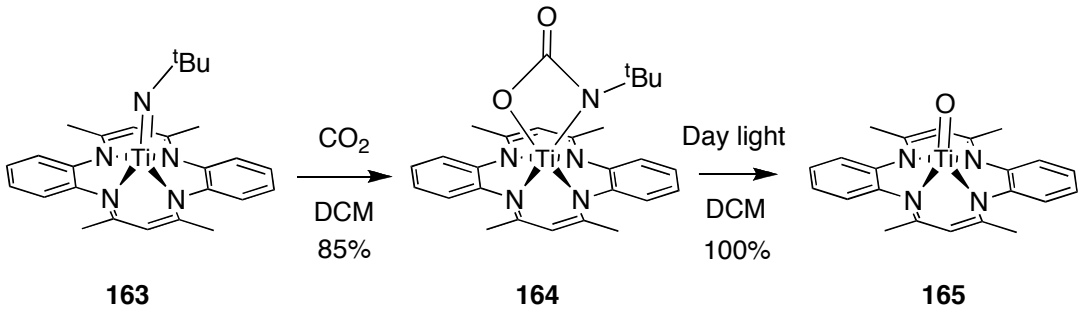
It has been seen in section 1.4.1, that this is an unfavorable process and as it is an equilibrium, generally favoring the reverse process due to the formation of carbon dioxide. In fact, the examples in the literature for the desired process are very rare. The

reverse reactivity is a well known and established method for the generation of metal-imido complexes.

1.5.1 Generation of Isocyanates

According to the literature, titanium is the only reported transition metal that does not follow the normal expected behavior of the transition metals, regarding reactivity with carbon dioxide and isocyanates. There have been only four examples published where titanium-imido complexes react with carbon dioxide to generate titanium-oxo complexes or isocyanates.

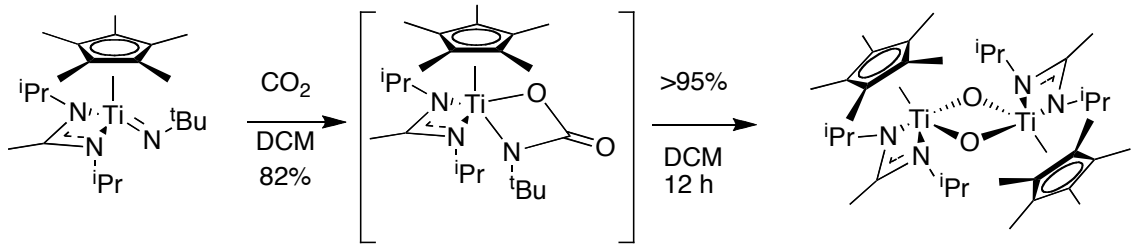
The first appearance in the literature of a titanium-imido complex reacting with carbon dioxide was reported by Mountford *et at*., isolating titanium-oxo species in high yield.[96] As was mentioned earlier, there were two steps involved in the process. X-ray diffraction studies of an intermediate showed a four membered ring metallocycle (**164**) which had inserted carbon dioxide after a [2+2] cycloaddition to generate a reasonably stable complex. In solution **164**, under ambient light decomposed *via* a [2+2] retro-cycloaddition to the titanium-oxo species **165** (Scheme 1.59). No detection of isocyanate, as the expected by-product, was recorded.



Scheme 1.59: Heterocumulene metathesis using carbon dioxide.

The same research group published the second reaction of titanium-imido complexes with carbon dioxide few years later.[97] The first reaction in 1999, showed a titanium-imido 12-electron complex reacting with carbon dioxide to form a four membered ring metallocycle; however, in 2001 a 10-electron titanium-imido complex (**166**) was

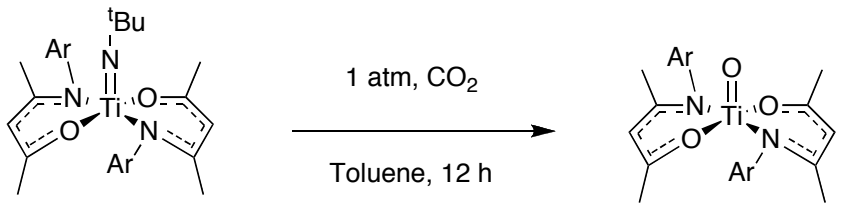
published which reacted in the same fashion giving the same result in similar yield. This 10-electron titanium-imido complex quantitatively decomposed to a titanium-oxo complex which then dimerised (**168**) (Scheme 1.60). In this case, like in the first reaction, no isocyanate was detected, and also no detection of the titanium-oxo complex monomer was obtained.



166 **167** **168**

Scheme 1.60: Heterocumulene metathesis using carbon dioxide.

Huang and Co-workers were another research group that reported heterocumulene metathesis between a titanium-imido complex and carbon dioxide.[98] The application of one atmosphere of carbon dioxide to complex **169** generated titanium-oxo complex (**170**) in 76% yield (Scheme 1.61). In their early work, no mention of the assumed four membered metallocycle intermediate was made. There was no mention either of the detection of the assumed ^{t}butyl isocyanate by-product of the reaction.

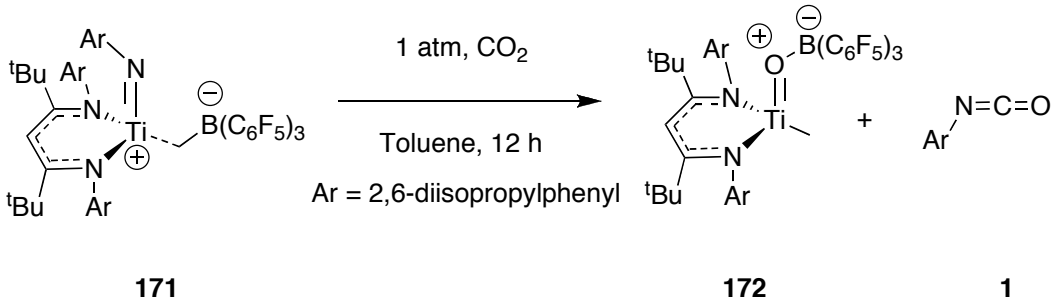


169 **170**

Scheme 1.61: Heterocumulene metathesis using carbon dioxide.

The most recently reported example of this reactivity was by Mindiola *et al*. In their research, quantitative conversion of carbon dioxide into an isocyanate *via* a metathesis reaction with titanium-imido zwitterion complex **172** was achieved.[99] The reaction is

believed to undergo a [2+2] cycloaddition - retro-cycloaddition as proposed in the mechanism which provided titanium-oxo complex **172** and isocyanate **1** (Scheme 1.62).

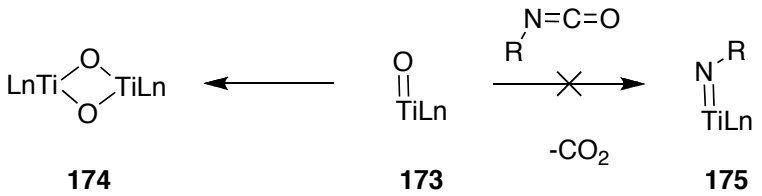


171 **172** **1**

Scheme 1.62: Heterocumulene metathesis using carbon dioxide.

In this particular case, the need for a latent low coordinate titanium-imido ligand is proposed to be crucial for the reaction to occur, in order for the titanium to activate and react with carbon dioxide. As it can be seen, a 10-electron complex is involved in the reaction. It is suggested that the reaction proceeds *via* displacement of the labile borate ligand $[CH_3B(C_6F_5)_3]^-$ by carbon dioxide and subsequent [2+2] cycloaddition to afford a hypothetical carbamate metallocycle, which then undergoes [2+2] retro-cycloaddition to yield titanium-oxo **172**. This represents the first heteroatomic reaction between carbon dioxide and a titanium-imido complex which reports the formation of a isocyanate and titanium-oxo complex, as well as the first example whose imido group was derived from aniline.

The generation of titanium-oxo complexes from titanium-imido complexes and carbon dioxide has been reported in the literature as a difficult, and not very common process, which only selected complexes with determined characteristics follow. On the other hand, there is no precedent in the literature of the reverse reaction where titanium-oxo complexes (**173**) react with isocyanates to generate titanium-imido complexes (**175**) and carbon dioxide (Scheme 1.63). The strong titanium - oxygen double bond does not undergo metathesis reactions with isocyanates, and dimerisation *via* a [2+2] cycloaddition is observed instead. Such a dimerisation generates a very stable oxo-bridged compound (**174**), inert in most of the previously reported processes.



174 **173** **175**

Scheme 1.63: Reactivity of Ti=O.

With these precedents in the literature an obvious starting point is to consider titanium as a candidate for the role of metal centre for our desired process. However, the bulkiness around the metal centre is a very important factor as it hinders the ability to the oxo-dimerisation.

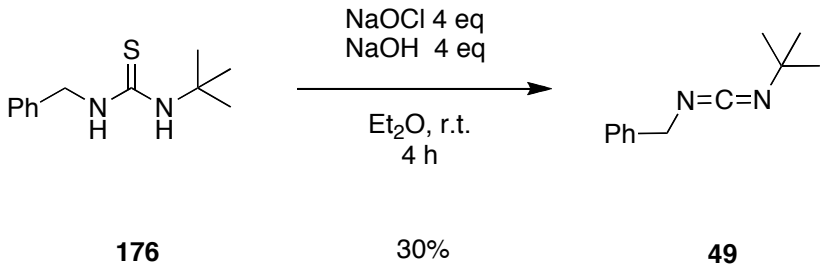
1.5.2 Generation of Carbodiimides

As was seen in section 1.1.5, carbodiimides are versatile functional groups which have been used as precursors for many interesting functional groups in both medicinal chemistry and total synthesis. The interest for their generation began more than 35 years ago, however, the lack of a standard route still remains. Since the first synthesis several methods have been studied and developed for their generation.

1.5.2.1 Dehydration of Ureas and Derivatives

The dehydration of ureas has proven to be a harsh method for the generation of carbodiimides due to the conditions needed for the reaction. However, when urea derivatives such as thio-ureas or seleno-ureas are used, elimination occurs under milder conditions.

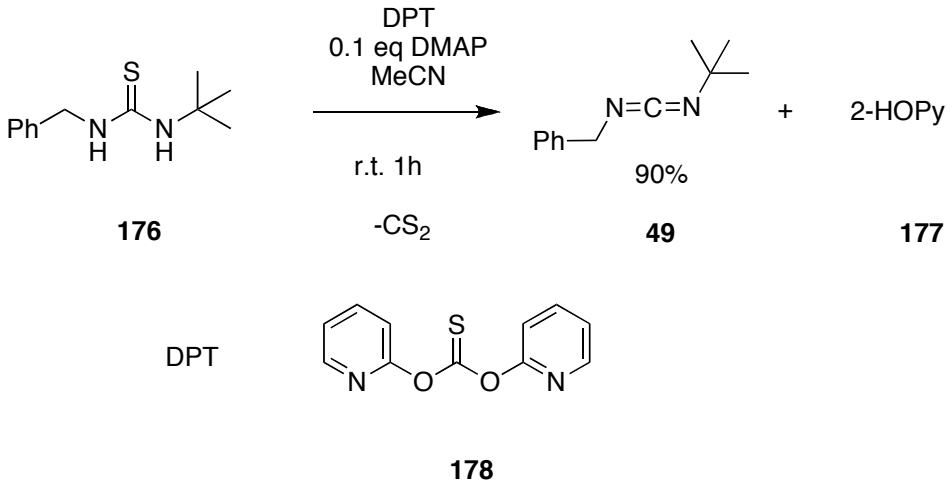
Using sodium hypochlorite and sodium hydroxide at room temperature, Wragg and co-workers transformed thio-ureas (**176**) into carbodiimides (**49**) by removal of hydrogen sulfide (Scheme 1.64).[100] Although the reaction was complete at room temperature over a period of 4 h, the applicability of this method is limited due to the need for strong oxidising agent.



176 30% **49**

Scheme 1.64: Synthesis of carbodiimides 1.

The same transformation was later developed using different reactions conditions by Kim *et al.*[101] Their development was based on the formation of carbon disulfide as by-product instead of removal of hydrogen sulfide (Scheme 1.65). By the employment of di-2-pyridyl thiocarbonate **177**, thiourea **176** was activated to react and promote the formation of the carbodiimide **49** in high yields. This methodology gave an advantage compared to that developed by Wragg and co-workers due to milder conditions and higher yields.

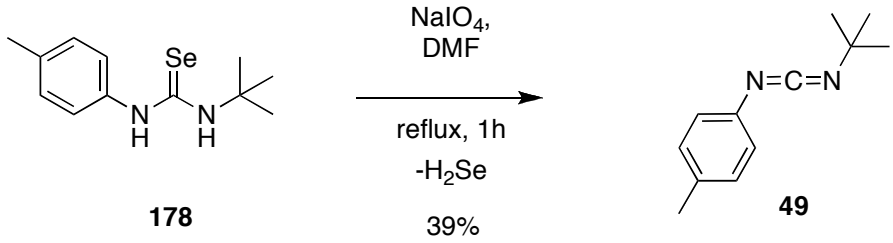


176 **49** **177**

178

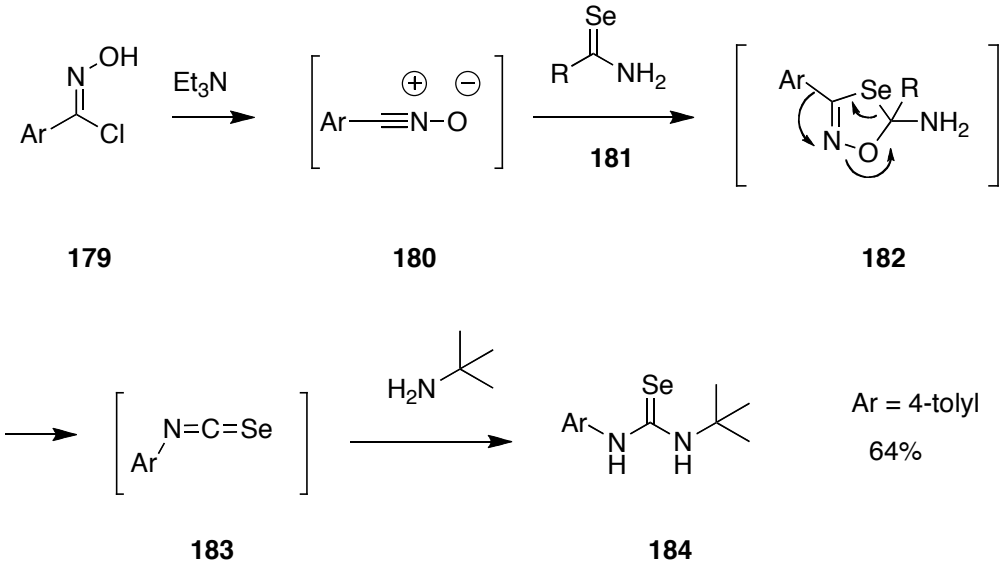
Scheme 1.65: Synthesis of carbodiimides 2.

Although the formation of carbodiimides by this method was very successful under very mild conditions, Koketsu *et al*. improved the yields and the scope of the process by applying similar methodology to selenoureas.[102] This methodology generated carbodiimides (**49**) from selenoureas (**178**) in a facile manner in moderate to high yields (Scheme 1.66).



Scheme 1.66: Synthesis of carbodiimides 3.

Although generation of the carbodiimide by deselenation of selenoureas proved to be a facile and efficient method it has not been extensively used due to the use of strong oxidising agents, such as sodium periodate, and the difficulty in generating seleno-ureas. Alternative reaction of nitrile oxide **180**, generated *in situ* from chlorooxime **179**, with selenamide **181** can generate a five-membered intermediate **182**. Rearrangement and migration of the Ar group generated the intermediate selenocyanate **183**, which finally reacted with a variety of amines to yield seleno-ureas (**184**) in moderate yields (Scheme 1.67).

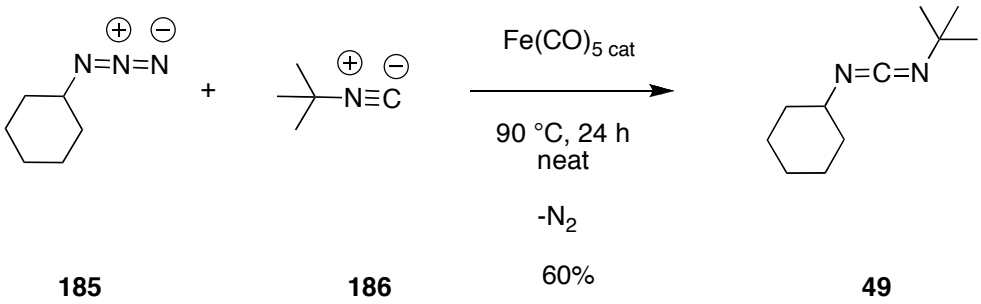


Scheme 1.67: Generation of seleno-ureas.

1.5.2.2 Catalytic Amination of Isocyanides

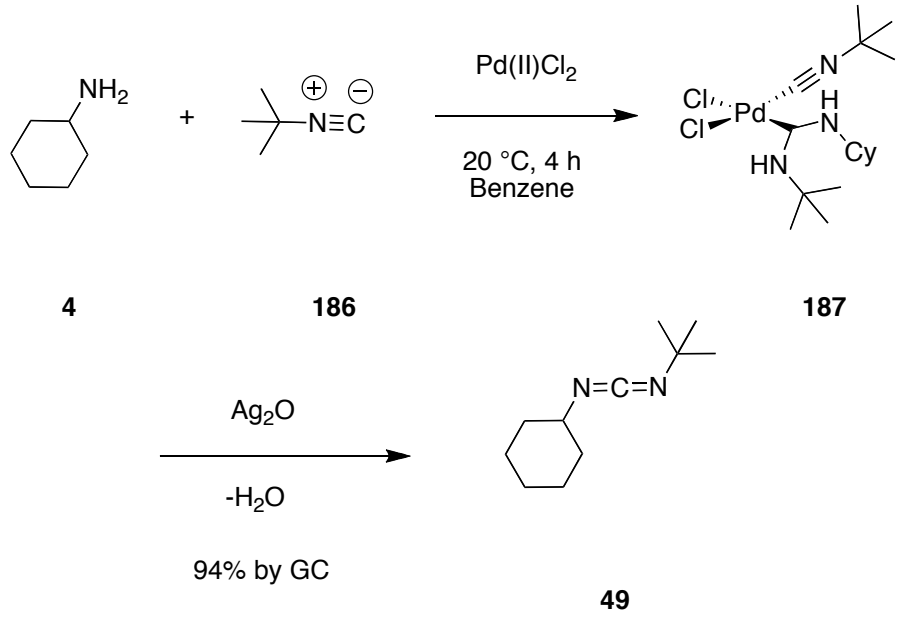
Despite the development of the facile route above to carbodiimides, the use of strong oxidising agents limits its potential application. At a similar period a catalytic process

was developed by Saegusa and co-workers.[103] In their research, $Fe(CO)_5$ catalyses the formation of carbodiimides **49** by reaction of isocyanides **186** with azides **185** in moderate yield (Scheme 1.68). No formation of symmetrical carbodiimides was observed in any of the examples. Supported by some literature precedent, it is believed that the iron catalyst reacts with the azide to form an intermediate ferro-nitrene species which then reacts with isocyanide to generate an unsymmetrical carbodiimide.[104]



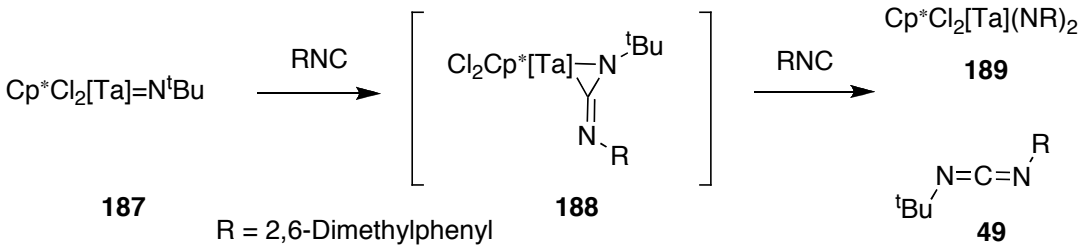
Scheme 1.68: Synthesis of carbodiimides by catalytic amination of isocyanindes.

The same research group developed this reaction further by substitution of the azide with simple amines as starting material.[105] With this clever development the reaction not only became easier to handle, but also gave carbodiimides in better yield and with broader scope. This novel development employed palladium(II) chloride as a catalyst to form a palladium(II) carbene intermediate **187**, with the addition of an isocyanide ligand from amine **4** and isocyanide **186**. Subsequent reaction with silver oxide generated carbodiimide **49** and water as a by-product (Scheme 1.69). One disadvantage of the reaction is the requirement of stoichiometric amounts of silver oxide to form the product and two equivalents of isocyanade.



Scheme 1.69: Amination of isocyanides by palladium to generate carbodiimides.

In a similar approach, previously prepared tantalum imido complex **187**, was reacted with three equivalents of isocyanide to generate carbodiimide **49** in high yield.[106] The mechanism was believed to follow a [2+2] cycloaddition to form a three-membered metallocycle **188**, followed by decomposition to form carbodiimide **49** and a new tantalum complex **189** with two other isocyanide ligands (Scheme 1.70).

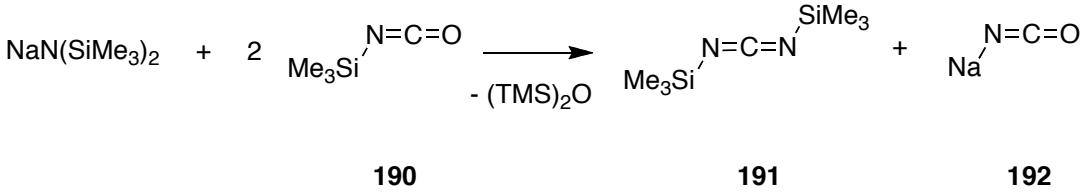


Scheme 1.70: Stoichiometric [2+2] of isocyanides and Ta=N.

1.5.2.3 Stoichiometric Activation by Tin

The reactivity of silylamides has been studied extensively and they show similarities with respect to the same unprotected amine in terms of reactivity. Wannagat and co-workers have previously shown that sodium hexamethyldisilazide reacts with two equivalents of trimethylsilylisocyanate **190** to produce bis-trimethylsilylcarbodiimide

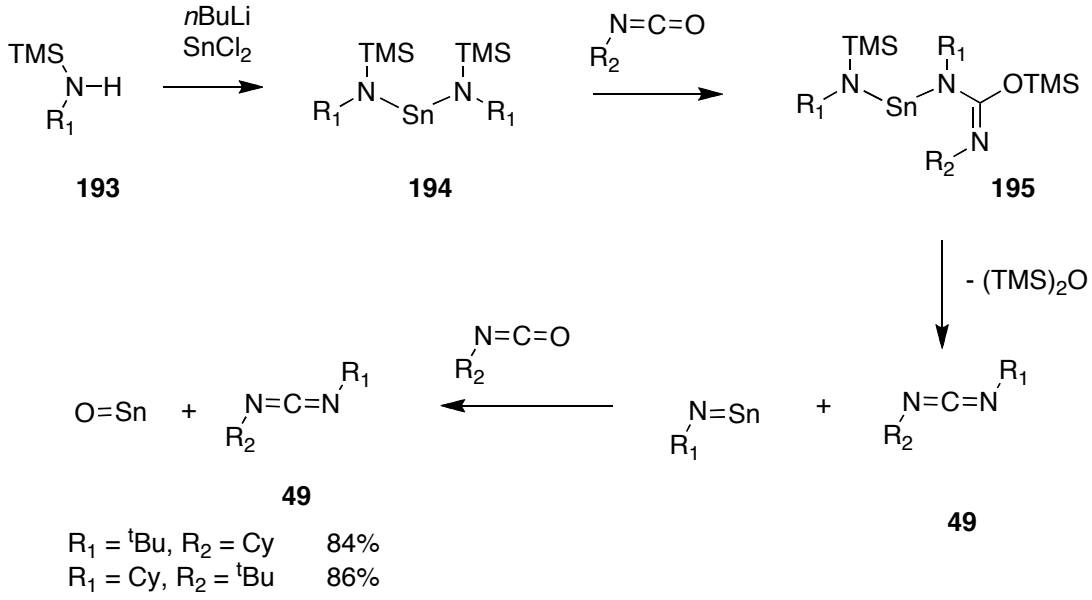
191 (Scheme 1.71).[107] The second equivalent of trimethylsilylisocyanate is required to react with the TMS alkoxide and avoid side reactions. A similar variation has been carried out using thioisocyanates, however only low yields were obtained.[108]



190 **191** **192**

Scheme 1.71: Generation of symmetrical carbodiimides.

Following a similar idea, Sita and co-workers studied a method to eliminate the use of sodium hexamethyldisilazide, which could be extended to isocyanates with substituents other than trimethylsilyl.[109] The reaction of monomeric tin(II) bisamide **194** with two equivalents of isocyanate generated carbodiimide **49** in 94 - 95% yield, showing high yields under mild reaction conditions. Yet again this reaction requires the use of one equivalent of isocyanate to react with the alkoxide by-product. In addition, the limitation in the availability of the tin(II) bisamide species reduces the scope of the reaction. Deprotonation of silylamine **193** and addition of half an equivalent of tin(II) chloride allowed formation of the tin-bisamide *in situ*, followed by reaction with isocyanate to generate carbodiimide **49** in high yield with broad scope of reactivity (Scheme 1.72).



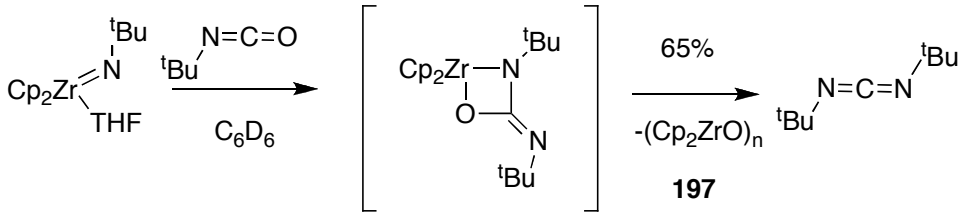
193 **194** **195** **49** **49**

Scheme 1.72: Synthesis of symmetrical carbodiimides by activation with Sn.

Other versions of similar methodology have also been developed using silicon, tin(IV) and germanium(IV) with similar results and have been extended to isocyanates and thioisocyanates.[110]

1.5.2.4 Heterocumulene Metathesis

Heteroatom metathesis is another method which could be used for the synthesis of carbodiimides. Several groups have reported their success in this area. It is interesting to notice that this methodology is similar to the method we proposed for our synthesis of carbodiimides. Walsh *et al*. showed how imido zirconocene **195** could be transformed into oligomeric zirconocene oxide **197** and carbodiimide **49** by simple reaction at room temperature in a sealed NMR tube (Scheme 1.73).[111] No proof of a four membered metallocycle was reported and is only assumed based on previous literature precedents.[112]

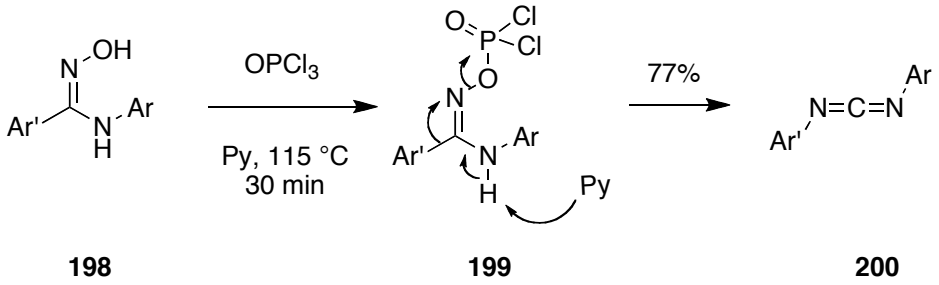


195 **196** **49**

Scheme 1.73: Heterocumulene metathesis with isocyanates to generate carbodiimides.

1.5.2.5 Tiemann Rearrangement

During the 1970's, rearrangement of electron-deficient amidoximes, as a source of carbodiimide, was developed.[113] A very facile method where amidoximes **198** reacted with phosphorus oxotrichloride was developed to form an electron-deficient amidoxime **199** *in situ*. Deprotonation, rearrangement and elimination of the phosphorus oxide generated carbodiimide **49** (Scheme 1.74). One limitation in the scope of this reaction is the use of only electron-rich aromatic substrates.

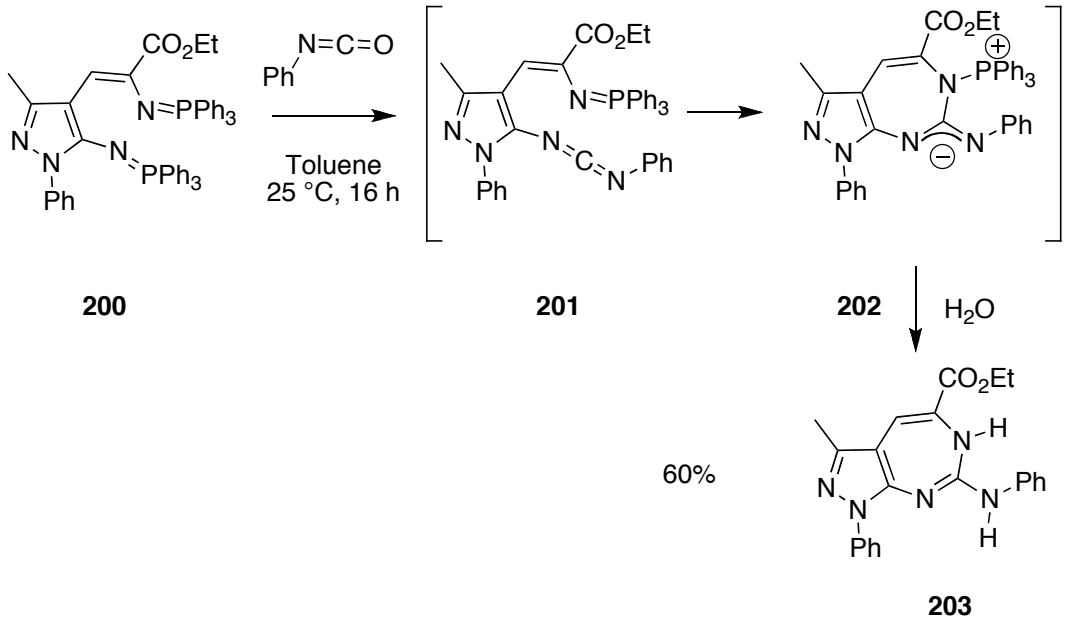


198 **199** **200**

Scheme 1.74: Synthesis of carbodiimides by dehydration of amidoximes.

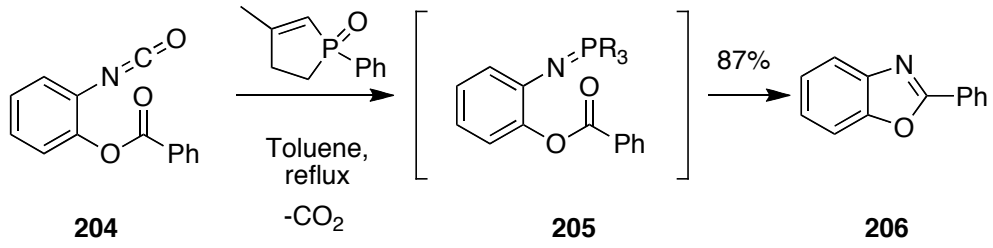
1.5.2.6 Aza-Wittig Reaction

A very successful method developed over the past 20 years and fully explored for the generation of carbodiimides has been the aza-Wittig reaction. This reaction is a variation of the Wittig reaction, where the substrate is a phosphine-amide as a ylide. Our interest lies when it is used with isocyanates, as partners in the reaction. In these cases, the product is a carbodiimide and was originally developed to generate symmetrical products by formation of the phosphine-amide *in situ*.[114] In more recent years, the reaction has evolved to the formation of the phosphine-amide and subsequent aza-Wittig reaction. As carbodiimides are unstable and are usually generated as precursors for more complicated structures, they are generated *in situ* and subsequently reacted with other functional groups (Scheme 1.75). Molina and co-worker have developed the generation of guanidines by an aza-Wittig reaction followed by a nucleophilic addition and hydrolysis in high yield using mild conditions.[115]



Scheme 1.75: Synthesis of carbodiimides by aza-Wittig.

The aza-Wittig reaction has also been used for the generation of imine derivatives in a two-step process by Marsden and co-workers.[116] In the first instance, isocyanate (**204**) and phosphine-oxide form phosphine-amide (**205**) and carbon dioxide as by product. This intermediate can undergo an aza-Wittig reaction with carbonyls (Scheme 1.76). This methodology can also be used for the generation of heterocycles.



Scheme 1.76: Generation of heterocycles.

Due to the excellent reactivity of phosphine-oxides with isocyanates, this methodology cannot be used in our research, our interest relies in reversing this reactivity. However, this reaction (Scheme 1.76) is driven by the formation of carbon dioxide and phosphine-oxide.

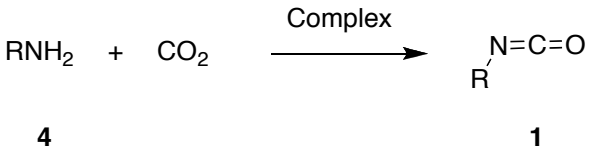
CHAPTER 2:

STUDIES ON IMIDO-MOLYBDENUM COMPLEXES

CHAPTER 2: STUDIES ON IMIDO-MOLYBDENUM COMPLEXES

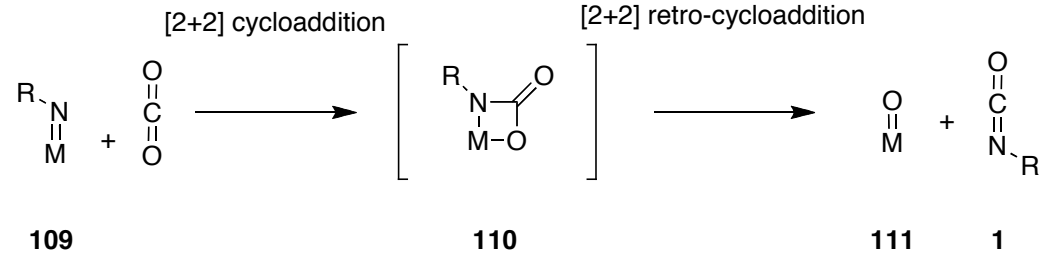
2.1 Introduction

The goal of this project is the design and synthesis of a complex capable of transforming an amine into an isocyanate by activation and reaction with carbon dioxide (Scheme 2.1).



Scheme 2.1: Aim of the project.

This chapter discusses the generation of molybdenum-imido complexes and their reactivity with carbon dioxide. With the metal-imido complexes in hand, the desired process involves a heterocumulene metathesis ([2+2] cycloaddition - [2+2] retro-cycloaddition) mechanism where carbon dioxide adds across the previously formed metal-imido complex to form a four-membered metallocycle **110**. Decomposition of the metallocycle intermediate would form the isocyanate **1** and metal-oxo complex **111** (Scheme 2.2).



Scheme 2.2: Heterocumulene metathesis.

The first step is the selection of the right transition metal for the design and preparation of the complex. For the selection of the metal centre several key factors had to be considered according to the proposed reactivity.

- Facile formation of imido and oxo bonds with the metal centre.
- The metal-heteroatom double bond must undergo [2+2] cycloaddition with cumulated double bonds.
- Selective cycloaddition with carbon dioxide in the presence of isocyanates.

Once the metal centre had been chosen, the properties of the complex could be varied by ligand tuning.

Other factors considered were:

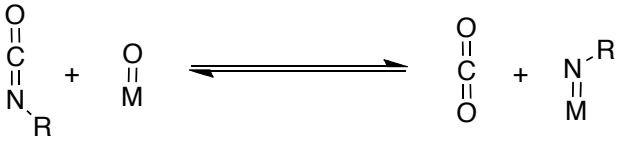
- The stability of the complex towards air and moisture.
- The compatibility of the metal complex with the reagents.

Considering all of the above points, the [2+2] cycloaddition of the metal-heteroatom double bond reacting with cumulated double bonds (metathesis reaction) is the most important of all the processes. The number of transition metal complexes that follow this reactivity is immense (section 1.4.1). However, when limiting this reactivity between isocyanates or carbon dioxide and cumulated double bonds, only a few transition metals can be considered as suitable candidates. Some of these transition metals, such as tungsten, niobium, rhenium, vanadium, tantalum and molybdenum were presented in section 1.4.

2.2 Studies on Molybdenum Complexes

Our interest lies in a transition metal complex capable of forming isocyanates from carbon dioxide *via* heterocumulene metathesis (as explained in section 1.2). However, most of the complexes reported to undergo this reactivity follow the reverse reaction to which we are interested; the formation of metal-imido complexes (**109**) and carbon dioxide by the reaction of metal-oxo complexes (**111**) and isocyanates (**1**) (Scheme 2.3).

The process is considered an equilibrium between all the components, and several factors are involved.

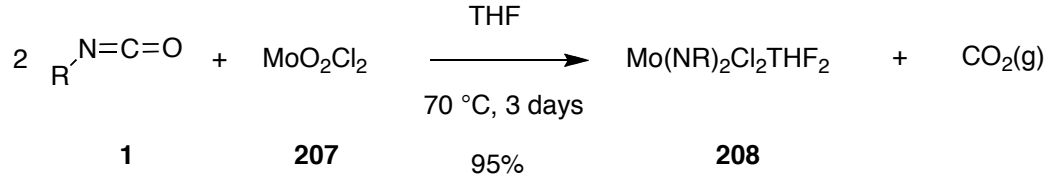


1 **111** **109**

Scheme 2.3: Heterocumulene metathesis equilibrium.

The thermodynamic stability of the complexes **111** and **109** generally favors the metal-oxo complexes **111** as they are more stable and less reactive than metal-imido complexes **109**. Concerning the cumulated double bonds, carbon dioxide is more stable and less reactive than isocyanates **1**. The nature of these opposing effects makes it very difficult to predict the direction of the equilibrium, and each particular case should be analysed carefully. In unsealed systems LeChatelier's principle contributes to the direction of the equilibrium as carbon dioxide is a gas, allowing its removal from the reaction.

Of all the transition metals, molybdenum complexes have the greatest number of reports in the literature for these types of reaction.[117] The potential of molybdenum-oxo complexes to undergo this transformation was seen by Osborn and co-workers when they heated a bis oxo-molybdenum complex (**207**) with an isocyanate (**1**) and generated the bis imido-molybdenum complex (**208**) (Scheme 2.4). The high yield of the reaction shows that the equilibrium is completely displaced to the formation of **208**, however, the requirement of refluxing THF (70 °C) for 3 days suggests that the reaction possesses a high activation energy.

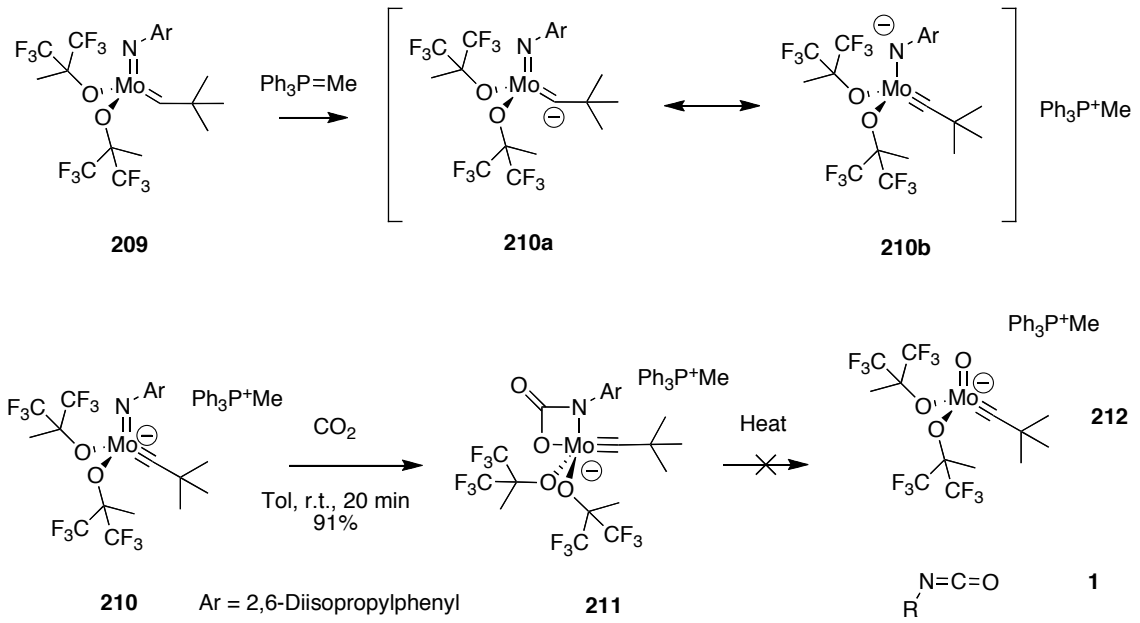


1 **207** 95% **208**

Scheme 2.4: Formation of M=N complexes.

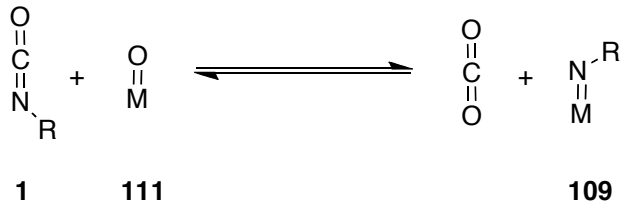
This reaction has become a standard methodology for the generation of metal-imido complexes from metal-oxo complexes and isocyanates. It is a clean reaction with carbon dioxide as the only by-product. However, as the conditions are quite harsh and the yields are in general moderate, it suggests that this reaction is not strongly thermodynamically favorable and only driven to completion by the loss of carbon dioxide (LeChatelier's principle). By the same principle, when adding an excess of one of the reagents (CO_2), the equilibrium may be able to be displaced towards the formation of the isocyanate.

In the literature the examples of molybdenum-imido complexes reacting with carbon dioxide are very rare. In 2006 Schrock and co-workers showed that imido-alkynyl-molybdenum complexes (**210**) can react with carbon dioxide to generate a four-membered metallocycle **211** in high yield.[118] The starting complex was a mono-anion generated by deprotonation of the alkylidene in complex **209** (Scheme 2.5). This enhanced the nucleophilicity of the imido ligand through a resonance effect (**210a** and **210b**). Reaction with carbon dioxide generated a metallocycle, which did not undergo [2+2] retro-cycloaddition to isocyanate or oxo-molybdenum complex, despite all their efforts. This example suggests that electron-rich molybdenum-imido complexes could be activated and, therefore react with carbon dioxide in the desired fashion. In this case the alkylidyne increases the electron-density of the metal, which increases the electron density of the imido ligand, activating it to react with carbon dioxide.



Scheme 2.5: Synthesis and reactivity of Schrock's Mo=N complex.

Previous to the work in this thesis, Anderson *et al*. developed a synthesis of molybdenum-imido complex **157** by the reaction of molybdenum-oxo complex (**156**) and isocyanates (**1**) (Scheme 1.54 in section 1.4.1). By comparison of complex **157** and **210**, it can be suggested as a general rule that the reaction between molybdenum-imido complexes and carbon dioxide (to yield molybdenum-oxo complexes and isocyanates) is more energetically favorable than the reverse process due to the formation molybdenum-oxo complexes which are more thermodynamically stable (Scheme 2.6). It is the formation and removal of carbon dioxide which drives the reverse reaction.



Scheme 2.6: Heterocumulene metathesis equilibrium

The X-ray crystal data of the two compounds shows a longer Mo=N bond length for Schrock's complex (1.813 Å), compared with 1.736 Å for Anderson's complex. Also the Mo-N-C bond angle is smaller in Schrock's complex (141°) compared with 173° for Anderson's complex. The bond angles and bond length suggests double bond (sp^2)

character between the nitrogen and the metal centre in Schrock's complex. The shorter bond length and larger bond angle in Anderson's complex suggests more sp character and potentially a stronger triple bond; this stronger bond may make reaction with carbon dioxide more difficult. In Schrock's complex (**210**) the anionic alkylidyne ligand occupies the orbital that could accept the two electrons from imido ligand lone pair. Thus the imido ligand in complex **210** is a 4-electron donor. In Anderson's complex (**157**) the imido lone pair can interact with an empty orbital and become a 6-electron donor.

1.813 Å
141°

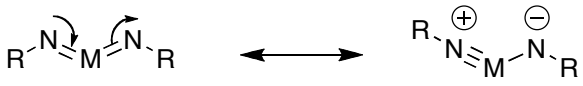
210

1.736 Å
173°

157

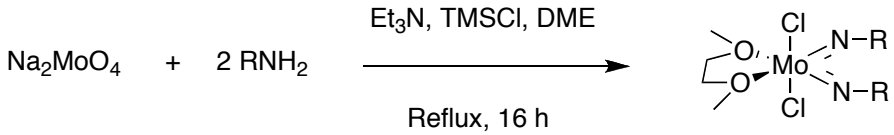
Scheme 2.7: Lengths and bond angles.

We wanted to investigate the synthesis of molybdenum-imido complexes and their reactivity with carbon dioxide and were interested in the generation of a complex with properties between the two above (**157** and **210**). A complex with more electron-density on the metal centre than Anderson's complex, but not as much as in Schrock's complex could react with carbon dioxide to form a metallocycle and may decompose to form an isocyanate. A bisimido complex was considered due to the spectator ligand effect where one of the imido ligands can be more electron donating than the other. The donation of electron-density by one of the imido ligands into a *d*-orbital of the metal may increase the electron-density in the other imido ligand, as they are competing for the same *d*-orbital (Scheme 2.8). This would increase the nucleophilicity of the imido ligand and, therefore, the reactivity against electrophiles such as carbon dioxide.



Scheme 2.8: Spectator ligand effect in bis-imido complexes.

Following Schrock and co-workers' procedure, literature complexes bisimido complex **214a,b** were successfully synthesised when the R group was an aromatic group.[119] However, this was unsuccessful for a novel non-aromatic amines such as benzylamine (Scheme 2.9). In one single step bisimido molybdenum complexes can be synthesised from the available starting material Na_2MoO_4 with moderate to good yield.



213 **4** **214**

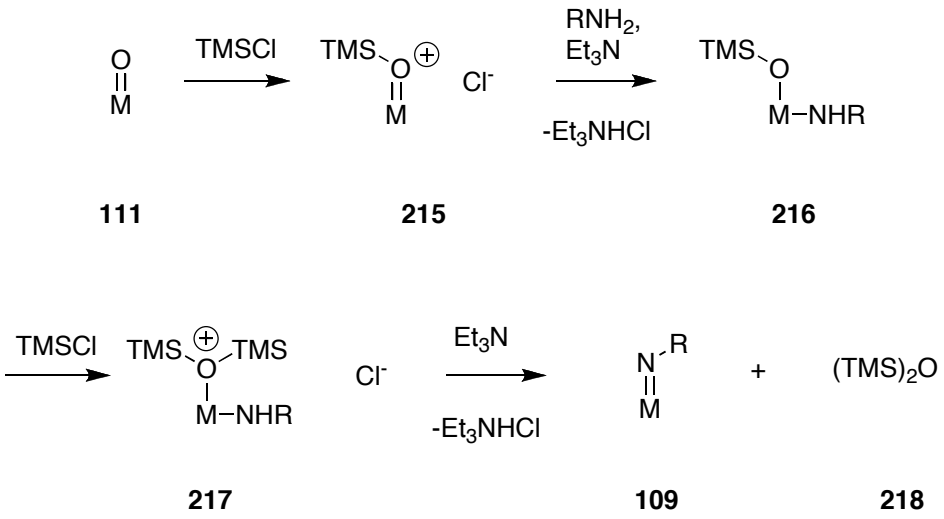
Scheme 2.9: Synthesis of bisimido-molybdenum complexes.

Entry	R	Yield %
214a	2,4,6-Trimethylphenyl	50
214b	2,6-Diisopropylphenyl	98
214c	Benzyl	-

Table 2.1: Synthesis of bisimido-molybdenum complexes.

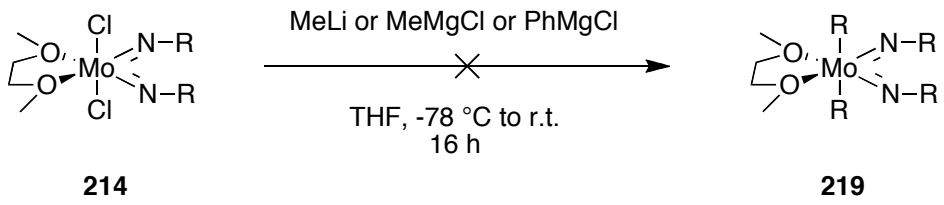
Compound **214c** was synthesised as an oil in poor yield and low purity, therefore no further investigation was attempted. On the other hand, compound **214b** was produced in excellent yield and high purity. Following a similar procedure, **214a** was prepared in moderate yield (50%, lit 99%, see experimental), but high purity. The reactivity of compounds **214a** and **214b** was tested with 1 atmosphere of carbon dioxide at room temperature in Et_2O and CH_2Cl_2. However, no reaction was observed in either of these cases and only degradation was observed over time.

The synthesis of the bis-imido complexes has proved to be fast, easy, high yielding and produced bisimido complexes in high purity when using anilines. Although the reactivity of these complexes was unsuccessful when reacted with carbon dioxide, their generation provided valuable information for future work. It showed a possible route to transform metal-oxo complexes into metal-imido complexes, and, at the same time, change the by-product from water (which poisons the catalyst) to less harming bistrimethylsilyl ether **218** (Scheme 2.10).



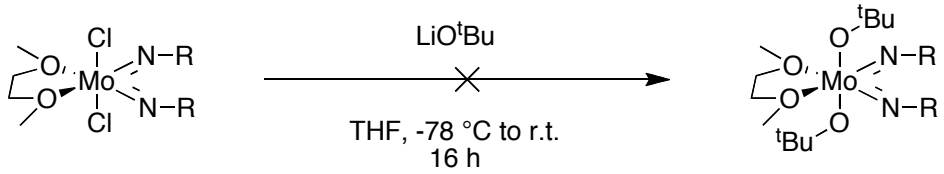
Scheme 2.10: Oxo-imine exchange mechanism.

In an attempt to modify the nature of the complex and change the electron-density on the metal centre, it was decided to exchange the chlorine ligands for alkyl and aryl substituents. The reactivity of these new compounds could be examined and compared to **157** and **210** (Scheme 2.11). However, by using lithium or Grignard reagents only decomposition was observed.



Scheme 2.11: Molybdenum ligand exchange.

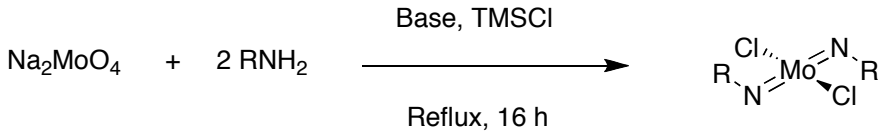
Our attention turned towards alkoxide ligands. However, no successful reaction was obtained after the treatment of compound **214** with lithium *tert*-butoxide (Scheme 2.12).



214 **219**

Scheme 2.12: Molybdenum ligand exchange.

As none of the modifications mentioned above produced any promising results, it was decided to change the nature of the complex. The original synthesis was analysed and it was decided to change the solvent from DME to a non-chelating solvent. This new reaction would produce a complex with an electron-deficient metal centre as the surrounding ligands will be reduced (Scheme 2.13). At this point it had to be considered that some low coordination molybdenum-imido complexes can dimmerise.

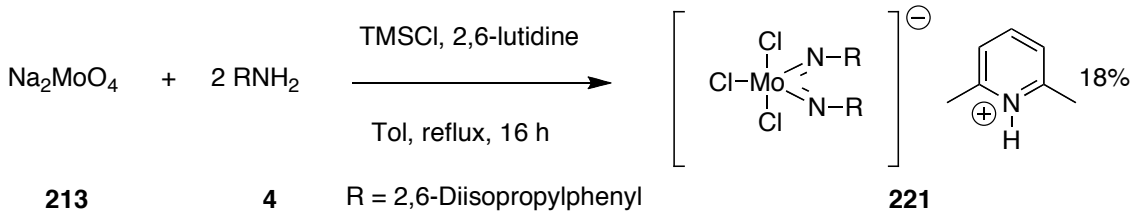


213 **4** **220**

Scheme 2.13: Generation of low coordinated molybdenum complex.

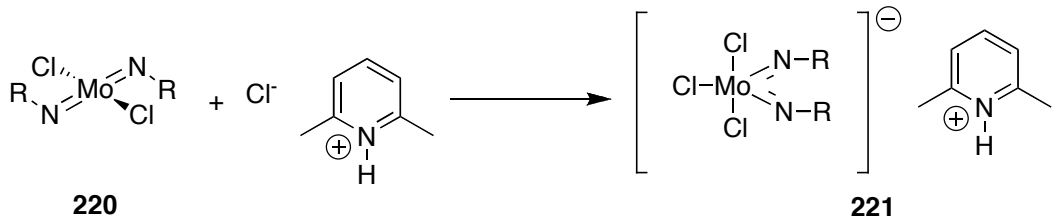
Although making the metal centre more electron-deficient is contrary to the original desired effect, it would generate a more reactive metal centre which would be able to achieve better coordination with an oxygen of carbon dioxide and promote the cycloaddition. Following this idea, the base was also changed to a non-nucleophilic, hindered base. The chosen solvent was toluene and 2,6-lutidine the base. After the reaction (Scheme 2.14), a red crystalline compound was isolated in low yield (18%). Spectroscopic data allowed us to characterise the red solid as bisimido molybdenum complex **221**. ^{1}H NMR spectra showed a ratio of two anilines *vs* only one lutidine, which led us to believe that the complex formed could have the same structure as **220**

with an additional lutidine. Mass spectroscopy showed the mass of the product and the isotope pattern suggested the possibility of having one molybdenum and three chlorines. These data suggested the possibility of complex **221**, which was confirmed by X-ray diffraction. This compound was found to exist as an anion having as a counterion protonated lutidine.



Scheme 2.14: Generation of novel bisimido-molybdenum complex.

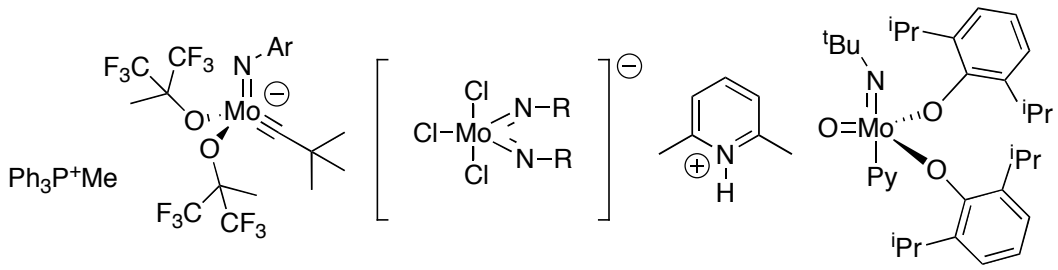
Attempts to increase the yield by adding more/less equivalents of the amine base, by refluxing for longer/shorter periods of time and by changing the order of addition were unsuccessful. It is known that a by-product of the original reaction was the hydrochloride salt of 2,6-lutidine. Therefore, formation of compound **221** could be explained by addition of Cl^- (in the presence of protonated 2,6-lutidine as counter ion) to complex **220** (Scheme 2.15).



Scheme 2.15: Proposed mechanism.

This novel compound had some interesting characteristics. The Mo=N bond lengths were 1.748 Å and 1.763 Å. The Mo-N-C bond angles were 173° and 149° respectively. Although both imido double bonds in our complex were similar to those in Anderson's complex (**157**), their bond lengths and angles were between those in **157** and **210** (Figure 2.1). These data indicated that both multiple bonds had triple bond character and therefore both ligands were 6-electron donors. This behavior contradicts common

bisimido complexes, where generally one imido ligand should have triple bond character and the other double bond character. However, the nature of this particular complex allows the metal centre to have two empty *d*-orbitals which receive electron-density from the imido ligands.



1.813 Å
141°

1.748 Å
173°

1.763 Å
149°

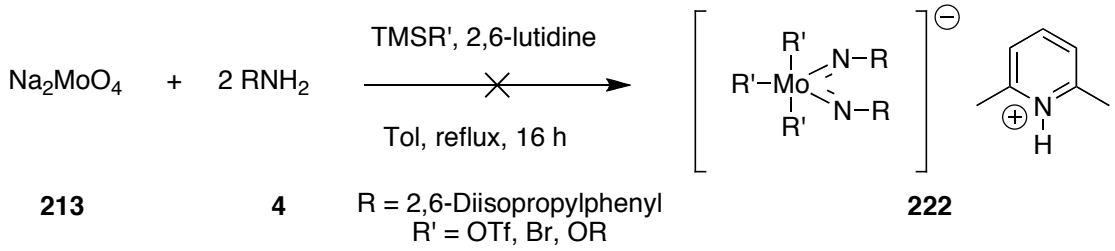
1.736 Å
173°

210 **221** **222**

Figure 2.1: Molybdenum-imido lengths and bond angles.

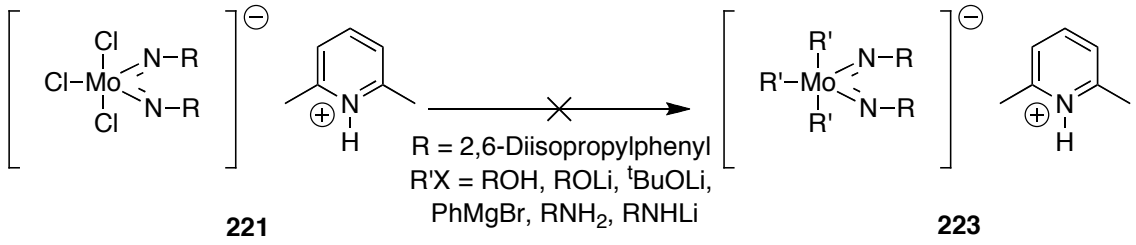
Despite the controversial deductions from the X-ray structural data, we attempted the reaction of complex **221** with carbon dioxide. Unfortunately, no reaction was observed after two hours and only complete degradation of the complex, possibly due to reaction with water, was observed. This supports the triple bond character for both multiple bonds and as both imido ligands behave as 6 electron donors, neither is able to enhance the nucleophilicity of the other. Therefore no spectator ligand effect to increase the reactivity of these complexes was observed in this particular case.

In order to generate analogs of complex **221** and study their reactivity, it was decided to change the ligands around the metal centre. The first strategy was to change the chlorine ligands to more electron-rich ones by using an alternative to the TMSCl method (Figure 2.1). With this change it was expected to obtain complex **222** with different ligands which could have an effect on its reactivity (Scheme 2.16). Unfortunately no desired products were observed, and only unidentified material could be obtained.



Scheme 2.16: Unsuccessful variation in the synthesis.

The second strategy was the reaction of complex **223** with different nucleophiles to effect ligand exchange. However, no reaction was observed with oxygen, amine and Grignard nucleophiles. Degradation was observed in all cases (Scheme 2.17).



Scheme 2.17: Unsuccessful ligand exchange.

The final attempted modification in this synthesis was changing the anilines used in the reaction. This difference would change the nature of the imido-molybdenum bond and the electron density around the metal centre. When using 4-nitroaniline and ethyl 4-aminobenzoate, no reaction was observed. However, 2,4,6-trimethylaniline produced the desired complex (**223**) in low yield and some impurities which could not be removed.

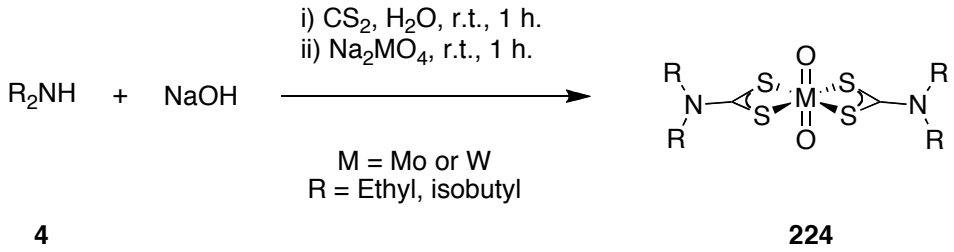
Due to the lack of results and the difficulties associated with work with these type of complexes, it was decided to abandon the molybdenum studies and try an alternative approach, with the aim of possibly returning to molybdenum in later stages of the project.

2.3 Conclusions

It has been shown previously that molybdenum-imido complexes **157** and **210** could react with carbon dioxide in the desired fashion. However, they need to be active and not all complexes are capable to react with carbon dioxide. A novel bisimido molybdenum anion complex has been synthesised in low yield. Its lack of reactivity was disappointing for our research. The study for the transformation of metal-oxo complexes into metal-imido complexes using bistrimethylsilyl ether and base to consume the by-product water has also been observed, leading to a strategy for the catalytic cycle.

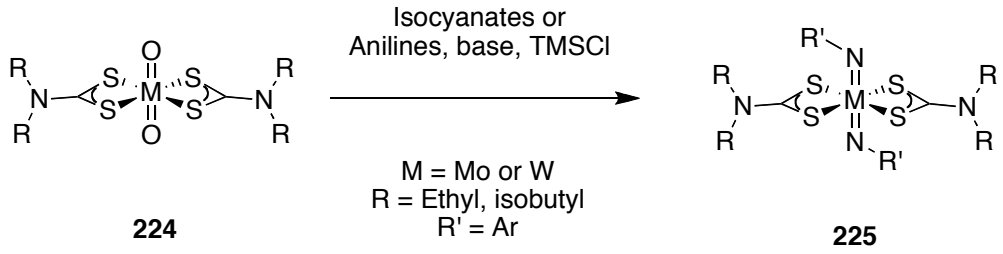
2.4 Future Work

In recent years, some novel bisthiocarbamate ligands have been developed for molybdenum and tungsten-oxo and imido-complexes, giving them more stability and allowing their handling in open atmospheres.[120] Some of these bisimido metal complexes are very reactive in [2+2] cycloaddition reactions and are synthesised by reaction between the metal-oxo complex and isocyanates (Scheme 2.18).



Scheme 2.18: Generation of molybdenum-oxo thiocarbamate ligands.

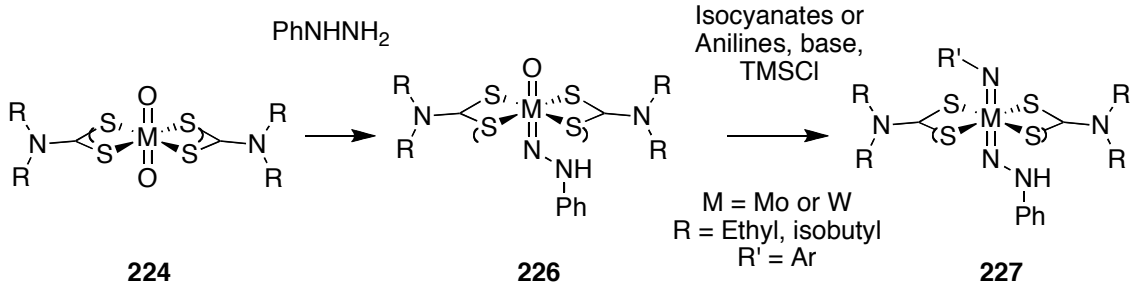
In this field two possible research branches could be followed. The first one will be the study of the generation of metal-imido complexes **225** from metal-oxo complexes **224** by other routes, such as the above described in Scheme 2.4 and Scheme 2.9 (Scheme 2.19).



224 **225**

Scheme 2.19: Reaction of Mo=O to generate Mo=N.

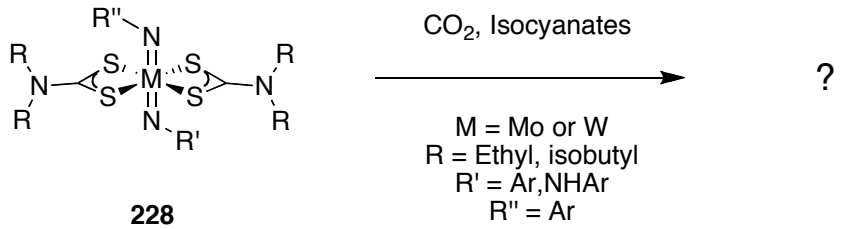
The transformation of dioxo complex **224** into oxo-imido complex **226** by the use of one equivalent of phenylhydrazine could also be investigated.[121] The mixed hydrazido oxo-imido complex (**226**) could then be transformed into unsymmetrical hydrazido imido complexes **227** by one of the methods developed above. These complexes would have completely different reactivity to the bisimido complex (**225**) (Scheme 2.20).



224 **226** **227**

Scheme 2.20: Proposed route to Mo=N.

The second possible research branch would be testing the [2+2] cycloaddition reaction (or heterocumulene metathesis) of these metal-imido complexes with isocyanates, carbon dioxide and other cumulated double bonds (Scheme 2.21).



228

Scheme 2.21: Possible reaction of Mo=N with carbon dioxide.

This future work has generated a new research project which is being studied within our group.

CHAPTER 3:

GENERATION OF UNSYMMETRICAL CARBODIIMIDE *VIA* HETEROCUMULENE METATHESIS

CHAPTER 3: GENERATION OF UNSYMMETRICAL CARBODIIMIDES *VIA* HETEROCUMULENE METATHESIS

3.1 Introduction

Carbodiimides are rare subunits in natural products and drug candidates, however, they are precursors for more common biologically active sites in many natural products and drugs, making them valuable functional groups in synthetic chemistry. Some of the functional groups derived from carbodiimides can be very difficult and laborious to synthesise by other routes or simply, their synthesis requires certain conditions that only can be easily achieved *via* a carbodiimide. For example, ureas, amidines, amido carbamates, guanidines, imido oxazolidinones, heterocycles (pyridines, indoles, tetrazoles...), and polymers have been synthesised from carbodiimides, as seen in section 1.1.5.

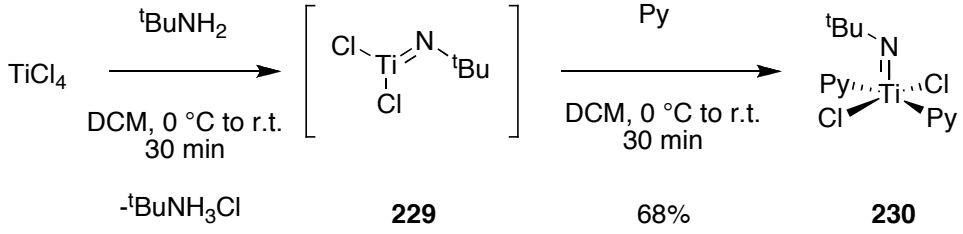
3.2 Development of the Carbodiimide Synthesis

As described, the aim of the research was to generate isocyanates by the reaction of metal-imido complexes with carbon dioxide (according to the research proposal). Initially it was decided (by reasons explained in section 4.1) to begin the research with the synthesis of simple titanium-imido complexes.

3.2.1 Preliminary Studies

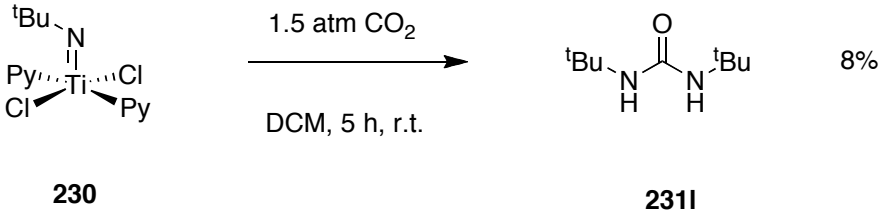
One of the simplest routes to metal-imido complexes found in the literature is an excellent piece of work by Mountford and co-workers.[122] In their synthesis, simple starting materials such as $TiCl_4$ and $^tBuNH_2$ react to form dichloro ^{t}butylimido titanium(IV) (**230**) as an intermediate in the process. The synthesis requires the use of at least two extra equivalents of the amine to remove two chlorines as $^tBuNH_3Cl$ (Scheme

3.1). Finally, the generation of the complex is completed by the addition of 2.3 equivalents of pyridine, which coordinate to the metal centre and stabilise the complex.



Scheme 3.1: Mountford's methods for generation for Ti=N.

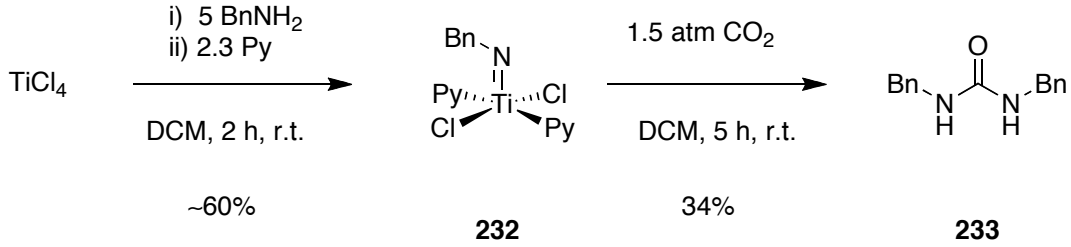
In our work, when compound **230** was reacted with carbon dioxide under 1.5 atmosphere of pressure, symmetrical urea **231l** was generated in very poor yield after aqueous work-up (according to the proposed mechanism two molecule of complex **230** generate one molecule of urea **231l**) (Scheme 3.2). The obvious origin of the carbonyl was carbon dioxide, therefore complex **230** must have activated and subsequently reacted with it. This experiment identified this family of compounds as suitable candidates for our purposes.



Scheme 3.2: Synthesis of urea by activation of carbon dioxide.

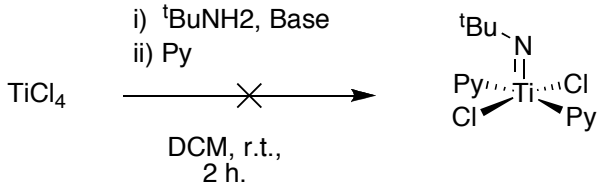
To elucidate the reactivity and mechanism of the reaction it was decided to generate another analogue and study the differences and similarities in the process. The simple modification of changing $^{t}BuNH_2$ for benzylamine allowed us to synthesise what believed to be complex **232** in moderate yield (Scheme 3.3). Unfortunately, the reaction yielded an inseparable mixture of complex **232** and benzylamine hydrochloride which showed similarities in solubility and which we could not separate by crystalisation. When submitting complex **232** and its impurities to the carbon dioxide reaction conditions, symmetrical urea **233** was obtained in low yield. The formation of the

complex is necessary for the reaction, as control experiments showed no reactivity between amines and carbon dioxide under the same conditions.



Scheme 3.3: Synthesis of Ti=N complex and reaction with carbon dioxide.

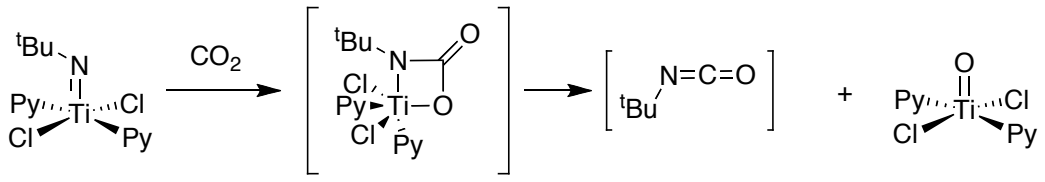
It can be seen that the formation of both complexes is extremely similar, with the only difference being the choice of amine. Excess amine is required to act as a base and eliminate two equivalents of HCl which is formed as a by-product of the reaction. In an attempt to improve the yield of the reaction and the purity of complex **232**, we decided to screen a series of organic bases in addition to the nucleophilic amine partner in Scheme 3.1. The experiment involved the addition of one equivalent of the desired nucleophilic amine and three equivalents of the base. The pKa values of $^{t}BuNH_2$ and benzylamine are 10.5 and 9.5 respectively, which gave us an indication of the approximate pKa range of bases which could be tested. As the metal complexes were incompatible with air or moisture, only organic bases could be used. As nitrogen-containing bases are the most abundant members of this family, a range of amines were tried. Some of the bases tried were DBU (12.0), quinuclidine (11.0), triethylamine (10.7), diisopropylethylamine (11.4), DMAP (9.2), 2,6-lutidine (6.7) and pyridine (5.2). However, degradation of the metal-imido complex was observed or low yields were obtained (Scheme 3.4). The low yield obtained was believed to be the result of not having a strong enough base, and therefore $^{t}BuNH_2$ was consumed as the base instead of being the nucleophilic amine. None of the methods produced clean product, which showed no advantage with respect to the original synthesis.



230

Scheme 3.4: Unsuccessful modification of Mountford's synthesis.

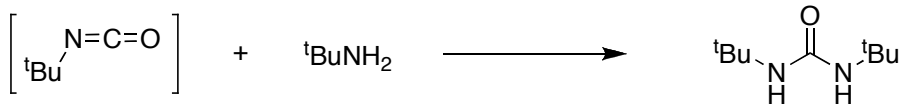
It is clear that the carbonyl in the urea product has been obtained by the activation and reaction of carbon dioxide. Therefore, we can assume that these two titanium complexes (**230** and **232**) activate carbon dioxide. Although the formation of symmetrical ureas was not the predicted result, the reactivity found in these two complexes was intriguing. As a hypothesis of the possible mechanism for the two reactions, two different ideas were postulated. Both of the ideas started with the assumption that the titanium-imido complex **230** reacted with carbon dioxide *via* a [2+2] cycloaddition to generate a four membered ring metallocycle **234**. Decomposition of the intermediate *via* a [2+2] retro-cycloaddition would then generate titanium-oxo complex **235** and isocyanate **1l** (Scheme 3.5). Under the reaction conditions the isocyanate was not detected or isolated.



230 **234** **1l** **235**

Scheme 3.5: Mechanism for the reaction with carbon dioxide.

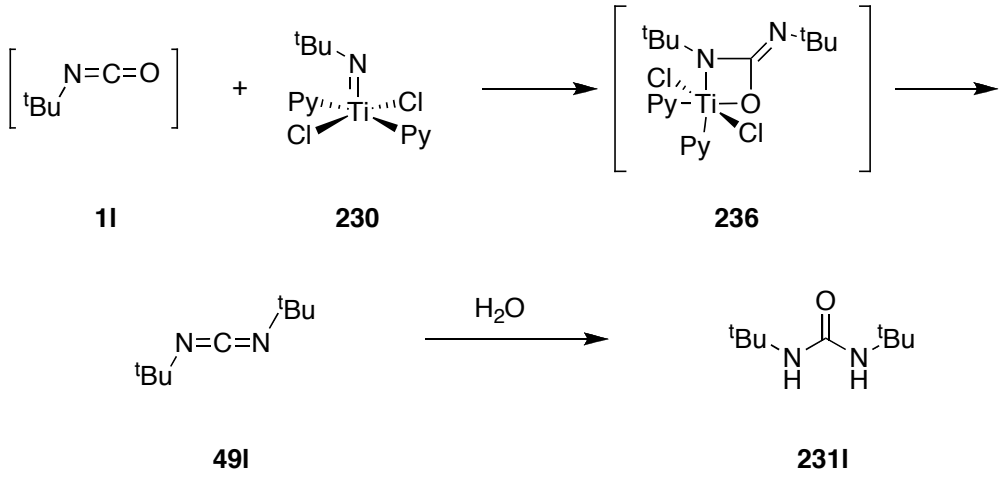
The first and more simple hypothesis is the reaction between isocyanate **1l** and amine **4**, which is a known reaction for the formation of ureas (Scheme 3.6). In the case of the ^{t}butyl analogue, $^{t}BuNH_2$ could only be formed by the degradation of complex **230** by adventitious water. On the other hand, for the benzyl analogue, it also could be provided by the free benzylamine hydrochloride in the reaction mixture.



1l **4** **231l**

Scheme 3.6: First possible pathway for the reaction.

The second hypothesis involves a completely different approach but began with the initial formation of isocyanate. The isocyanate is much more reactive than carbon dioxide. There exists the possibility that as soon as the isocyanate was generated it acted as a competitor and reacted with complex **230** by a second heterocumulene metathesis reaction to generate carbodiimide **49l**, *via* a new metallocycle **236** intermediate in the process. Finally, hydrolysis of the carbodiimide during work-up would generate urea **231l** as the final product (Scheme 3.7).



1l **230** **236**

49l **231l**

Scheme 3.7: Second possible pathway for the reaction.

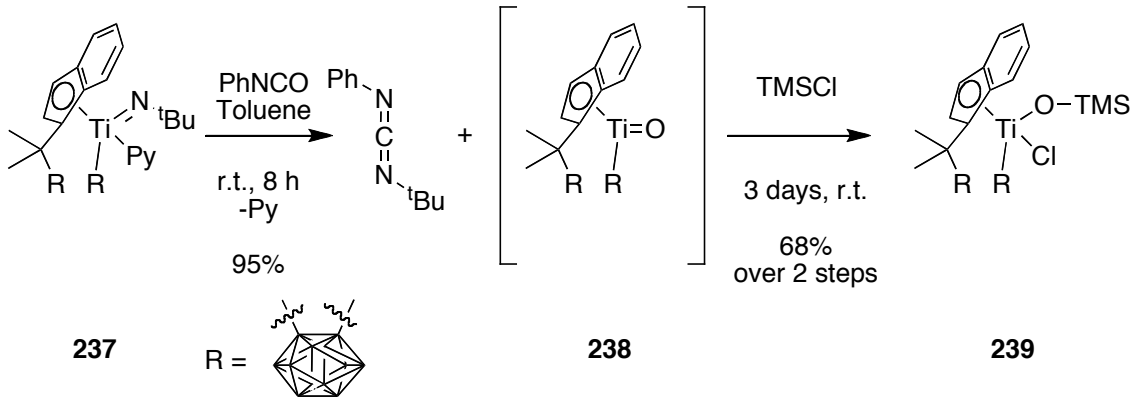
In order to prove that the second pathway could be considered as a plausible mechanism, a second experiment between 4-chlorophenylisocyanate and titanium-imido complex **230** was performed. The reaction was carried out using the same reaction conditions as the experiments where titanium-imido complexes were reacted with carbon dioxide, using dichloromethane as solvent, stirring for five hours at room temperature. The reaction yielded *N*'-(4-chlorophenyl)-*N*-^{t}butyl carbodiimide (**49l**) in

35% yield in unoptimised conditions (Scheme 3.8). No titanium-oxo compound was isolated as a by-product of the reaction, presumably due to degradation.

Scheme 3.8: First heterocumulene metathesis reaction to generate carbodiimides.

This experiment not only proved that the second pathway was a plausible mechanism for the reaction, but it also opened a possibility for a new methodology for the generation of carbodiimides.

Previous to our discovery, only three examples of titanium-imido complexes reacting with isocyanates to generate carbodiimides had ben reported in the literature. However, the general interest in those examples was to study the formation and stability of the titanium-oxo product. The earliest of the examples was developed by Xie and co-workers in 2005, where they generated a hindered titanium-imido complex **236** that could react with isocyanate **1** to produce carbodiimide **49** and titanium-oxo complex **238** (Scheme 3.9).[123] The steric interactions around the metal centre prevented dimerisation on the metal centre. Treatment with TMSCl allowed the formation of chloro titanium-silyl ether **238**. This example supports our hypothesis that silyl reagents could be used to activate titanium-oxo complexes.



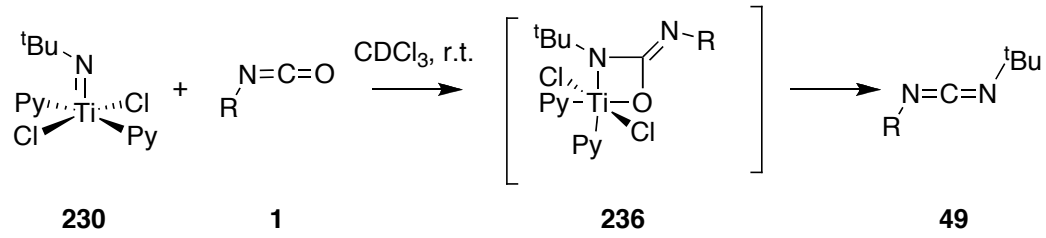
Scheme 3.9: Literature precedent of heterocumulene metathesis.

The rest of the examples show the same heterocumulene metathesis reactivity using different titanium-imido complexes, but none of them report activation of the titanium-oxo complex.[124]

3.2.2 Optimisation

Optimisation of the reaction conditions of the heterocumulene experiment between titanium-imido **230** and isocyanate **1a** (Scheme 3.4) was necessary due to the low yield of carbodiimide in the preliminary experiment. The reactions required the use of a solvent which maintained a homogenous mixture during the reaction process. The only other solvent which allowed this in addition to the original solvent was THF. However, no improvement in the yield of the reaction was observed when it was used at room temperature. The use of higher temperatures only increased the generation of impurities and by-products. At lower temperatures the reaction was slow and longer reaction times resulted in lower yields. The use of 0.5 and 2 equivalents of isocyanate did not increase the yield of the reaction.

The most important and laborious part of the optimisation process was altering the reaction time. Considering the instability of the compounds in air and moisture, no chromatographic techniques could be used to elucidate the progression of the reaction. An alternative technique was to perform experiments in sealed NMR tubes and record ^{1}H NMR spectra at given times. By comparing the data, an approximate idea of the optimum reaction time could be obtained. In the optimisation experiment a 1 : 1 mixture of isocyanate **1** and titanium-imido complex **230** were used. The solvent chosen for the reaction was deuterated chloroform due to its availability and similarity to the usual reaction conditions. In order to study the reactivity of the process and to define its scope, a wide range of analogues were studied. Different aromatic isocyanates with electron-withdrawing, electron-donating, electron-neutral and halogen-containing functionalities, as well as a range of aliphatic isocyanates were studied. The results from the spectroscopic data, showing the ratio of the products after certain time intervals, are summarised in Table 3.1.



230 **1** **236** **49**

Scheme 3.10: Optimisation reaction.

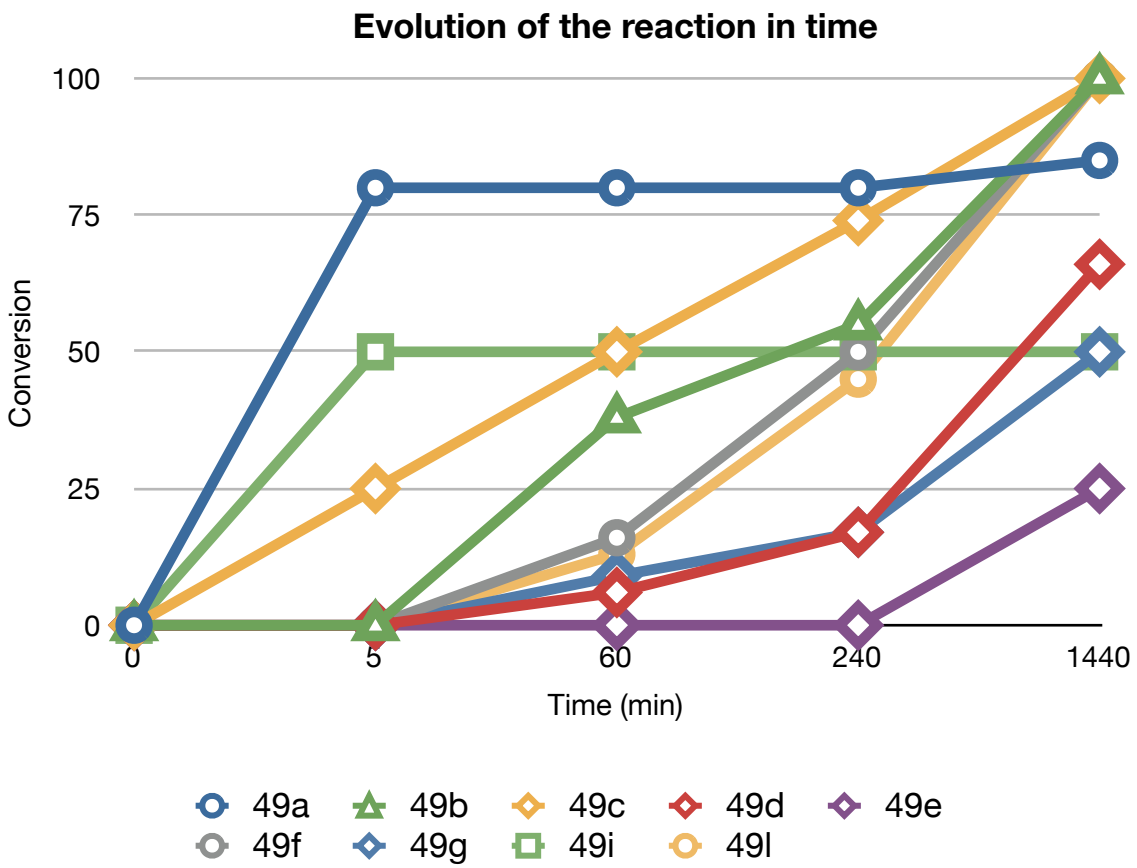
This table shows ratios of **236** and **49**.

Entry	R	5 min	1 h	4 h	24 h	4 d
49a	4-ClC_6H_4	100 : 0	94 : 6	83 : 17	33 : 66	0 : 100
49b	4-$EtO_2CC_6H_4$	100 : 0	62 : 38	45 : 55	0 : 100	0 : 100
49c[b]	4-$O_2NC_6H_4$	75: 25	50 : 50	26 : 74	0 : 100	-[a]
49d[b]	4-$MeOC_6H_4$	20 : 80	20 : 80	20 : 80	15 : 85	5 : 96
49e	4-$Me_2NC_6H_4$	100 : 0	100 : 0	100 : 0	75 : 25	14 : 86
49f	Bn	100 : 0	84 : 16	50 : 50	0 : 100	0 : 100
49g	$Ph(CH_2)_2$	100 : 0	91 : 9	83 : 17	50 : 50	12 : 88
49i	Cy	100 : 0	100 : 0	87: 13	55 : 45	0 : 100
49l	tBu	50 : 50	50 : 50	50 : 50	50 : 50	50 : 50

a = Degradation. b = No formation of major intermediate, ratio **1**:**49**.

Table 3.1: Optimisation of the reaction time.

The reaction described in Table 3.1 is composed of two parts: [2+2] cycloaddition and [2+2] retro-cycloaddition. Theoretically, starting material, intermediates and products could be found in the reaction mixture. However, in all the cases, after 5 minutes of reaction no starting materials could be observed by ^1H NMR. Therefore, the ratio described in the table corresponds to a major intermediate *vs* carbodiimide.

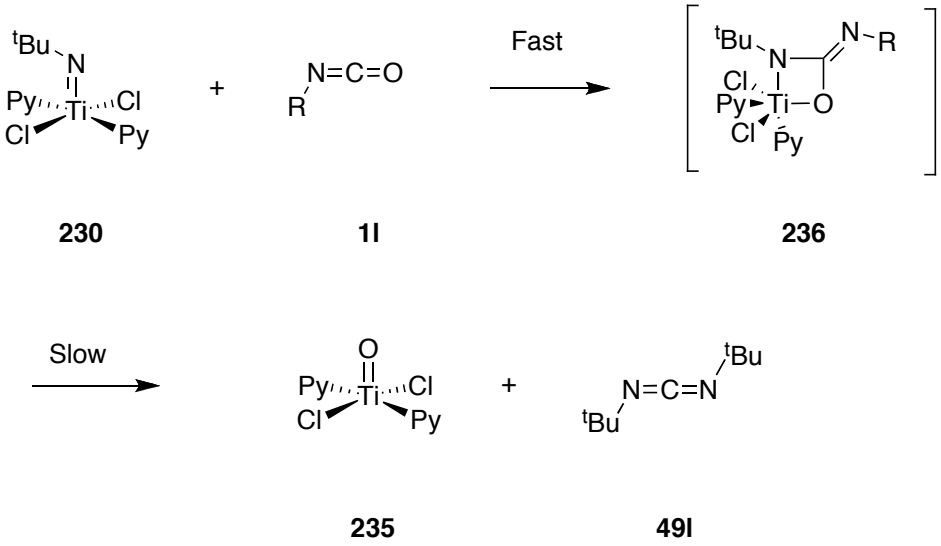


Graph 3.1: Evolution of the reaction on time.

As it can be observed in graph 3.1, there were only two examples (**49c** and **49d**) that did not form a major intermediate, or there was no difference between the ^{1}H NMR spectra of the starting materials and the major intermediate. No apparent electronic reasoning could explain this observation, as one is electron-deficient and the other electron-donating.

It has to be noted that these experiments were performed in a sealed NMR tube and no stirring, mechanical or ultrasound, was applied, therefore, the stirred reaction could require shorter periods. In all the examples, minor intermediates were formed during the reaction, but only major intermediates were recorded in Table 3.1. After 4 hours, the reaction had not progressed enough for it to be considered an optimum reaction time. After 24 hours the ratio of products to starting material was at least 50 : 50, with three of the cases (**49a,b,f**) showing complete consumption of starting material and major intermediate. Only **49e** showed slower reactivity, with only 25% completion. Despite the advanced stage of the reaction, considerable amounts of by-products and

degradation product started to appear in the background. It was considered that the optimum time for the reaction was going to be 16 h, which produced better yields than 4 h and improved purity over 24 h. Another observation obtained from the above data, is that consumption of starting material was very fast and presumably represents the formation of a reaction intermediate, possibly the imido-carbamate metallocycle. The formation of product was then much slower, suggesting that decomposition of the metallocycle intermediate by a retro-cycloaddition was the rate determining step (Scheme 3.11). Only **49c** and **49d** did not follow this behavior.



Scheme 3.11: Rate determining step on the process.

Although the formation of a number of intermediates was apparent in most of the analogues, when ^{t}butyl isocyanate (**1l**) was used, only one intermediate **236l** was detected by ^{1}H NMR spectroscopy. The stability of this intermediate was higher, allowing its existence for longer periods and, as seen in Table 3.1, a constant 1 : 1 mixture of intermediate **236l** : product **49l** was observed during the whole reaction timescale. Only at longer periods of time were by-products and degradation products observed. This constant mixture, together with the simplicity of the ^{1}H NMR spectra, allowed us to record and obtain valuable data from ^{13}C NMR spectra. The information showed the appearance of a quaternary carbon at 165 ppm (Figure 3.1). This peak could correspond to the quaternary imine carbon in the imidocarbamate metallocycle. Few similar compounds have been reported in the literature, however, many examples have

been reported containing carbamate and urea metallocycles.[125] The chemical shift of the quaternary carbon of the novel compounds shows a similar chemical shift to those in the literature. It exist the possibility of having **236l** as intermediates in the reaction, it is not clear which of the two structures is predominant under which conditions.

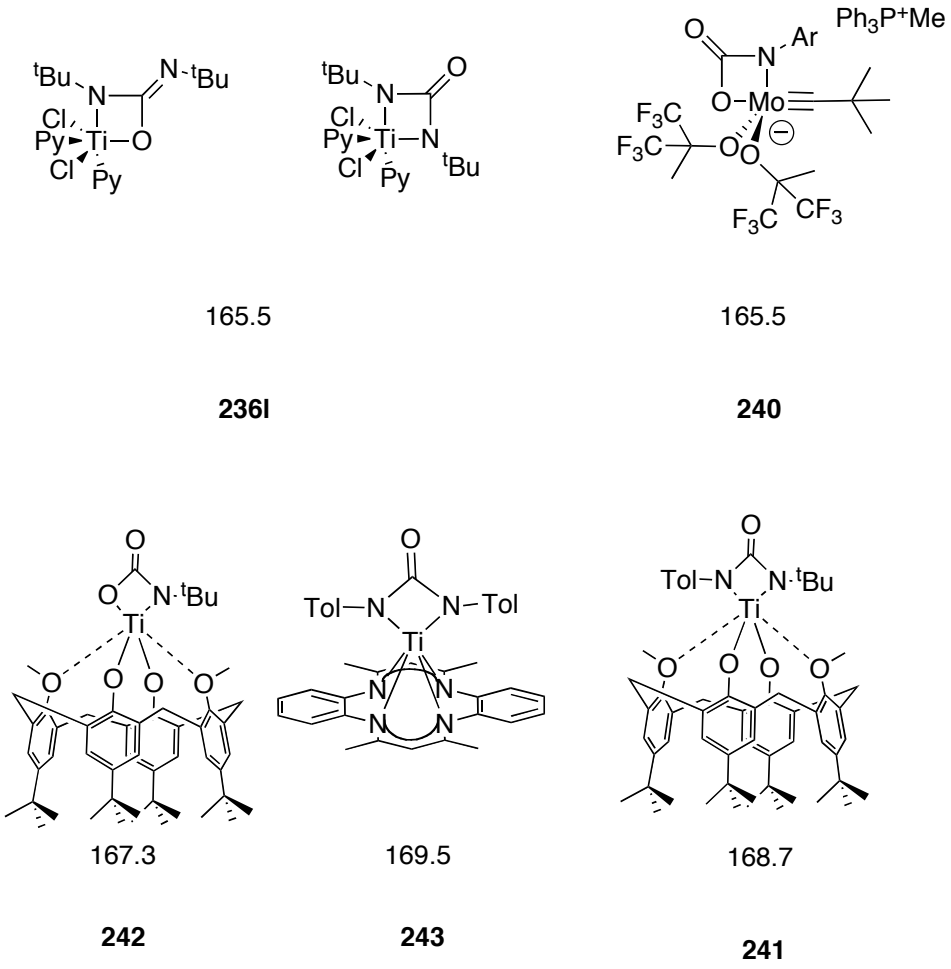
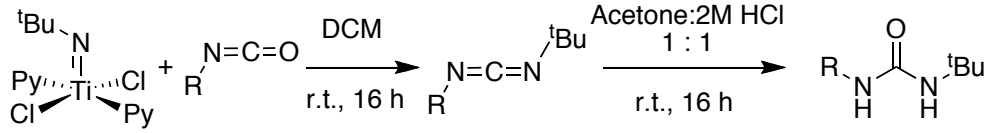


Figure 3.1: Similar literature examples of metallocycle.

3.2.3 Heterocumulene Metathesis for the Synthesis of Carbodiimides

Once the initial studies were finished, the optimum reaction conditions were established to be a 50 : 50 ratio of starting materials, using dichloromethane as solvent, and allowing the reaction to proceed at room temperature over 16 h. The experiments were performed according to these conditions with the same substituted isocyanates that were used in the optimisation process and with the addition of two new isocyanates (Scheme 3.12). Up to now, all the aromatic analogues used were *p*-substituted, minimizing the

possible steric interaction in the substituted aromatic isocyanates. However, the two new examples represented the addition of steric hindrance in the form of 2,6-disubstituted phenyl isocyanates. In addition, after isolation and characterisation, hydrolysis of carbodiimides to the corresponding ureas (**231**) was performed. This sequence, not only allowed us to enhance the use of the methodology, but also allowed us to work with more stable compounds such as ureas.



230 **1** **49** **231**

Scheme 3.12: Generation of unsymmetrical ureas by heterocumulene metathesis and hydrolysis.

Entry	R	Yield **49** %	Yield **231** %
231a	4-ClC_6H_4	46	93
231b	4-$EtO_2CC_6H_4$	49	94
231c	4-$O_2NC_6H_4$	64	98
231d	4-$MeOC_6H_4$	80	65
231e	4-$Me_2NC_6H_4$	-[a]	-[a]
231f	Bn	76	89
231g	$Ph(CH_2)_2$	68	76
231h	4-MeC_6H_4	38	89
231i	Cy	85	98
231j	2,6-$Me_2C_6H_3$	-[a]	61
231k	2,6-$^{i}Pr_2C_6H_3$	-[a]	20
231l	^{t}Bu	32	16

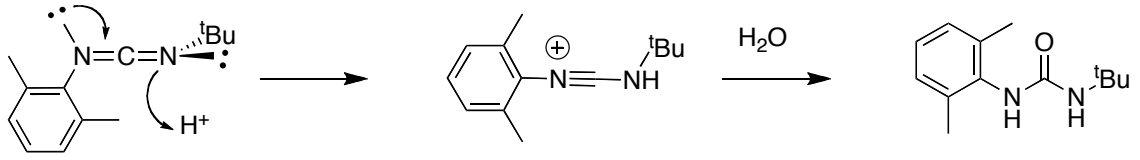
a = Not detected or isolated.

Table 3.2: Generation of unsymmetrical ureas by heterocumulene metathesis and hydrolysis.

The isolated yield of the carbodiimide varies from moderate to good, with higher yields generated for the aliphatic isocyanates. The exception of the aliphatic amines was entry **231l**, corresponding to the most hindered of the aliphatic examples. Although the steric interaction could make a significant difference to the conversion, the low yield obtained is believed to be due to isolation problems. Consecutive trituration with toluene and pentane before passing the carbodiimides through a silica gel column were performed, as explained in the experimental section.

When comparing the aromatic isocyanate with *p*-substituents, it can be seen that the yield of carbodiimide in entry **231d** was higher than the rest. This result is in agreement with the ^{1}H NMR experiments where at short periods of time, the reaction was quicker for *p*-methoxyphenyl isocyanate than other aryl isocyanate. Another electron-rich substituted isocyanate (**231e**) showed some isolation problems presumably due to solubility in the solvents used and could not be isolated in enough purity to quantify and in small amount. The final electron-rich aromatic isocyanate (**231h**), unlike entry **231d**, generated the carbodiimide in lower yield than the electron-poor aromatic isocyanates (**231b** and **231c**). With these varying results it is not possible to identify which electronic effect enhances the reactivity of the isocyanate.

In the examples where the substrates contained steric hindrance in the form of 2,6-disubstituted phenyl isocyanates (**231j** and **231k**), carbodiimides were not isolated or detected. Instead, ureas were obtained directly under the same reaction and isolation conditions. Assuming the reaction underwent the same mechanism in these two examples, strain created across the cumulated double bond by the 2,6-substituents, possibly made the carbodiimide very reactive and it was, therefore, easily hydrolysed to the corresponding urea (Scheme 3.13). In the rest of the cases where these substituents were not present, there was no such strain and the carbodiimides were isolated under normal conditions, requiring addition of acid for hydrolysis. One possible explanation for the higher reactivity of hindered carbodiimides, compared to alkyl or aryl analogues, could be that steric compression encourages reaction with acid.



49j **244** **231j**

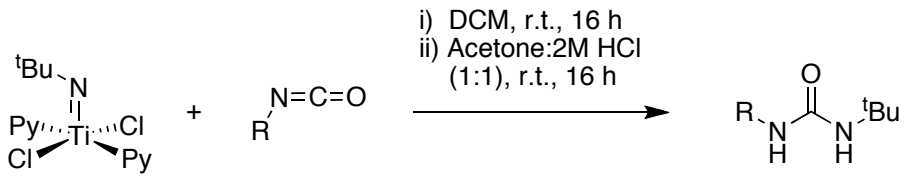
Scheme 3.13: Carbodiimide hydrolysis promoted by acid

Structure **49j** relieves steric compression by the fact that the nitrilium ion is linear. This would then quickly react with water and would form urea. The initial protonation step with alkyl and simple aryl substituents would be slower as there would be no destabilisation of the ground state structure due to steric compression.

Acid hydrolysis of carbodiimides was generally a high yielding process, with the exception of entry **231e** and **231k**. Urea **231e** was not isolated or detected at any point of the reaction. No explanation could be found for this observation. In the case of urea **231l**, problems with isolation might have been the reason for the low yield.

3.2.4 One Pot Process for the Generation of Ureas

In the isolation of carbodiimides, it was thought that some product could be lost in the process due to consecutive extractions with toluene, pentane and silica gel column chromatography. This could explain the poor yields obtained in some cases. To address this problem, some parallel experiments were carried out. On one side (experiment already discussed in section 3.2.3), a two-step process was performed by heterocumulene metathesis, isolation of the carbodiimide, hydrolysis and subsequent isolation of the urea. In the new experiment we had intended to quench the carbodiimide *in situ,* without any purification, to obtain the urea. Thus, a one pot process by heterocumulene metathesis, hydrolysis of the intermediate carbodiimide and isolation of the urea would be attempted. If our hypothesis was correct, by removing the carbodiimide isolation step, the yield of isolated urea should increase. The experiments were performed according to the experimental procedure below and the results are describe in Scheme 3.14.



230 **1** **231**

Scheme 3.14: One pot generation of ureas.

Entry	R	Yield **231** %
231a	4-ClC_6H_4	63
231b	4-$EtO_2CC_6H_4$	93
231c	4-$O_2NC_6H_4$	85
231d	4-$MeOC_6H_4$	77
231e	4-$Me_2NC_6H_4$	-[a]
231f	Bn	82
231g	$Ph(CH_2)_2$	67
231h	4-MeC_6H_4	78
231i	Cy	87
231j	2,6-$Me_2C_6H_3$	60
231k	2,6-$^iPr_2C_6H_3$	35 (47)
231l	^{t}Bu	-[a]

a = Not isolated or detected.

Table 3.3: One pot generation of ureas.

Generally the yields of the reaction were higher, with the exception of **231e** and **231k**, which suffered from the isolation problems mentioned above. The difference in yield between aliphatic and aromatic compounds was not as significant as before, with all yields falling within the same range of 60 - 93%. Concerning the *p*-substituted aromatic compounds, the results suggested that electron-deficient aromatic isocyanates reacted with higher yields than the electron-rich ones. Once more, additional steric hindrance in

the isocyanate gave a lower yield in the reaction. The generation of urea **231k** was complemented by the formation of 2,6-diisopropylaniline in 47 % yield. The explanation for this could be that the reaction had not gone to completion when quenched, and there was a significant amount of remaining isocyanate. At this point, the addition of 2M HCl hydrolysed the isocyanate to the aniline and the carbodiimide to the urea.

There were three main components in the reaction mixture at the point of the hydrolysis: carbodiimide **49**, isocyanate **1** and complex **230**. The carbodiimide was hydrolysed to urea, and depending on which of the other two compounds was hydrolysed first, two different results could be obtained (Figure 3.2). Hydrolysis of isocyanate (**1**) would lead to aniline (**4**) and amine. There is also the possibility that the acid could first hydrolyse complex **230** to $^{t}BuNH_2$. In this case the product would be urea by reaction between the amine (**4**) and the isocyanate (**1**). These two hydrolysis reactions could be in competition. However, as the product in the reaction was aniline and no significant increase in the amount of urea was observed, this suggested that the isocyanate hydrolysed before a significant amount of complex **230** had been hydrolysed.

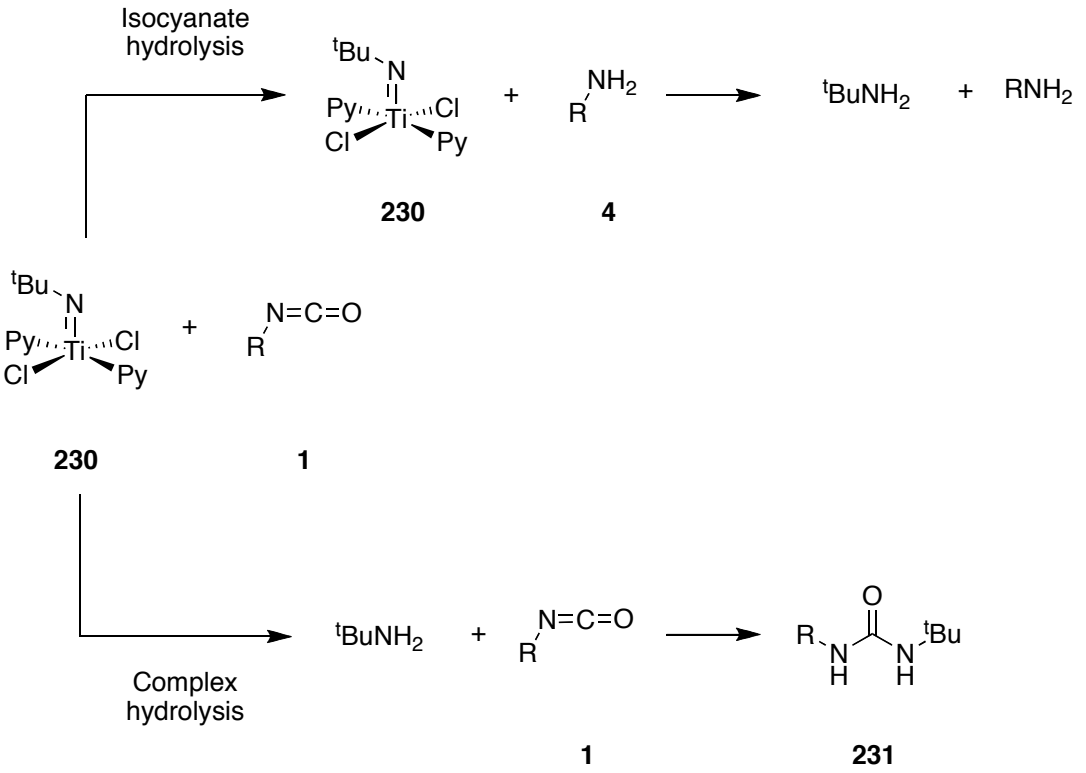
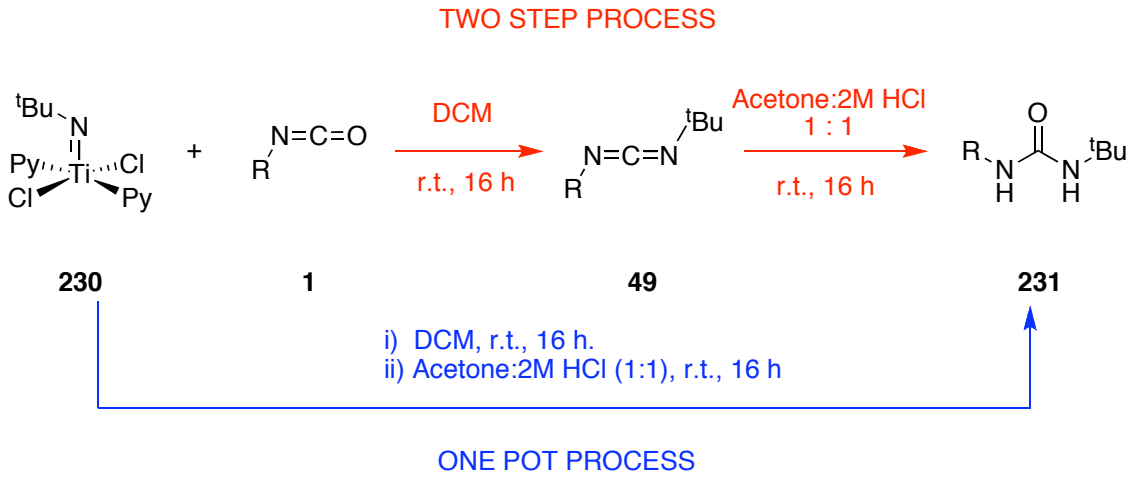


Figure 3.2: Possible pathways for hydrolysis.

3.2.5 Two Step *vs* One Pot process

When comparing the results of the two step process and the one pot process, it can be seen that the one pot process generated the ureas in higher yields (Scheme 3.15), with the exception of the hindered substrates, where the yields were quite similar. The low yields obtained for the hindered substrates in both the one pot and the two step processes support an original hypothesis that the poor yield result from a problem with product isolation.

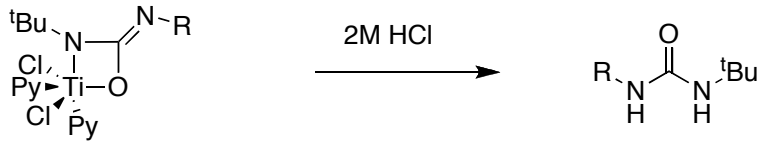


Scheme 3.15: Comparison between two step and one step process.

Entry	R	Yield Urea **231** % Two Step	Yield Urea **231** % One Pot	Difference Yield %
231a	4-ClC_6H_4	43	63	+20
231b	4-$EtO_2CC_6H_4$	46	93	+47
231c	4-$O_2NC_6H_4$	63	85	+22
231d	4-$MeOC_6H_4$	52	77	+25
231f	Bn	68	82	+14
231g	$Ph(CH_2)_2$	52	67	+15
231h	4-MeC_6H_4	34	78	+44
231i	Cy	83	87	+4
231j	2,6-$Me_2C_6H_3$	61	60	-1
231k	2,6-$^iPr_2C_6H_3$	20	35	+15

Table 3.4: Comparison between two step and one pot process.

Although it was believed that performing a one-pot process increased the generation of carbodiimide, the presence of intermediates in the reaction mixture when hydrolysis was performed had not been considered. The hydrolysis of the four membered ring metallocycle intermediate could also generated urea, but not *via* carbodiimide (Scheme 3.16). Therefore, it is not strictly correct that by doing a one-pot process the yield of the carbodiimide generated *in situ* was increased.

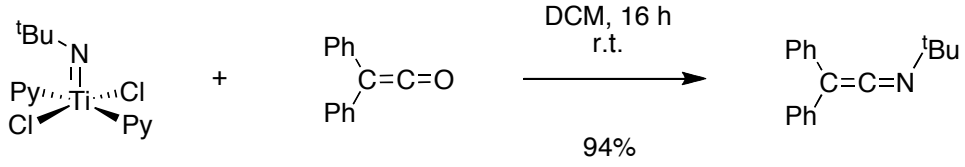


236 **231**

Scheme 3.16: Hydrolysis of metallocycle.

3.2.6 Extension of the Methodology

In an attempt to extend this methodology and discover its scope and limitations, a different substrate was used. In this case, freshly prepared diphenylketene was reacted with complex **230** to generate ketenimine **245** in high yield (Scheme 3.17).[126] It was demonstrated that ketenimine synthesis was possible with our developed heterocumulene metathesis and, therefore, provides an opportunity for further expanding the utility of these titanium-imido complexes in the future.



230 **245** **246**

Scheme 3.17: Synthesis of ketenimines.

3.3 Conclusions

The first conclusion taken from the preliminary studies is that very simple titanium-imido complexes, such as **230** and **232**, activate carbon dioxide and react by heterocumulene metathesis under only 1.5 atmospheres of pressure. These experiments confirm our original hypothesis of reactivity. Despite the fact that the synthesised complexes react with carbon dioxide, the yield of the reactions were low and the products were not the expected ones. It has been shown that the reaction of complexes **230** and **232** with carbon dioxide proceeds to produce symmetrical ureas being formed

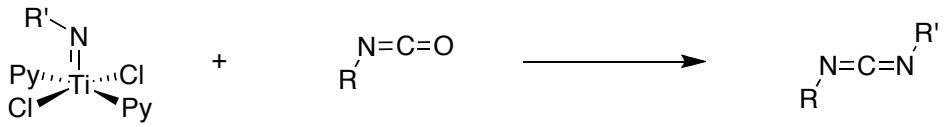
instead of the desired isocyanates. Mechanistic studies showed the possibility of isocyanate formation; however, the product (isocyanates) were more reactive than carbon dioxide and they were further reacting in a second heterocumulene metathesis to form carbodiimides.

A novel procedure for the synthesis of unsymmetrical carbodiimides in moderate to high yields was developed based on this reaction. In our examples, one of the carbodiimides substituents was ^{t}butyl (due to the limitation of the complex synthesis) but the other could be either aliphatic or aromatic. The limitation in the isocyanate synthesis was the steric bulk around the isocyanate. Too sterically hindered substrate impeded the formation of carbodiimide and decreased the yield of urea. This methodology could be extended by the generation of different analogues of complex **230**. Carbodiimides were hydrolysed to ureas under mild conditions by reaction with 2M HCl. These two steps could be performed in one pot to increase the yield of the urea. These experiments showed that the yield of the carbodiimides generated *in situ* could be higher than the isolated yield of carbodiimides.

Development of heterocumulene metathesis for the generation of ketenimines from ketenes, was also demonstrated in one case.

3.4 Future Work

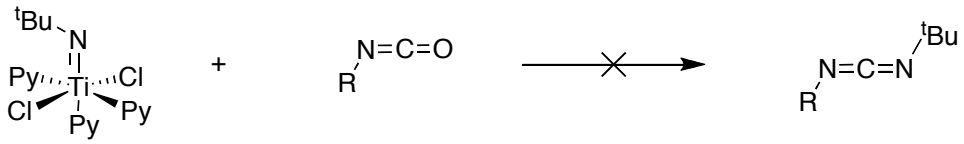
The examples of heterocumulene metathesis studied during our investigations are based on only one titanium-imido complex as a substrate and have highlighted some limitations on the isocyanate substrate. The next step in the methodology would be to study the complex substrate in more detail (Scheme 3.18). A method for the generation of families of complexes with different substituents in the imido ligand would be necessary.



230 **1** **49**

Scheme 3.18: Possible future studies in the expansion of the methodology.

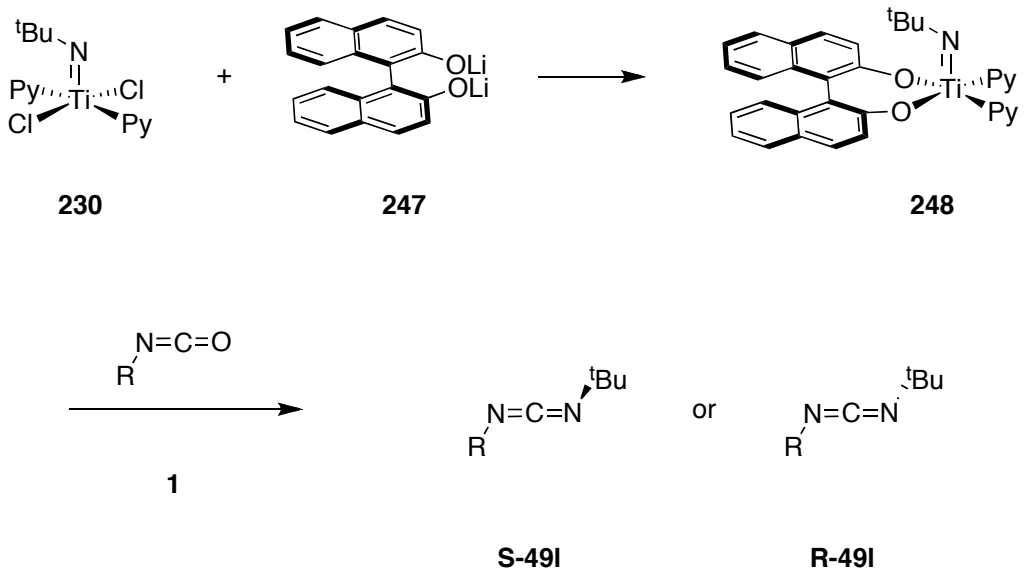
It is important to note at this stage that the titanium complex (**230**) is required to be a 12 electron complex, as no reaction occurred when titanium-imido **246**, which is a 14 electron complex, was used (Scheme 3.19).



246 **1** **49**

Scheme 3.19: Unsuccessful heterocumulene metathesis using 14-electron Ti=N.

The idea of generating unsymmetrical carbodiimides, also enables the possibility of producing an asymmetric approach to carbodiimides, through the generation of axial chirality. The racemisation energy barrier for carbodiimides and ketenimines varies depending on the substituents. According to experiment by Jochims and co-workers the process requires low energy in general.[127] However, other compounds with more bulky substituents such as diferrocenylcarbodiimides have higher barrier energies and have been resolved, allowing determination of their absolute configuration.[128] A possible strategy would involve the generation of asymmetric titanium-imido complexes, which will transfer the asymmetry to the carbodiimide. As will be explained in chapter 5, the chlorine ligand in complex **230** can be exchanged by an alkoxide. It may, therefore, be possible to use 1,1'-bi-2-naphthol (BINOL) as a chiral ligand (Scheme 3.20).



Scheme 3.20: Proposed generation of unsymmetrical carbodiimides.

Some other chiral ligands such as phosphine or nitrogen base could also be used in the study. The possible application of these chiral molecules in asymmetric synthesis is not obvious and more thought is necessary.

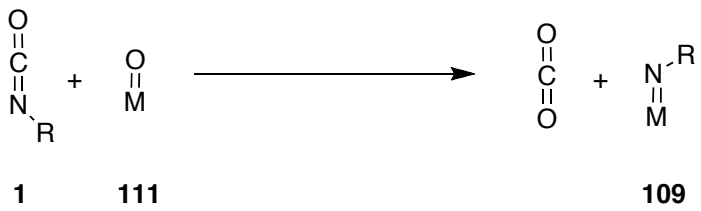
CHAPTER 4:

HETEROCUMULENE METATHESIS STUDIES USING CARBON DIOXIDE

CHAPTER 4: HETEROCUMULENE METATHESIS STUDIES USING CARBON DIOXIDE

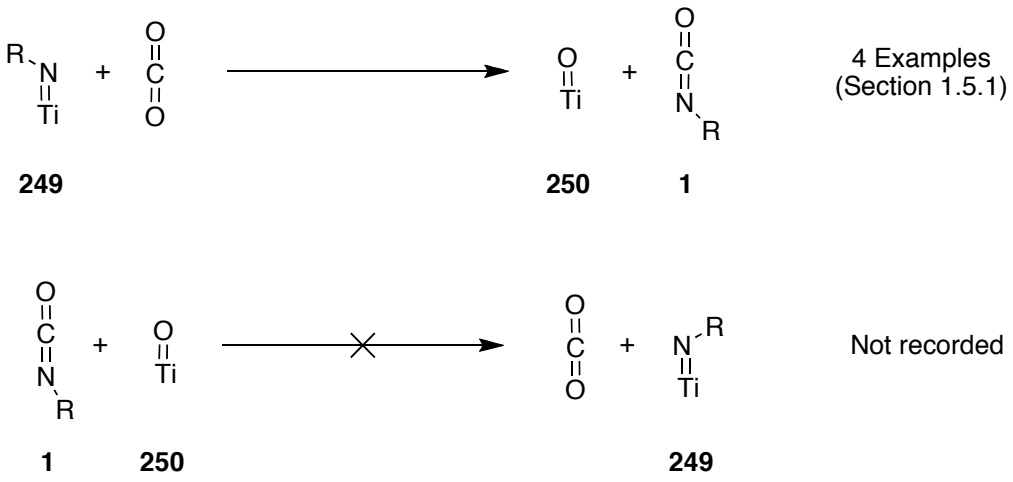
4.1 Generation of the Complexes

In order to succeed in our research there were several key factors which had to be considered. Careful selection of the metal centre and design of the complex were crucial to obtain the desired reactivity. Most transition metals recorded in the literature that undergo heterocumulene metathesis have been used to generate carbon dioxide and metal-imido complexes (**109**) from isocyanates (**1**) and metal-oxo complexes (**111**) (Scheme 4.1). Examples in which the reactivity is reversed are very rare.



Scheme 4.1: General heterocumulene metathesis reactivity

The only transition metal which does not follow the general heterocumulene metathesis reactivity is titanium. There are only a few examples in the literature that show heterocumulene metathesis reactivity between titanium-imido complexes and carbon dioxide (section 1.5.1). More important the reaction between isocyanates (**1**) and titanium-oxo complexes (**250**) to generate titanium-imido complexes (**249**) has not been reported in the literature (Scheme 4.2).



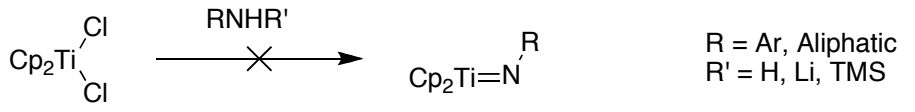
Scheme 4.2: Titanium heterocumulene reactivity.

After considering the precedents in the literature, it was decided that titanium would be a good starting point for our research. It presented a good chance of undergoing the desired heterocumulene metathesis reactivity. On the other hand, titanium-oxo complexes are known to be very stable and therefore, not very reactive. Furthermore, it is known that these complexes can oligomerise, which can inhibit further reactivity of the complex. To prevent this problem steric hindrance has to be generated around the metal centre, as previously shown in the literature.[129]

4.1.1 First Generation of Titanium-Imido Complexes

Previous titanium-imido complexes showing the desired reactivity with carbon dioxide were complexes synthesised in several steps using difficult procedures. Our aim was to simplify the titanium-complexes in order to use readily available starting materials, as well as decreasing the number of reaction steps. This would provide us with a simple and efficient synthesis of hopefully reasonably stable complexes.

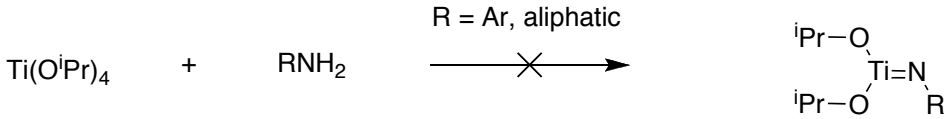
In order to suppress oligomerisation we focused on sterically hindered complexes. The most readily available titanium starting material was titanocene dichloride (**251**). Titanocene imido complexes are not easy to prepare, and only a few complexes have been reported in literature.[130] Our attempts to generate titanocene imido complex **252** by desired reaction of amine sources with $TiCp_2Cl_2$ were unsuccessful (Scheme 4.3). In all cases only starting material or unidentifiable reaction mixtures were observed.



251 **252**

Scheme 4.3: Unsuccessful generation of $Cp_2Ti{=}N$.

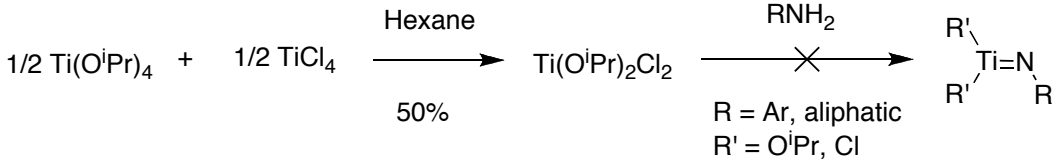
In a second attempt, titanium(IV) isopropoxide (**254**) was used as a source of titanium with no success (Scheme 4.4). The lack of reactivity with this substrate could be due to the hindrance produced by the four isopropoxide ligands on the titanium centre.



253 **4** **254**

Scheme 4.4: Unsuccessful formation of Ti=N complex.

In an attempt to improve the outcome and gain reactivity, an intermediate titanium(IV) bisisopropoxide dichloride complex (**254**) was synthesised in 50% yield; however, no titanium-imido complex could be formed by reaction of this complex with amines (Scheme 4.5).[131]

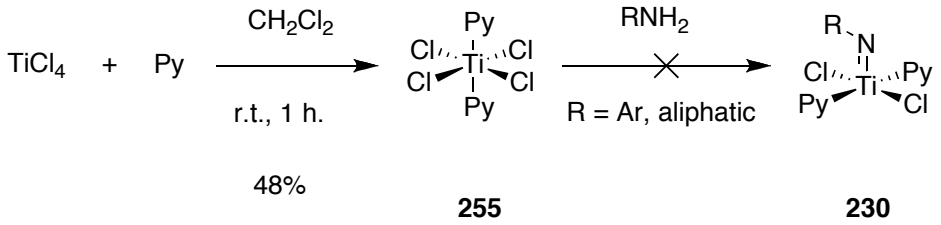


253 **254** **252**

Scheme 4.5: Unsuccessful generation of Ti=N.

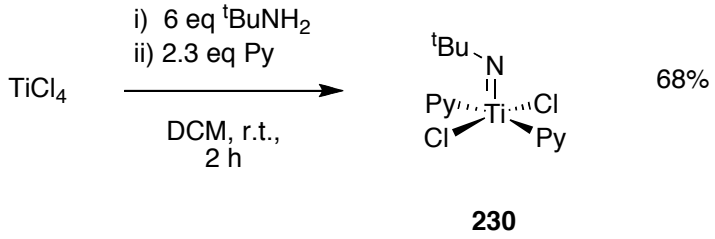
It is known that bispyridine titanium(IV) chloride is a stable titanium(IV) complex. It is produced by reaction between $TiCl_4$ and pyridine, which stabilises the metal centre by coordination and reduction of its reactivity (Scheme 4.6).[132] It is also a air/moisture

unstable solid, but is more stable so it can be measured out more accurately under anhydrous conditions. The complex (**255**) becomes insoluble in most solvents when formed, which prevented further reaction with added amine to form our desired complexes (**230**).



Scheme 4.6: Stabilisation of $TiCl_4$.

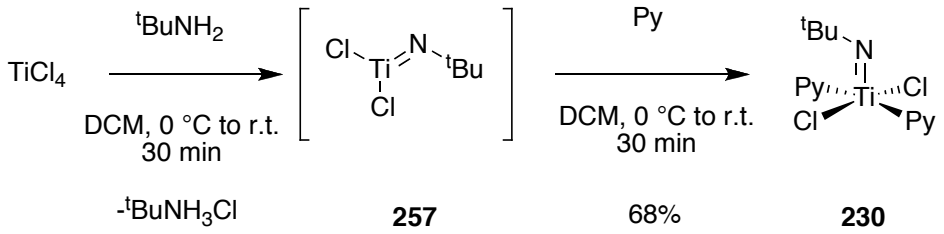
The easiest route to generate titanium-imido complexes was developed by Mountford *et al*. in one single step using readily available starting materials (Scheme 4.7). Borrowing this methodology, we can access an essential backbone for our complexes, which may be modified to enhance their reactivity. This reaction could be performed on multi-gram scale (~30 g) in reasonable yield. The ability to carry out this reaction on large scale is important if this route is to be used on an industrial scale.



Scheme 4.7: Synthesis of 12-electron Ti=N complex.

This strategy represents a very important reaction and source of titanium-imido complexes. However, we found that its versatility was very poor and limited when synthesising analogues by the same reaction. The suggested mechanism for the reaction describes the formation of titanium-imido intermediate **257** by reaction between $TiCl_4$ and $^tBuNH_2$, see section 3.2.1 (Scheme 4.8). The amine ($^tBuNH_2$) is added in excess, it

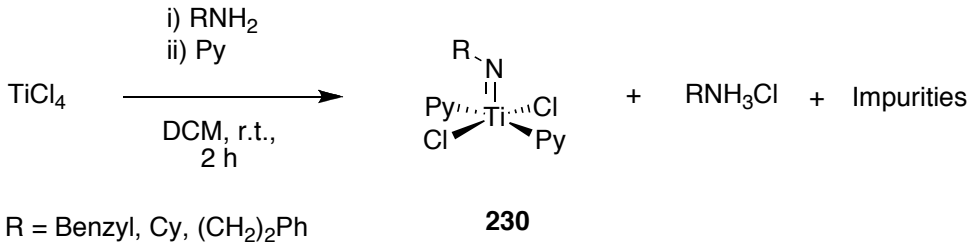
therefore acts as a nucleophile initially and then as a base to eliminate HCl in the form of $^{t}BuNH_3Cl$. Pyridine coordinates to the final complex to stabilise it.



Scheme 4.8: Mechanism for the generation of Ti=N complexes.

The ^{t}butylammonium chloride salt by-product was removed from the reaction mixture by filtration using CH_2Cl_2 then toluene : CH_2Cl_2 (10:1) consecutively. No recrystallisation was required due to the high purity in which the complex was obtained.

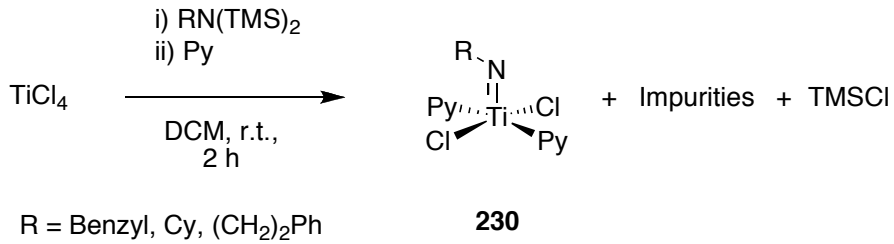
In an attempt to extend the scope of this reaction, to obtain more analogues to react with carbon dioxide, it was decided to use a variety of amines. Other aliphatic primary amines and benzyl amine were used following the exact procedure of Mountford *et al*. (Scheme 4.9). Unfortunately, all examples presented purification problems and no clean products could be isolated from any reactions.



Scheme 4.9: Attempted synthesis of analogues of Ti=N complexes.

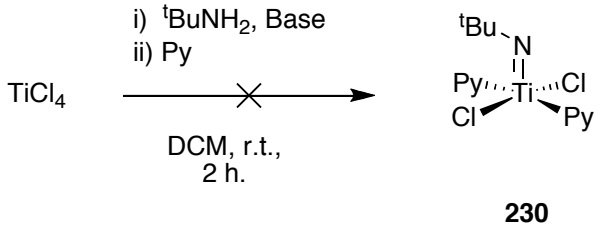
The difficulties in the isolation of these products lie in the separation of the product from the hydrochloride salt by filtration. It appeared that the product (**230**) and the by-product had similar solubilities, making separation by filtration or crystallisation very difficult. A proposed alternative was to change the amine for a bis-silyl protected amine (Scheme 4.10). This was believed to produce TMSCl as the by-product of the reaction,

which could be removed from the mixture by evaporation. However, due to the reactivity of the TMSCl formed other unidentified reactions occurred and some other impurities were present in the reaction. Once again, the separation proved to be very difficult.



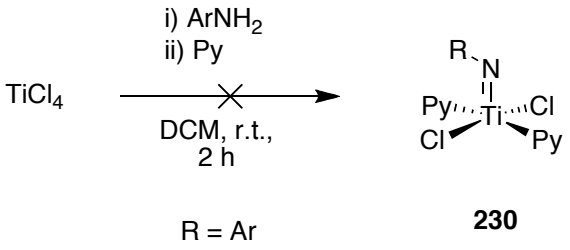
Scheme 4.10: Modification in the synthesis of Ti=N complexes.

To address this problem, an alternative route was devised where a different nitrogen containing organic base was used to remove the HCl from the reaction mixture (section 3.2.1). However no success was obtained (Scheme 4.11).



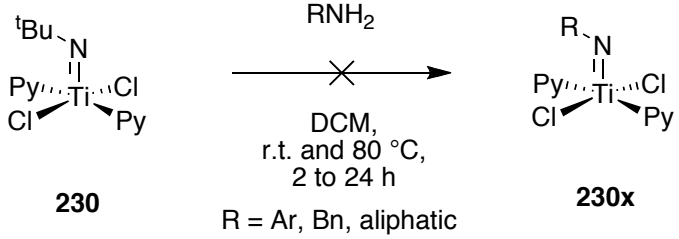
Scheme 4.11: Addition of bases to facilitate the reaction.

Although it was shown that no clean compounds could be isolated by the modifications, the success of the reaction for the generation of titanium-imido complexes from non-aromatic amines was suggested by ^{1}H NMR experiments. Another extension of the reaction was the use of anilines to prepare some other analogues under the same conditions (Scheme 4.12). In this case the reaction did not proceed, presumably due to the differences in pKa between the aniline (4.87) and the original amine (10.5), and the lower nucleophilicity of the anilines.



Scheme 4.12: Attempted synthesis of Ti=N complexes from anilines.

With the development of a standard route to titanium-imido complexes in one step being unsuccessful, another approach was investigated. After generating complex **230**, it was subjected to transimination reaction with other aromatic and non-aromatic amines (Scheme 4.13). A number of anilines and aliphatic amines were used under various conditions, however no successful reaction was obtained. Trasimination was believed to be an easy procedure due to gaining in stability.



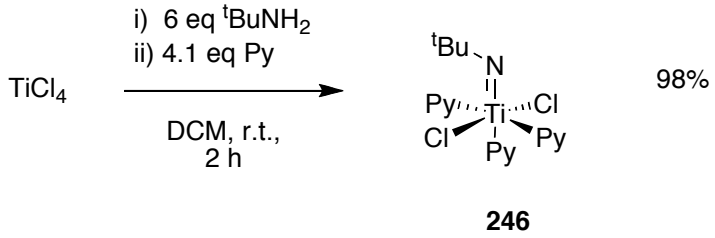
Scheme 4.13: Unsuccessful formation Ti=N using anilines.

Due to the above results, it was clear that this route to imido-titanium complexes was limited and therefore unsuccessful for the generation of a range of 12-electron titanium-imido complexes.

4.1.2 Second Generation of Titanium-Imido Complexes

The same research group that developed the synthesis of titanium-imido complex **230**, developed the formation of a 14-electron complex **246** in excellent yield, by increasing the amount of pyridine from 2.3 to 4.1 equivalents (Scheme 4.14). The third pyridine was coordinated to the metal centre in an axial position. This meant that the structure of the complex changed from a 12-electron pyramidal complex to a 14-electron octahedral

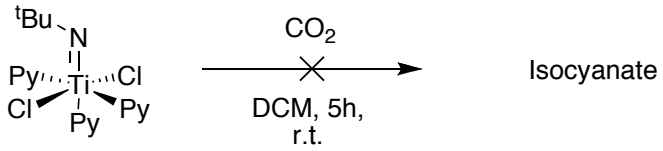
complex. The generation of complex **246** could also be performed on a multi-gram scale (~30 g) in high yields.



246

Scheme 4.14: Synthesis of 14-electron Ti=N complex.

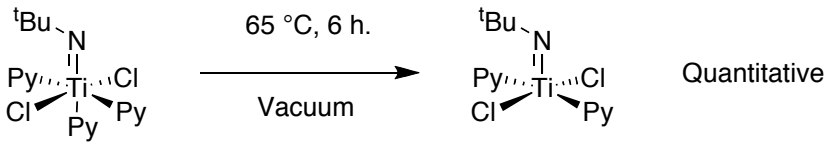
This novel complex has a completely different reactivity than the previously described titanium-imido complex **246**. By studies of the reaction with carbon dioxide, we discovered that 14-electron titanium-imido complexes, were unreactive against heterocumulene metathesis to form isocyanates (Scheme 4.15). However, its reactivity for transimination and ligand exchange meant that it could be a valuable intermediate for the synthesis of other complexes.



246

Scheme 4.15: Unsuccessful formation of isocyanate.

In addition, complex **246** undergoes another reaction to obtain 12-electron titanium-imido complexes (**230**), by de-coordination of the axial pyridine (Scheme 4.16). The reaction achieved complete conversion by heating at 65 °C under vacuum for 6 h.

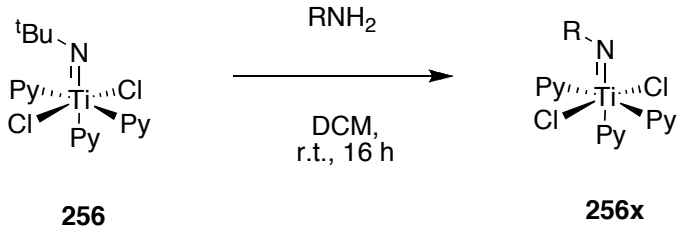


246 **230**

Scheme 4.16: Pyridine decoordination.

This reaction suggested that other trispyridine titanium complexes which contain 14-electrons, could be converted in high yield into the 12-electron analogs by removal of the axial pyridine.

Transimination is the other characteristic reactivity that complex **256** undergoes as reported by Mountford and co-workers. This reaction also proceeded in moderate to high yield, allowing us to access a wide range of novel complexes **256c,d,e,f** and literature **256a,b,g** in a very simple process after isolation by recrystalisation (Scheme 4.17).



256 **256x**

Scheme 4.17: Transimination reaction.

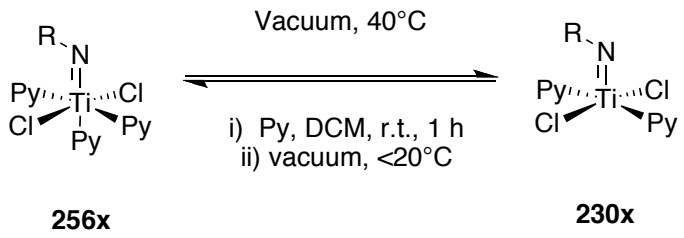
Entry	R	Yield **256** %
256a	4-ClC_6H_4	56
256b	4-$O_2NC_6H_4$	70
256c	4-$MeOC_6H_4$	64
256d	4-$Me_2NC_6H_4$	32[a]
256e	4-$EtO_2CC_6H_4$	68
256f	2,4,6-$Me_3C_6H_2$	76[a]
256g	2,6-$^iPr_2C_6H_3$	84
256h	4-$H_2NC_6H_4$	Mixture

a = Mixture of starting material aniline and product.

Table 4.1: Yields for a variety of amines in transimination reaction.

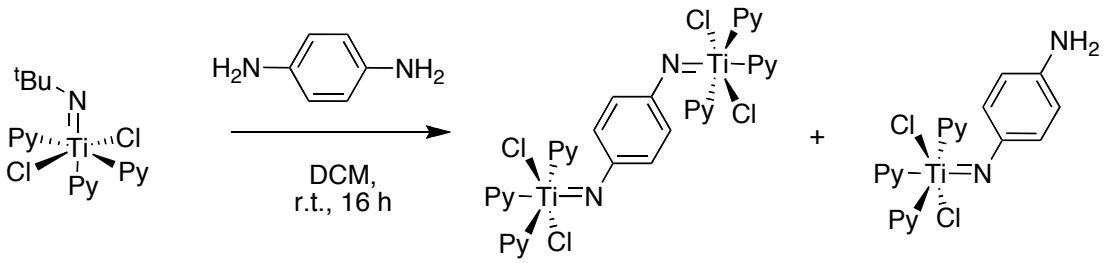
Analysis of the crude reaction mixture by ^{1}H NMR showed complete conversion (with the exception of **256f** and **256g**). Unfortunately, the isolated yield after purification proved to be much lower in all cases. When the aniline used had an electron-donating substituent (**256c** and **256d**), the isolated yields were less than those with electron-withdrawing substrates (**256b** and **256e**). The use of *p*-*N*,*N*-dimethylaniline (**256d**) gave some difficulties in the isolation process; the product was derived in low yield (32%) and purity (86%), due to the solubility of starting material and products.

When sterically hindered 2,6-disubtituted anilines (**256f** and **256g**) were used, the reaction was slower (as described in the experimental section 5.7). In the case of entry **256f** a mixture of starting material and product was isolated as the reaction could not be driven to completion by prolonging the reaction time up to 4 days. It was also found that complex **256g** could be transformed into the 12-electron complex **230** by applying vacuum at 40°C with complete conversion after 4 h. This reaction could be reversed quantitatively by adding one equivalent of pyridine and evaporating the solvent at 20°C (Scheme 4.18).



Scheme 4.18: Variation between 12- and 14-electron complex.

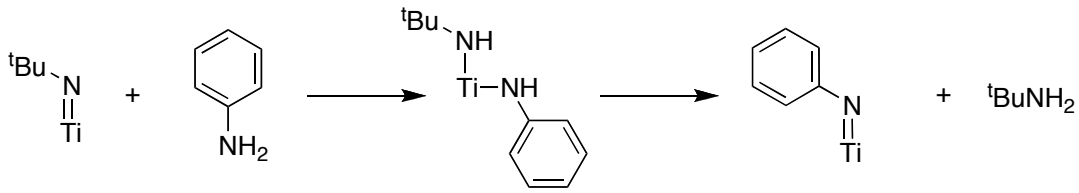
The use of 1,4-diaminobenzene (**256h**) (Scheme 4.19) was of particular interest due to the similarities with diisocyanates that are used for the generation of polyurethanes, which contain disubstituted aromatic species. Although the conversion proceeded in a similar level to the other amines, an unseparable complex mixture was formed. Unfortunately, it proved difficult to characterise the compounds formed, but the experiment gave us the necessary information to suggest the formation of a complex.



256 **257** **256h**

Scheme 4.19: Transimination to form dimers.

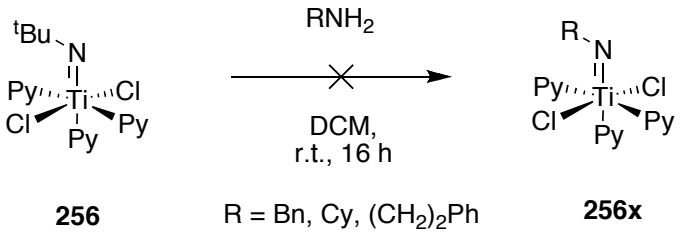
The ^{1}H NMR spectrum of the crude reaction mixture showed complete consumption of the starting material. We can consider the transimination process as an equilibrium, which is displaced towards the formation of the most thermodynamically stable complex. In our particular case the titanium-imidophenyl complexes **256x** are thermodynamically more stable than the corresponding aliphatic complexes **256** (Scheme 4.20). Possibly the addition of an aromatic group in the imine stabilises the complex.



256 **258** **256x**

Scheme 4.20: Mechanism for transimination reaction.

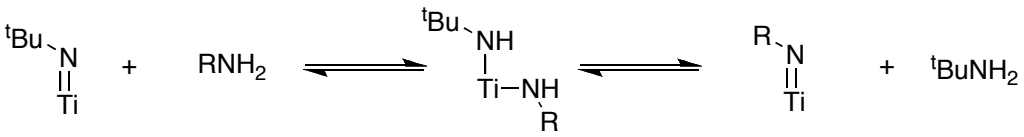
This reaction worked very well when anilines were used, however, aliphatic amines produced a mixture of compounds (Scheme 4.21). In these cases, the thermodynamic stability of the starting complex **256** and the product complex **256x** are similar, therefore the equilibrium cannot be displaced to favour the formation of the products.



256 R = Bn, Cy, $(CH_2)_2Ph$ **256x**

Scheme 4.21: Unsuccessful transimination using anilines.

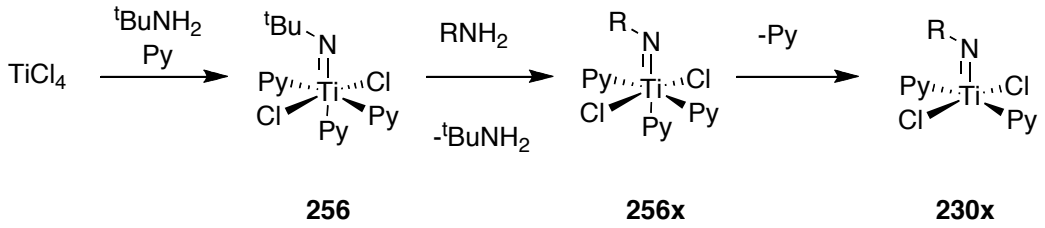
Assuming that the reaction is an equilibrium process in order to drive the reaction to completion, removal of $^tBuNH_2$ (due to its low boiling point compared to benzylamine) was attempted by distillation from the reaction in Scheme 4.22 as the reaction was advancing. However, only degradation was observed. An alternative procedure involved a sequence of evaporation and addition of solvent (CH_2Cl_2) until $^tBuNH_2$ was completely removed. It was thought that the equilibrium would be displaced towards the formation of the product, but once again degradation was observed. These two experiments led us to believe that the imido-titanium complexes were unstable to heat.



256 **258** **256x**

Scheme 4.22: Transimination equilibria.

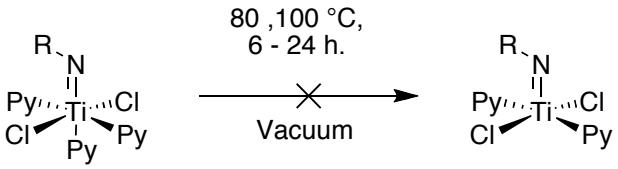
Despite the unsuccessful generation of titanium-imido complexes with aliphatic amines, a wide range of analogs containing aromatic amines were obtained. The idea behind the generation of these compounds was the formation of 12-electron titanium-imido complexes by a three-step sequence from available starting materials (Scheme 4.23). The route involved generation of ^{t}butylimido titanium complex **256**, transimination with the desired aniline to complex **256x** and pyridine de-coordination to yield titanium-imido complex **230x**.



256 **256x** **230x**

Scheme 4.23: Sequence for the generation of 12-electron Ti=N analogues.

The family of 14-electron titanium-imido complexes **256a-f** was submitted to the conditions for de-coordination of the axial pyridine to obtain the corresponding 12-electron complexes (Scheme 4.24). Disappointingly, none of the substrates showed complete conversion and a mixture of compounds and degradation was observed. The reactions were carried out at 80 and 100 °C, for 6 and 24 h under vacuum (0.1 mmHg).



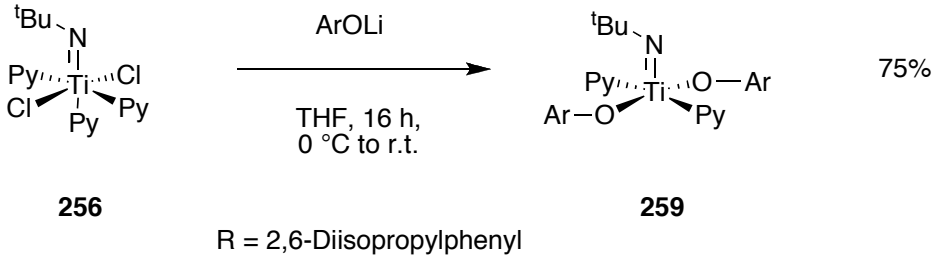
256x **230x**

Scheme 4.24: Unsuccessful pyridine decoordination.

Failure of the pyridine de-coordination could be explained by the fact that tbutyltitanium-imido complex **256**, possesses a bulky substituent attached to the nitrogen. This group generates steric interactions with the equatorial substituents (pyridine and chlorine), forcing them towards the bottom of the molecule and enlarging the bond length between the axial pyridine and the titanium. For the rest of the substituents this steric interaction may not be so large (as the substituents were not so bulky) producing a shorter bond for the axial pyridine, therefore this bond was stronger, and more difficult to break. At this stage another strategy for the generation of 12-electron titanium-imido complexes was investigated.

4.1.3 Third Generation of Titanium-Imido Complexes

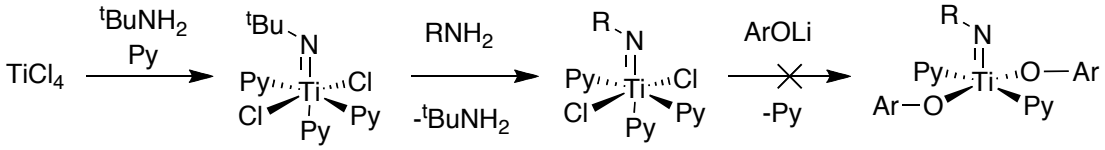
For the generation of 12-electron titanium-imido complexes it was required to generate either another route or modify the complexes already obtained. Mountford and co-workers showed that substitution of the chlorine ligands in complex **256** by alkoxides could be easily achieved by reaction with lithium alkoxides (Scheme 4.25).[133] The yield of the reaction was high (75%) and was also a simple modification which could be carried out on at multi-gram (~30 g) scale without considerable decrease in the yield.



Scheme 4.25: Ligand exchange.

The steric bulk provided by the alkoxide ligands forms a metal centre which is highly congested, therefore the axial pyridine is easily removed to achieve a 12-electron titanium-imido complex. In fact, the trispyridine complex was never observed. The other effect produced by changing the ligand was the donation of electron-density into the metal centre, providing a more electron-rich complex which should enhance the nucleophilicity of the nitrogen lone pair. This effect may increase the reactivity towards heterocumulene metathesis reactions by the spectator ligand effect.

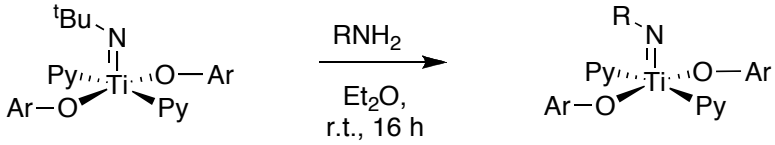
The ligand exchange strategy could be applied to the 14-electron titanium-imido complexes (Scheme 4.25) to generate a wider range of complexes for our study. By analogy, it was believed that similar complexes would follow the same reactivity and generate 12-electron titanium-imido complexes. The complexes would be generated in a three-step synthesis from commercially available starting materials (Scheme 4.26). Unfortunately the chlorine ligand exchange for complexes **256x** showed difficulties, and in some cases isolation of the desired product was not possible.



256 **256x** **259**

Scheme 4.27: Unsuccessful route to oxo-aryl Ti=N complexes.

Generation of complexes **259x**, where ᵗbutylamine has been substituted by an aromatic or non-aromatic amine, is an interesting goal as this family of complexes appeared to be good candidates to undergo hetercumlene metathesis. It was interesting to note that these compounds could be synthesised by transimination from complex **259**, therefore the experiments were performed in an attempt to give a range of 12-electron imido complexes (Scheme 4.26).



259 **259x**

Scheme 4.27: Transimination in oxo-aryl Ti=N complexes.

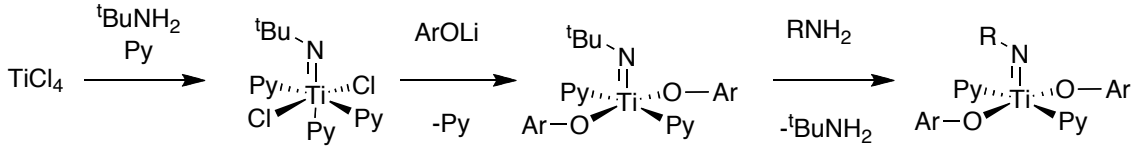
Entry	R	Yield **259** %
259a	4-$O_2NC_6H_4$	81
259b	4-$MeOC_6H_4$	50
259c	4-ClC_6H_4	76
259d	4-$EtO_2CC_6H_4$	41
259e	2,4,6-$Me_3C_6H_2$	53[a]
259f	2,6-$^iPr_2C_6H_3$	-
259g	4-$H_2NC_6H_4NH_2$	Mixture[b]

a = 53% product and 8% of aniline. b = Unidentified mixture.

Table 4.2: Transimination in oxo-aryl Ti=N complexes.

The yields of these reactions range from moderate to high, however, crude data analysis showed high levels of conversion for all reactions. The lower yields were due to difficulties in the isolation of the compounds. The reactions were performed in Et_2O where both starting material and product had low solubility, and after filtration and recrystallisation some of the compound was lost. As in previously described titanium complexes, transimination using hindered anilines produced lower yields and inseparable mixtures of starting material and product. In the case of entry **259e**, the transimination product could be isolated in 53% yield, but 8% of aniline impurity was present in the sample which could not be separated. The stability of this complex was shown to be very low, so only a ^1H NMR spectrum could be obtained by way of characterisation. Any other spectroscopic data showed degradation. When aniline **259f** was used, no reaction was observed, and only unreacted starting material isolated. When using 4-$NH_2C_6H_4NH_2$ (**259g**), spectroscopic data suggested the formation of a dimer, but an inseparable mixture of products was isolated. Presumably, the compounds could be monomer and dimer, although the ^1H NMR spectrum showed a very complicated spectrum.

The generation of complexes **259x** provided another route to 12-electron titanium-imido complexes. The strategy consisted of inversion of the order of chemical processes (Scheme 4.28). After generation of ^{t}butylimido-titanium complex **256**, chlorine ligand exchange produced titanium complex **259** and finally transimination produced a family of 12-electron titanium-imido complexes **259x**.



R = 2,6-Diisopropylphenyl

256 **259** **259x**

Scheme 4.28: Route to oxo-aryl Ti=N complexes.

We believe this route is more effective as a range of products can be accessed from a simple alkoxide complex **259**. As well as using akoxides in the modification of

titanium-imido complexes, ligand exchange with nitrogen-based nucleophiles could also be applied. Studies on the exchange of the chlorine ligands by a lithium salt of pyrrole have been performed successfully in 45 - 50%, without further development (see future work).

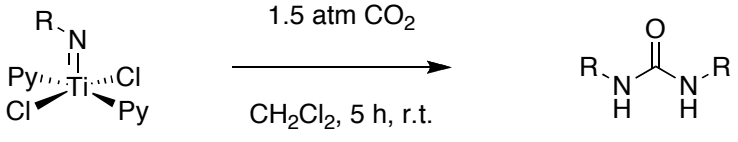
All of the titanium-imido complexes prepared, using any ligand set, were unstable to air and moisture. In some cases spectroscopic data could not be collected. In particular mass spectroscometric data was unable to be obtained from any of the samples.

4.2 Studies on the Activation and Reactivity of Carbon Dioxide

Once the 14- and 12-electron titanium-imido complexes had been synthesised and characterised, the complexes were treated with carbon dioxide in order to study their chemistry. All the experiments were performed using a solution saturated with carbon dioxide and 1.5 atmospheres of pressure. The reactions were also performed under a pressure of 8-10 bar, aiming to increase the yield or change the reactivity, however, decomposition of the complexes were observed under these high pressure conditions.

4.2.1 Studies on Isolated Titanium-Imido Complexes

The reaction between complexes **230x** with carbon dioxide and their success in the activation of carbon dioxide has previously been described in section 3.2.1 (Scheme 4.29). These two examples led us to believe that 12-electron titanium-imido complexes possessed the reactivity required to react with carbon dioxide.



230x

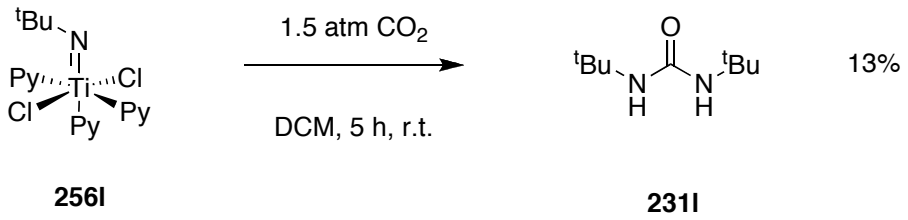
R = ^{t}Bu 8%
R = Bn 34%

231l
233

Scheme 4.29: Reaction of 12-electron Ti=N complexes with CO_2.

4.2.1.1 Studies on Purified Complexes

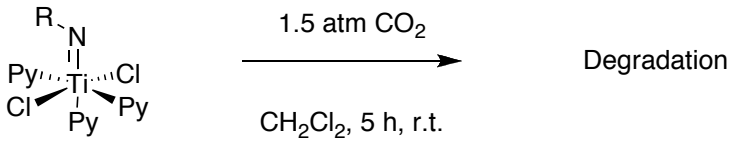
Our initial strategy was to generate simple 12-electron titanium-imido complexes and study their chemistry. However, due to the difficulties in the generation and the sensitive nature of the complexes we focussed on 14-electron complexes **256x** of which we had generated a number of analogues. The first of this family to be investigated was complex **256l**, the precursor for all the 14-electron complexes (Scheme 4.30). In spite of all our previous assumptions regarding the reactivity of the 12- and 14-electron complexes, this complex **256l** showed higher conversion to the symmetrical urea than its 12-electron complex analog (**231l**).



256l **231l**

Scheme 4.30: Reaction of 14-electron Ti=N complex with CO_2.

The increase in yield of this reaction, lead us to believe that the other analogues of complex **256x** (when ^{t}butylamine was replaced by anilines) could show some activity. However, when the reactions were performed under the same conditions, no product was obtained and only degradation was observed (Scheme 4.31).

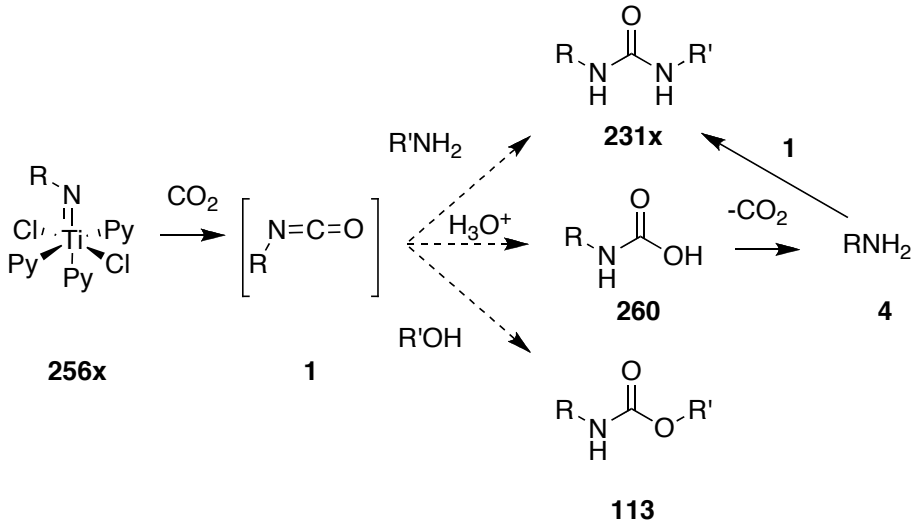


256x R = O_2NPh, MeOPh, EtO_2CPh, Me_2NPh, ClPh, 2,4,6-Me_3Ph, 2,6-$^i Pr_2$Ph.

Scheme 4.31: Unsuccessful reaction of Ti=N complexes with CO_2.

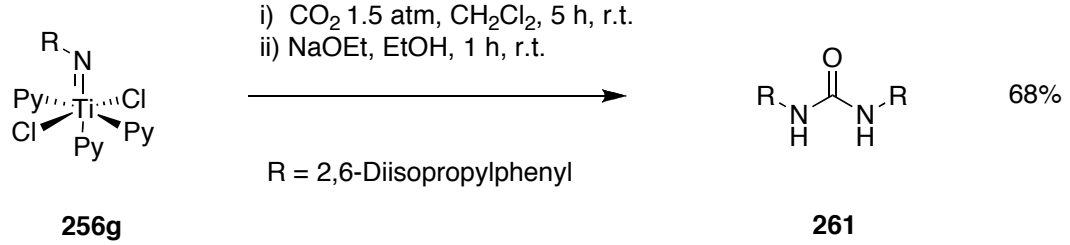
Considering the poor success of the reaction, it was decided to approach the reaction in another way. Assuming the formation of isocyanates in the desired reaction, these could

have been hydrolysed *in situ* to the corresponding amines (which degraded under reaction conditions). Therefore, it was decided to react the complexes **256x** with carbon dioxide and when the reaction was finished add a nucleophile which could react with the isocyanate to form various product (Scheme 4.32). The nucleophiles chosen were amines, that should lead to urea **231x**, alcohol (or alkoxides) that should lead to a carbamate and acidic water leading to an amine, *via* a carbamic acid which could conceivably add to a residual isocyanate to form urea.



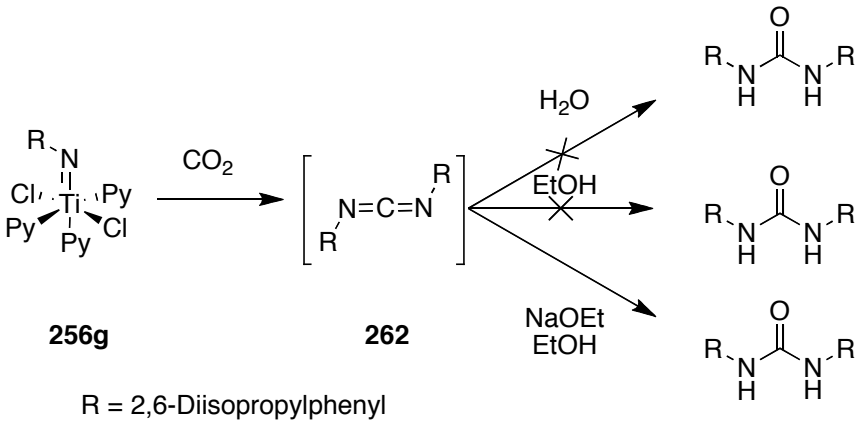
Scheme 4.32: Proposed strategy.

Unfortunately only one of the complexes (2,6-diisopropylphenylimido-titanium complex **256g**) showed reactivity when treated with carbon dioxide. The reaction showed degradation when quenched with an alcohol, not the expected carbamate. Surprisingly the addition of sodium ethoxide formed symmetrical urea **261** in excellent yield (68%) (Scheme 4.33).



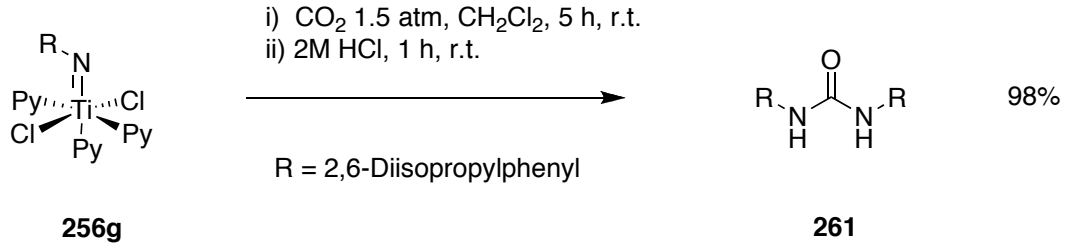
Scheme 4.33: Formation of symmetrical urea from CO_2.

If the reaction in Scheme 4.32 was proceeding *via* hydrolysis of carbodiimide **262**, the same result should have been observed when quenched only by water. Also, the addition of an alcohol should have produced the same result (Scheme 4.33). However, the difference led us to believe that the reaction (Scheme 4.34) was proceeding *via* a different mechanism or intermediates.



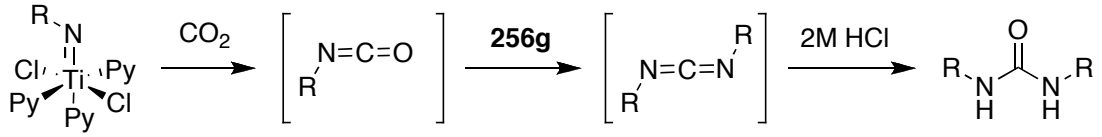
Scheme 4.34: Reactivity of Ti=N complex.

The same reaction showed in Scheme 4.32 was also quenched with 2M HCl with the hope of obtaining either the aniline or symmetrical urea. On this occasion urea **261** was isolated in nearly quantitative yield (Scheme 4.35).



Scheme 4.35: Formation of urea from carbon dioxide.

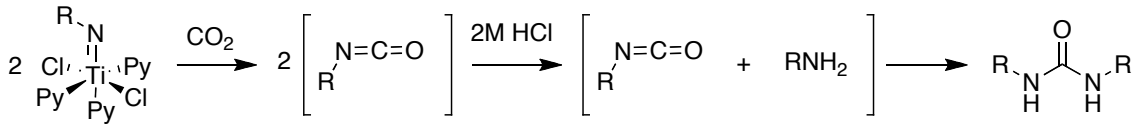
This result did not elucidate the mechanism of the reaction, as two possible pathways could explain the formation of **261** (Scheme 4.35). The reaction could proceed *via* acid hydrolysis of carbodiimide **262** (Scheme 4.36).



256g **1k** **262** **261**

Scheme 4.36: Carbodiimide hydrolysis.

Alternatively complete formation of isocyanate **1k**, followed by acid hydrolysis to aniline **4** and final urea (**261**) formation by addition of amine to isocyanate could occur (Scheme 4.37). Although it is known that amines and isocyanates react very quickly, it seems unlikely under the reaction conditions of hydrolysis.

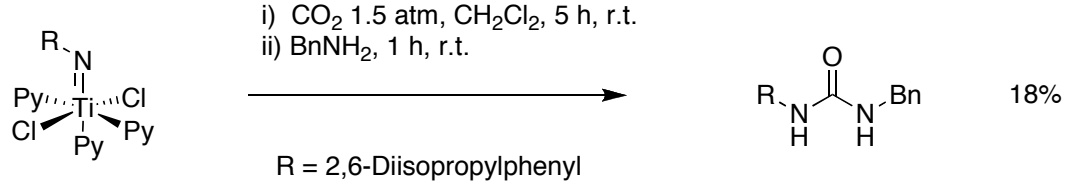


256g **1** **1** **4** **261**

R = 2,6-Diisopropylphenyl

Scheme 4.37: Isocyanate hydrolysis.

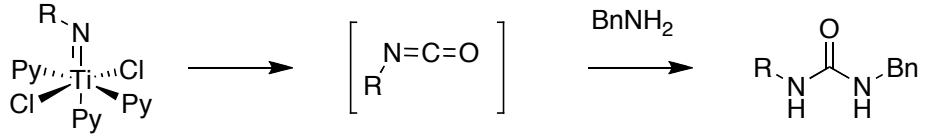
Both of the above reactions (Scheme 4.35 and 4.33) produced symmetrical urea **261** in moderate to high yield, but an explanation for the mechanism could not be elucidated from the experiments. The last reaction was the addition of benzylamine as a non-aromatic amine to form an unsymmetrical urea (**263**). This reaction worked as predicted, but only produced unsymmetrical urea **263** in low yield (Scheme 4.38).



256g **263**

Scheme 4.38: Formation of unsymmetrical urea from carbon dioxide.

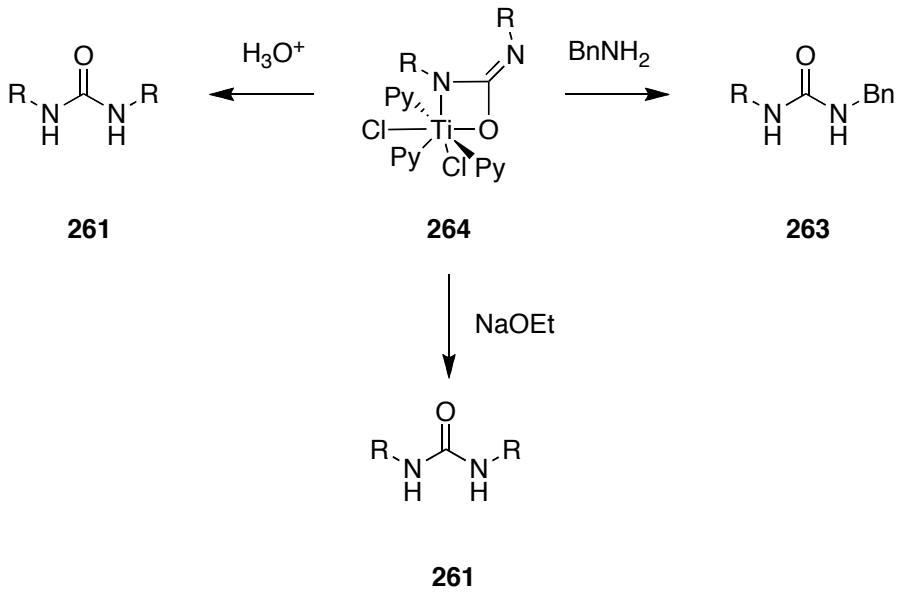
It was expected that some symmetrical urea **261** should have been formed. However, its absence suggests that the urea formation occurs *via* formation of isocyanate **1k**, followed by reaction with benzylamine (Scheme 4.39).



256g **1k** **263**

Scheme 4.39: Possible mechanism for the reaction.

The hypothesis of the carbodiimide formation was supported by some of the experiments (Scheme 4.33 and 4.35), but did not explain the benzylamine experiment (Scheme 4.38). The inconsistency between the above experiments may suggest a different mechanism may be operating in the reaction with carbon dioxide. It is possible that a four-membered metallocycle **264** could be formed, which could be stable or have a slower [2+2] retro-cycloaddition (as it was seen in section 3.2.2) (Scheme 4.40). Depending on which compound is added to quench the reaction ($BnNH_2$, H_3O^+ or EtONa), there would be a different isolated product. The addition of acidic water will decompose the complex to generate symmetrical urea. Benzylamine could add into the imido-carbamate and form an unsymmetrical urea. Sodium ethoxide will not react with metallocycle, instead it will react with the titanium and eliminate urea.

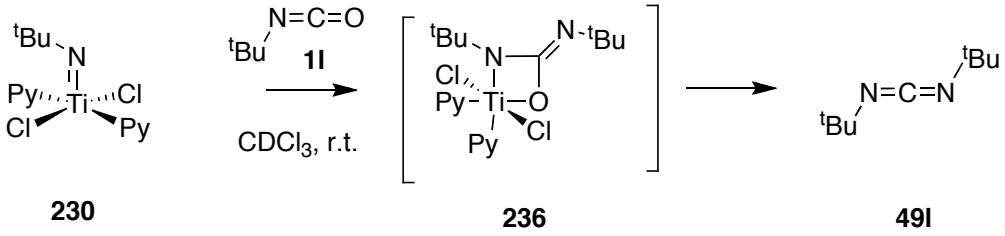


261 **264** **263**

261

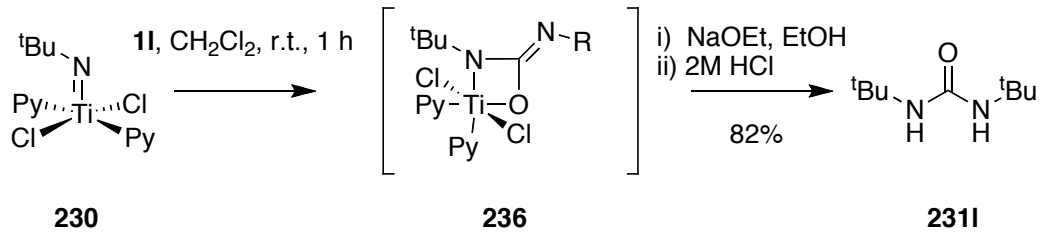
Scheme 4.40: Possible variation for the mechanism.

In section 3.2.2 the formation of carbodiimides from ^{t}butylimido-titanium complexes and isocyanates was studied. One of the examples (entry **49l**, Table 3.1) showed the possibility of a four-membered metallocycle **236**. The [2+2] cycloaddition reaction was a fast reaction (isocyanate starting material was consumed in approximately 5 min), and led to a reasonably stable intermediate **236** (Scheme 4.41). The possible intermediate proposed in Scheme 4.40 suggests that these processes (section 3.2.2 and Scheme 4.33, 4.35 and 4.38) react similar intermediates. Knowing that in the case of **49l** the intermediate formed had reasonable stability, we decided to use it to study the hypothesis in Scheme 4.40.



Scheme 4.41: Reaction between ^{t}butylimido-titanium complex **230** and ^{t}butylisocyanate.

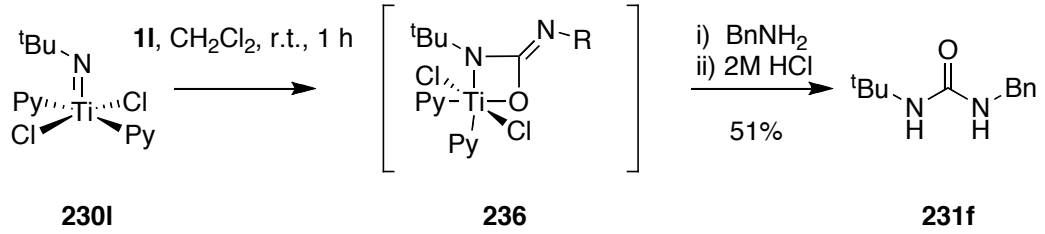
The reaction of ^{t}butylimido-titanium complex **230** and ^{t}butylisocyanate (**1l**) generated symmetrical urea in low 32% yield upon quenching under acidic conditions (Scheme 3.12). When the reaction was quenched with sodium ethoxide the result was again the isolation of symmetrical urea in 82% yield (Scheme 4.42).



Scheme 4.42: Heterocumulene metathesis - NaOEt quench experiment.

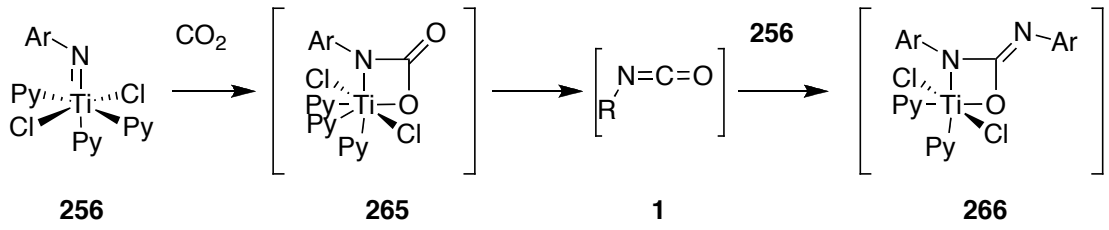
The last one of these family of experiments was to quench the intermediate with benzylamine and this gave the unsymmetrical urea **231f** in 51% yield (Scheme 4.43).

The symmetrical urea **231l** was not detected in the crude reaction mixture or isolated product.



Scheme 4.43: Heterocumulene metathesis - benzylamine quench experiment.

The results of these experiments (section 3.2.2, Scheme 4.33, 4.35, 4.38, 4.41, 4.42 and 4.43) suggest a similar four-membered metallocycle intermediate in the process. This leads us to the conclusion that in experiments shown in scheme 4.33, 4.35 and 4.38 we could be forming isocyanate **1** *in situ*, which undergoes a [2+2] cycloaddition to form intermediate **266** (Scheme 4.44). Depending on the compound added to quench the reaction, different ureas can be isolated.

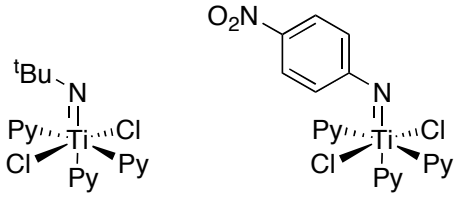


Scheme 4.44: Plausible mechanism for the reaction of Ti=N complexes with CO2.

Since only two of the 14-electron titanium-imido complexes showed reactivity with carbon dioxide, we could conclude that this family of complexes are generally unreactive towards carbon dioxide. We thought that the two complexes that did show some reactivity may help us to elucidate some characteristics or requirements to achieve and enhance reactivity.

According to the single crystal X-ray structures obtained, the Ti=N bond distance for complex **256l** (1.705Å) is smaller than the same bond in complex **256b** (1.722Å) (Figure 4.1). According to our hypothesis, this should increase the activity of **256b**,

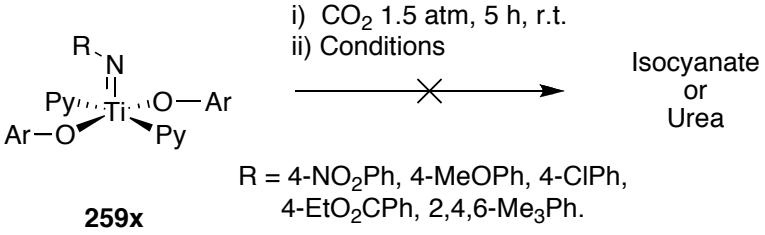
however, the experimental data shows the reverse behaviour. The Ti=N-C bond angles show 175° for complex **256l** and 180° for complex **256b**. Although the difference is small, this comparison suggests than complex **256l** should be more reactive. The disagreement between these observations has made it difficult to understand any requirements for the reactivity with carbon dioxide. It is conceivable that the steric interactions due to the bulkiness of the ^{t}butylimine in complex **256l** could produce the disagreement between the data, and therefore the difference in reactivity.



256l **256b**

Figure 4.1: Comparison beween Ti=N complexes.

With these experiments in hand, it only remained to test the reactivity of the 12-electron titanium-imido oxoaryl complexes (**259x**) with carbon dioxide. Although preliminary ^{1}H NMR experiments using complex **259l** showed the possible formation of ^{t}butylisocyanate, none of the compounds reacted with carbon dioxide (Scheme 4.45). These experiments were performed in the same way as for the 14-electron titanium-imido complexes (**266**) using a variety of conditions, but no reactivity was observed, only decomposition.

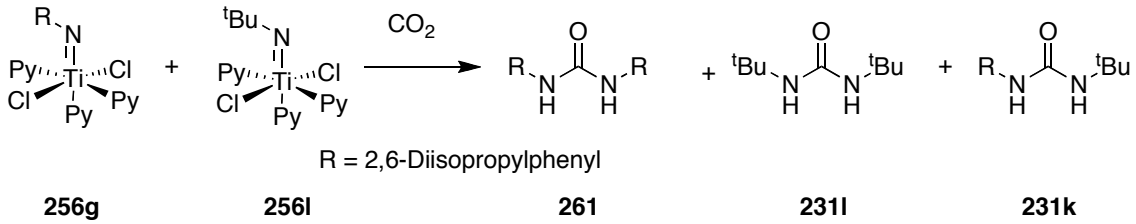


259x

Scheme 4.45: Unsuccessful reaction of oxo-aryl Ti=N complexes with CO_2.

4.2.1.2 Studies on Mixtures of Complexes

We have found that two 12-electron complexes (with non-aromatic amines) and two 14-electron complexes (one aromatic and one non-aromatic amines) reacted with carbon dioxide (Scheme 4.29, 4.30 and 4.35). In all the examples when the reactions were quenched in acidic media, symmetrical ureas instead of isocyanates were obtained. We decided to investigate this reaction by reacting a mixture of two complexes with carbon dioxide (Scheme 4.46). In theory, a mixture of three compounds could be obtained: symmetrical ureas (**261** and **232l**) and mixed urea (**231k**).



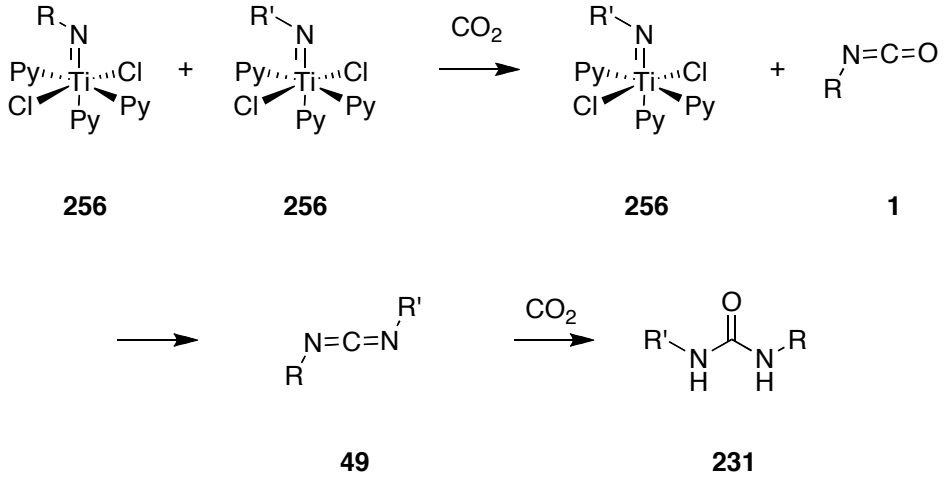
Scheme 4.46: Reaction of mixtures of complexes with carbon dioxide.

Entry	Ratio **256g** : **256l**	Yield **232k** %
231ka	70 : 30	36
231kb	36 : 64	21

Table 4.3: Reaction of mixtures of complexes with carbon dioxide.

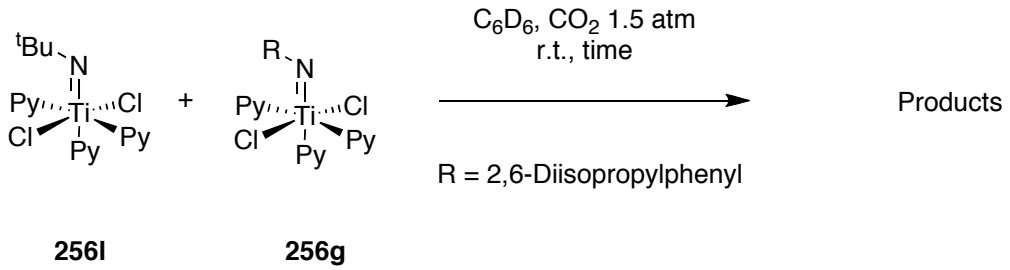
Two different mixtures of starting materials were reacted with carbon dioxide following the same reaction conditions as for the initial experiments (Scheme 4.46). Surprisingly, upon treatment of a mixture of complexes **256g** and **256l** with carbon dioxide (1.5 atmospheres) for 5 h at r.t. in CH_2Cl_2, followed by work up with 2M HCl, only unsymmetrical urea was isolated in both of the cases.

The formation of only unsymmetrical urea in both cases suggested that one of the complexes reacted much faster with carbon dioxide than the other (Scheme 4.47). The isocyanate formed could then react with the other complex to form a mixed carbodiimide. Finally, hydrolysis produced mixed urea **232k**.



Scheme 4.47: Mechanism for the reaction.

In order to assess the mechanism of the reaction, further experiments consisting of reaction of a known ratio of both starting materials were reacted with carbon dioxide (Scheme 4.48). To study the effect of the concentration of the two complexes in the reaction mixture. In this case the experiment were performed using C_6D_6 as solvent, to enable produced easier interpretation of the data. No differences in reactivity were observed between $CDCl_3$, CH_2Cl_2 and C_6D_6. ^1H NMR spectra were recorded at known times to monitor the evolution of the reaction (section 5.10.1).

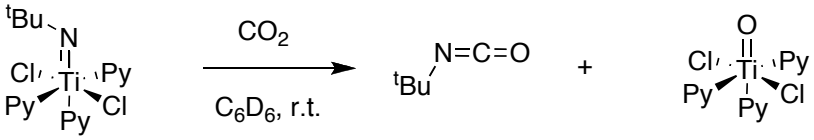


Scheme 4.48: ^1H NMR experiment to measure the evolution of the reaction.

Entry	Initial Ratio **256l** : **256g**	16 h Ratio **256l** : **256g**	40 h Ratio **256l** : **256g**
256a	20 : 80	4 : 96	0 : 100
256b	28 : 72	12 : 88	0 : 100
256c	52 : 48	37 : 63	26 : 74
256d	48 : 52	40 : 60	29 : 71
256e	60 : 40	50 : 50	43 : 57
256f	77 : 23	70 : 30	64 : 36

Table 4.4: Evolution of the reaction using different ratios of **256l** and **256g**.

Although the ratios described are relative values, by referring them to an external standard (mesitylene), it was observed that the concentration of complex **259g** remained constant during the process. Its lack of reactivity was shown (entries **256a** and **256b**) where complex **256l** was completely consumed, but complex **259g** still remained at the same concentration. The data collected showed that complex **256l** reacted with carbon dioxide, while complex **259g** remained intact. It was believed that the reaction between complex **256l** and carbon dioxide would produce ^{t}butyl isocyanate and titanium-oxo complex **267** (Scheme 4.49).

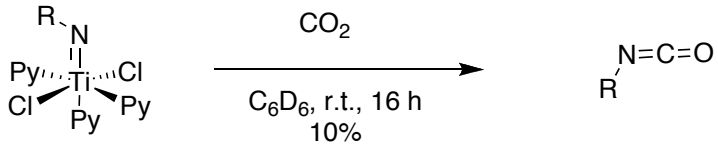


256l **1l** **267**

Scheme 4.49: Reaction between complex **256l** and CO_2.

The ^{1}H NMR spectrum showed the signal for the ^{t}butyl peak disappeared as the reaction progressed. However, the characteristic signal of the ^{t}butyl group did not appear anywhere else in the spectrum. When complex **256l** was reacted individually under the same reaction conditions with carbon dioxide, the result of the experiment changed. As complex **256l** was being consumed, another peak of an unidentified compound appeared. However, the result suggested that some product was disappearing as the

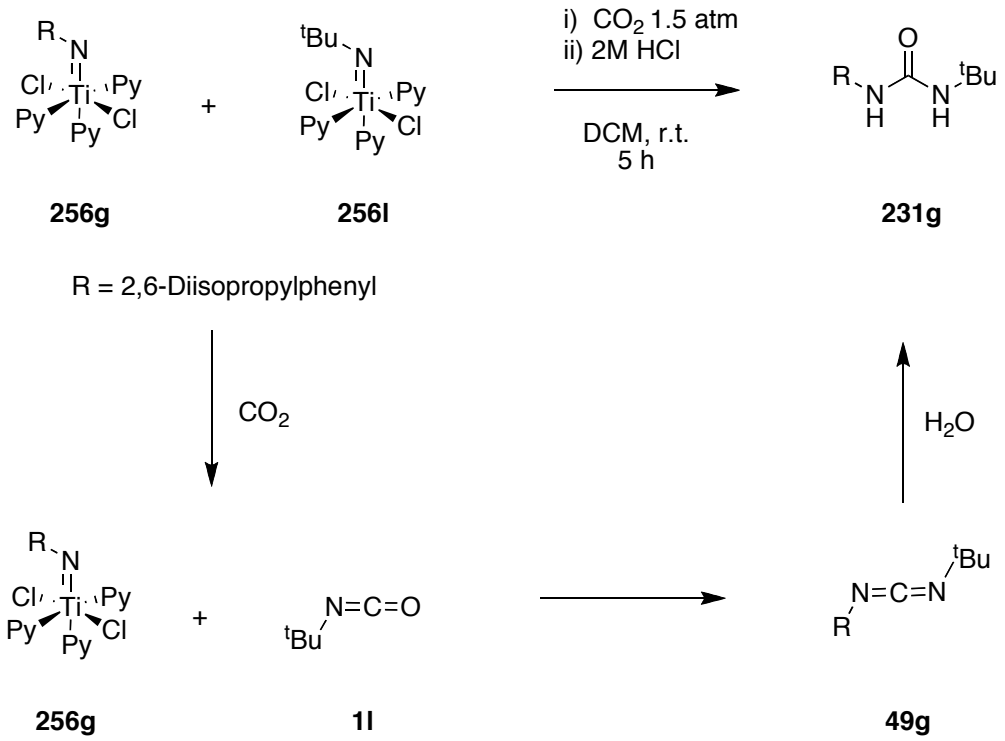
amount of complex **256l** and the amount of the new compound formed were lower compared to an external standard. On the other hand, when complex **256g** was treated individually with carbon dioxide, 10% conversion to isocyanate was observed (Scheme 4.50).



256 **1**

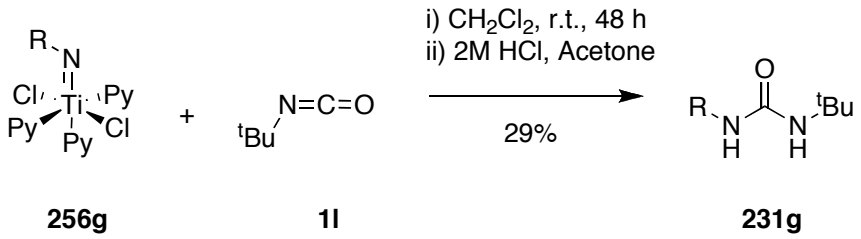
Scheme 4.50: ^{1}H NMR experiment for complex **256g**.

The results obtained from the ^{1}H NMR experiments (Table 4.4) concluded that complex **256l** reacted with carbon dioxide faster than complex **256g**. This allows us to suggest a plausible mechanism for the reaction. First a heterocumulene metathesis between complex **256l** and carbon dioxide generates isocyanate **1l**. In this first step complex **256g** did not play any role and acts as a spectator. It is in the second step of the reaction when the generated isocyanate (**1l**) reacts with the remaining complex **256g** *via* a second hetercumulene metathesis to generate unsymmetrical carbodiimide **49g**. Final hydrolysis yielded urea **231g** (Scheme 4.51).



Scheme 4.51: Suggested mechanism.

As previously described in section 3.2.3 the isolation of carbodiimide **49g** was very difficult due to its high reactivity, undergoing hydrolysis to the corresponding urea. Therefore, it was expected that isolation of carbodiimide **49g** was not possible. In order to support the mechanism of the reaction, it was shown that treatment of complex **256g** with isocyanate **1l**, gave urea **231g** in 29% yield (Scheme 4.52).

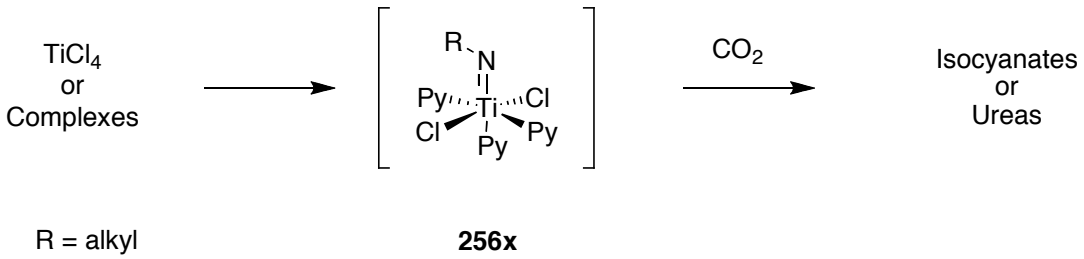


Scheme 4.52: Heterocumulene metathesis.

After performing the experiments of all the isolated titanium-imido complexes with carbon dioxide, no isocyanates were obtained, and only on isolated occasions did some complexes show reactivity.

4.2.2 Studies on *in situ* Formation of Non-Aromatic Amine Titanium-Imido Complexes

The results of the carbon dioxide reactivity experiments with arylimido-titanium complexes had shown generally unsuccessful activation with only poor reactivity in some isolated cases. The reactivity of non-aromatic titanium-imido complexes has not been tested, with the exception of complex **230** and **232**. It is known that non-aromatic amines are generally more nucleophilic and basic than aromatic ones, and therefore could generate different results than the aromatic complexes. For this reason it was thought that it would be interesting to study the possible *in situ* formation of complexes **256x** and then subsequent reaction with carbon dioxide (Scheme 4.53). These experiments could generate valuable information concerning the reactivity of the complexes.

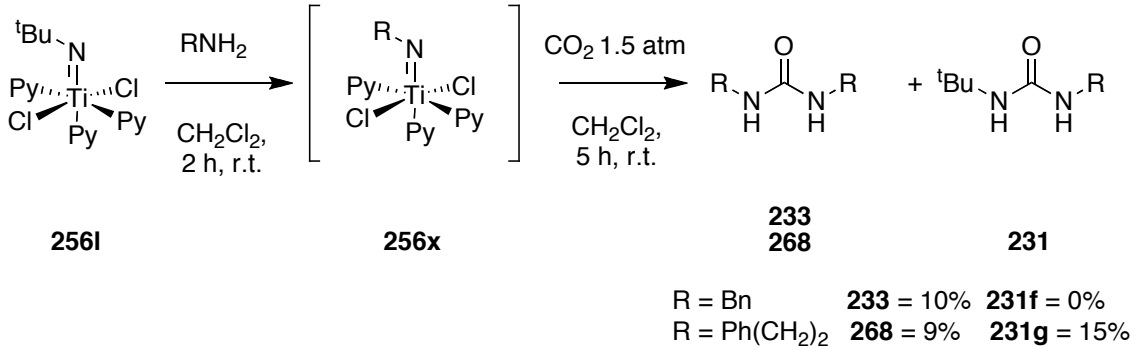


Scheme 4.53: Proposed *in situ* experiments.

4.2.2.1 Transimination

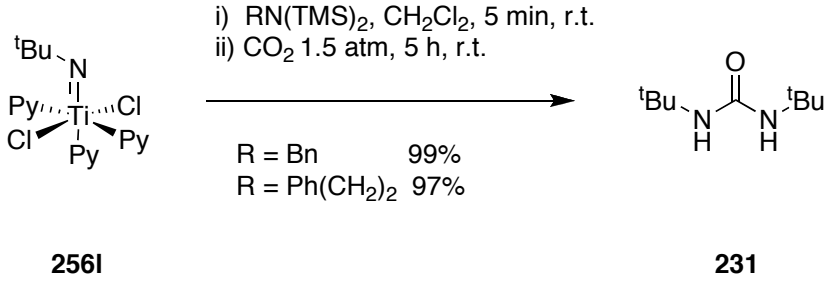
It has already been shown that a transimination reaction can be used to prepare analogues of complex **256** where R is an aromatic substituent. This reaction proceeds with complete conversion and good isolated yield using aromatic amines (section 4.1.2). However, when the transimination was attempted using a non-aromatic amine, the reaction did not go to completion and a mixture of starting material and products was obtained (see section 4.1.1). Due to difficulties in the separation and purification we decided to submit the mixtures directly to the carbon dioxide reaction conditions, obtaining low yields of symmetrical and unsymmetrical urea (Scheme 4.54).

Transimination experiments were performed using benzylamine and 2-phenylethylamine.



Scheme 4.54: One-pot transimination - CO_2 reaction.

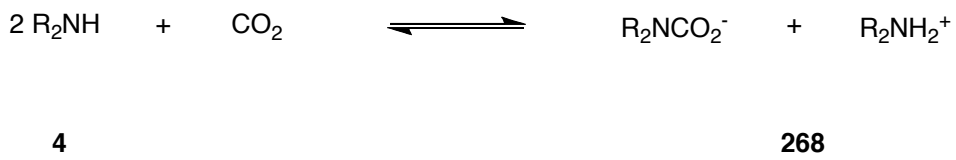
The yields obtained in the reactions were very low, and believed to be caused by the low reactivity between carbon dioxide and the impure complexes. As was explained previously, another way of synthesising the desired complexes was by using bis-silyl protected amines. In this case, the same *in situ* transimination and treatment with carbon dioxide conditions were applied, but the results were completely different (Scheme 4.55). The reaction generated the symmetrical urea **231** only, in almost quantitative yield. This excellent yield represent an improvement to those exposed in scheme 4.30 where the yield was only 13%.



Scheme 4.55: One pot transimination - CO_2 reaction using additives.

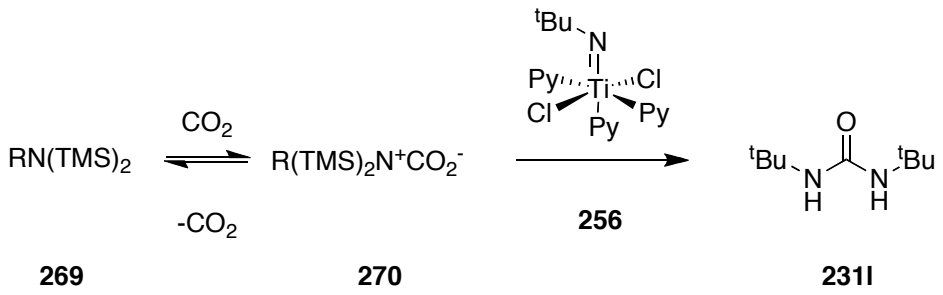
The fact that only urea **231** was obtained, led us to believe that no transimination was occurring in the reaction; however, the silylated amine was activating the complex to react with carbon dioxide. It is known that amines **4** can react with carbon dioxide to form an equilibrium with a carbamate salt **268** (Scheme 4.56). It is also known that bis-

silyl protected amines are more basic and nucleophilic, yet more hindered, than primary amines.



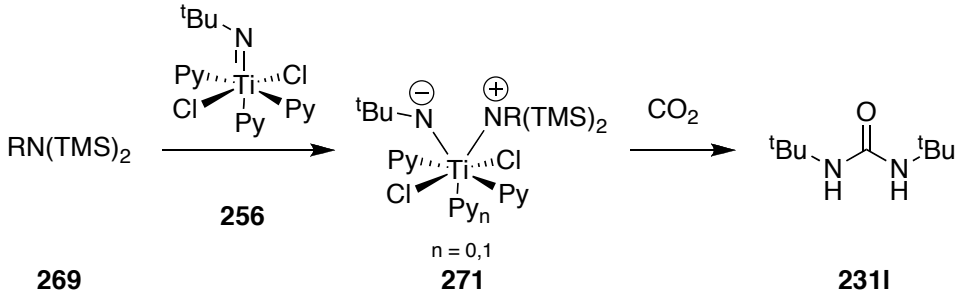
Scheme 4.56: Equilibria amines - carbamate.

Knowing these two facts, it could be possible that the bis-silyl protected amine was activating carbon dioxide to undergo heterocumulene metathesis (Scheme 4.57).



Scheme 4.57: Carbon dioxide activation.

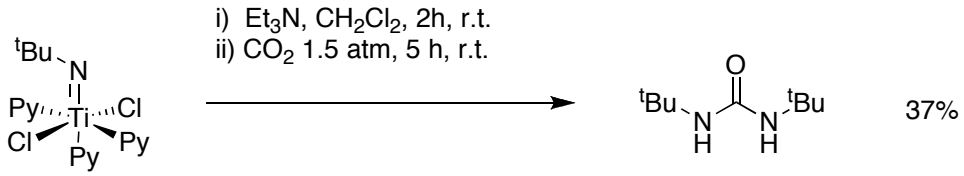
On the other hand, it could also activate the complex for the reaction (Scheme 4.58). No evidence to support these two processes was obtained.



Scheme 4.58: Complex activation.

It could be possible that under the reaction conditions decomposition of the silyl amine to form TMS^+ *in situ*, could also activate the tianium-imido complex to react with carbon dioxide. Again, no evidence for this possible mechanism was found.

The activation of the complex seemed a more complicated explanation due to steric interactions which would increase the instability of the complex **271**. The exact role of the bis-silyl protected amine in the reaction is not known. In an attempt to understand this behaviour, the experiment was repeated using a tertiary alkyl amine under the same reaction conditions (Scheme 4.59).



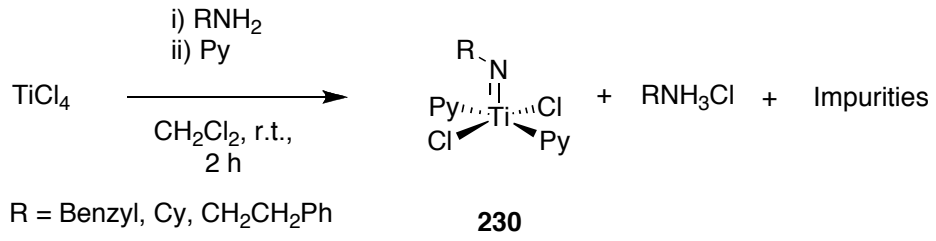
256 **231**

Scheme 4.59: One-pot transimination - CO_2 reaction using additives.

The yield in this reaction using triethylamine decreased to approximately one third of that when using $RN(TMS)_2$ (Scheme 4.55). This result confirms that amines activate the reaction and, more importantly, that the use of bis-silyl amines activates the process more efficiently than tertiary amines. This is a very important discovery for the future applications of this reaction.

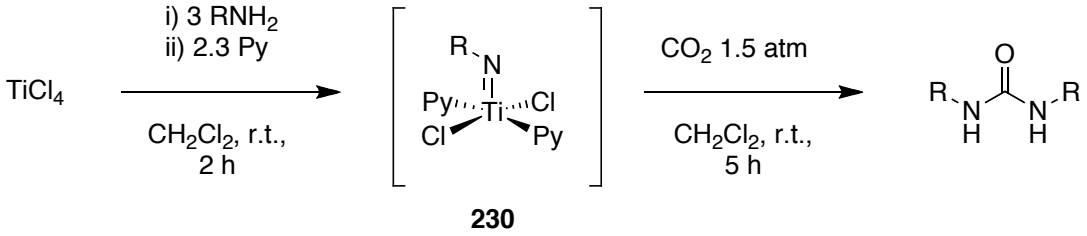
4.2.2.2 One-Pot Synthesis

Another conceivable route to non-aromatic imido-titanium complexes is their generation in one single step from $TiCl_4$ and non-aromatic amines (Scheme 4.60). This route provided moderate to good yields of the desired complexes, however, the formation of by-products with similar solubility made their purification difficult. ^1H NMR suggests the formation of complex **230**.



Scheme 4.60: Formation of Ti=N complexes using non-aromatic amines.

Despite the problems in isolation, a one pot reaction consisting of the formation of the complex *in situ* and heterocumulene metathesis reaction with carbon dioxide was performed (Scheme 4.61). The process showed good reactivity to produce a variety of symmetrical ureas.



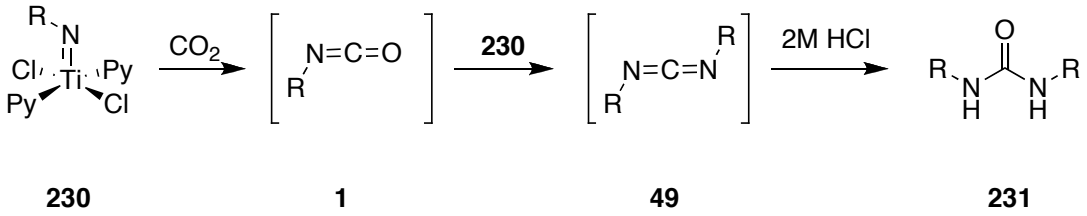
Scheme 4.61: Mechanism for one-pot synthesis - reaction with CO_2 using 3 equivalents of amine.

Entry	Compound	R	Yield urea %
230a	**233**	Bn	48
230b	**268a**	Cy	36
230c	**268b**	$Ph(CH_2)_2$	56
230d	**231l**	^{t}Bu	7

Table 4.5: One-pot synthesis - reaction with CO_2 using 3 equivalents of amine.

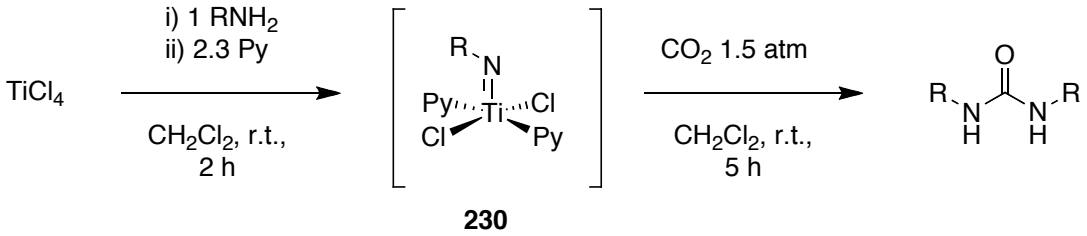
Using three different non-aromatic amines, the yield of the reaction varied from low to moderate. The addition of three equivalent of the amine is necessary as one acts as the imido ligand, whereas the remaining two act as a base to eliminate HCl. Before the addition of carbon dioxide, the amine is thought to be completely consumed. Therefore, the mechanism of this reaction is formation of the complex **230**, followed by

heterocumulene metathesis with carbon dioxide to form isocyanate **1**. Secondly heterocumulene metathesis occurs between complex **230** and isocyanate (**1**) to form carbodiimide **272**. This is followed by final hydrolysis to yield urea (Scheme 4.62). This mechanism requires two equivalents of $TiCl_4$ to form one equivalent of urea.



Scheme 4.62: Mechanism for the formation of symmetrical urea.

To confirm the requirement of three equivalents of amine, the same experiments were performed using only one equivalent of amine (Scheme 4.63). The results were, as predicted, approximately one third of the yield of isolated complex **230** compared to the above experiments.



Scheme 4.63: One pot synthesis - reaction with CO_2 using 1 equivalents of amine.

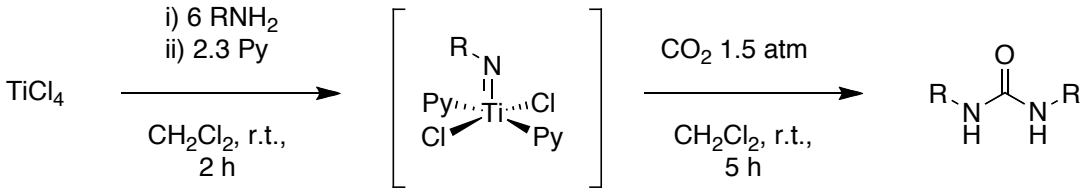
Entry	Compound	R	Yield urea %
230a	**233**	Bn	16 (48)
230b	**268a**	Cy	14 (42)
230c	**268b**	$Ph(CH_2)_2$	17 (51)
230d	**231l**	^{t}Bu	2 (6)

Yield based on $TiCl_4$. In brackets, extrapolated yields considering only 33% could occur.

Table 4.6: One pot synthesis - reaction with CO_2 using 1 equivalents of amine.

The yields of these reactions confirmed the need for three equivalents of amine. In parentheses are the extrapolated yields, considering that the reaction could only proceed to 33% conversion. Note they are very similar to these in Table 4.5.

The next step in this study was the addition of excess amine as we thought that this could increase the yield of urea. However, the use of 6 equivalents of amine caused a decrease in the yield of the reaction, with the exception of **231l** which gave an increase in the yield (Scheme 4.64). The unusual reactivity of this substrate **231l** is unfortunately not understood at this time.



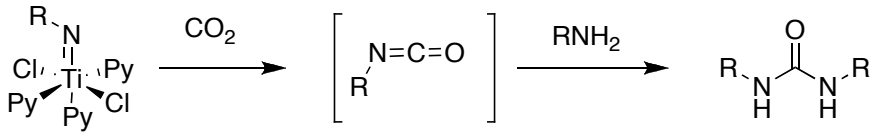
230

Scheme 4.64: One pot synthesis - reaction with CO_2 using 6 equivalents of amine.

Entry	Compound	R	Yield urea %
230a	**233**	Bn	34
230b	**268a**	Cy	19
230c	**268b**	$Ph(CH_2)_2$	42
230d	**231l**	^{t}Bu	26

Table 4.7: One pot synthesis - reaction with CO_2 using 6 equivalents of amine.

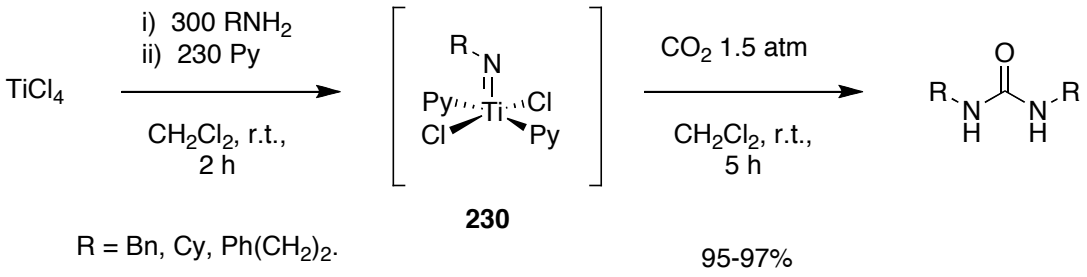
The mechanism for the reactions when 3 equivalents of amine are used requires the use of two equivalents of $TiCl_4$ to form one equivalent of urea. In the cases where an excess of amine is used, the mechanism for the reaction could be different. Once the complex **230** is formed, it presumably undergoes heterocumulene metathesis with carbon dioxide to form isocyanate **1** as before. The excess of amine present, can then react with the isocyanate **1** to form urea (Scheme 4.65). This mechanism requires only one equivalent of $TiCl_4$ to form one equivalent of urea and conceivably the yield could be double.



230 **1** **231**

Scheme 4.65: Mechanism for the formation of urea from CO_2 using excess amine.

Despite the decrease in yield when using an excess of amine (6 equivalents experiments), it is possible to obtain a nearly quantitative yield by adding a much larger excess (Scheme 4.66). To obtain a consistent, near quantitative yield in all cases, the addition of 300 equivalents was required.



230

R = Bn, Cy, $Ph(CH_2)_2$.

95-97%

Scheme 4.66: Quantitative generation of urea from CO_2.

Hypothetically if the titanium-imido complex was transformed quantitatively into urea, the by-product of the reaction should be the titanium-oxo complex. It was decided to attempt the activation of Ti=O by TMSCl to obtain Ti=N (Figure 4.2). This experiment would allow us to turn-over the metal complex and complete the catalytic cycle.

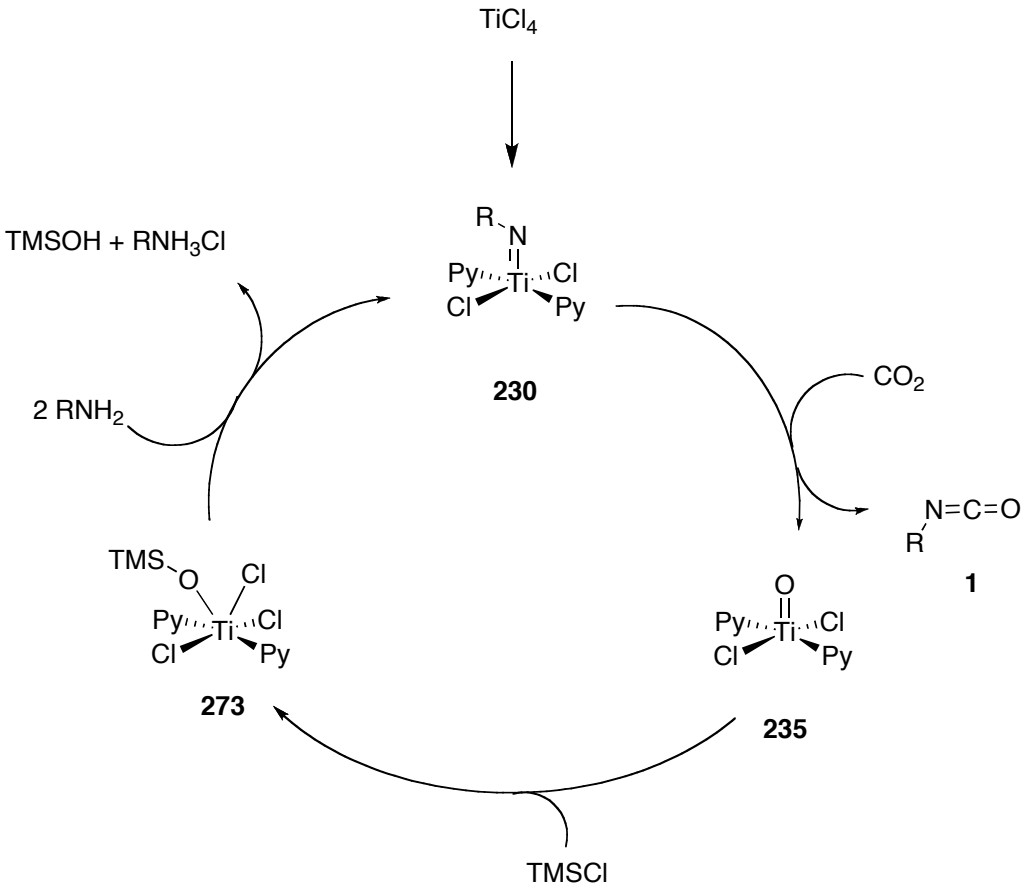
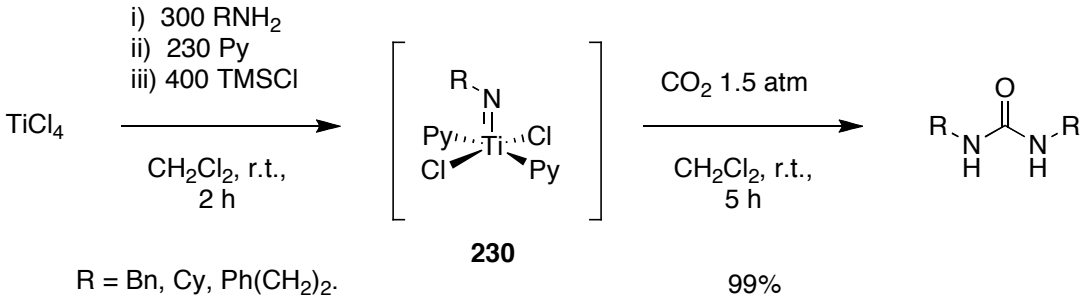


Figure 4.2: Proposed cycle.

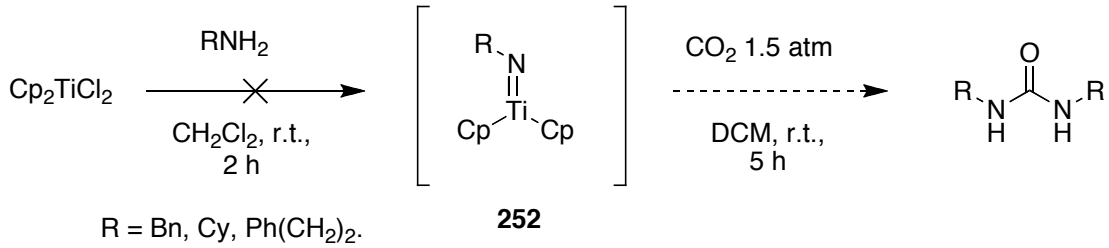
Repeating the experiment under the conditions with a vast excess of amine (as Scheme 4.66), but in the presence of a large excess of TMSCl (400 equivalents), gave urea in nearly quantitative yield with respect to $TiCl_4$ (Scheme 4.67). This result suggested that TMSCl did not activate the reaction to complete the cycle. Therefore, the addition of the Lewis acid did not make any difference in the reaction.



Scheme 4.67: Attempted catalytic reaction.

Other Lewis acids such as $Mg(OTf)_2$, Bu_3BOTf, Bu_3SnCl and $B(C_6F_5)_3$ were also tested under the same conditions to study the activation of Ti=O using a similar strategy. However, no activation was achieved and these other Lewis acids also inhibited the reaction and no urea was formed.

One of our first attempts to synthesise titanium-imido complexes was using titanocene dichloride, which was unsuccessful. Despite its lack of reactivity, we attempted *in situ* experiments to react Cp_2TiCl_2 with non-aromatic amines and carbon dioxide to form ureas (Scheme 4.68). However, the reactions showed no formation of the product and we concluded there was no evidence for the *in situ* formation of titanocene-imido intermediate.

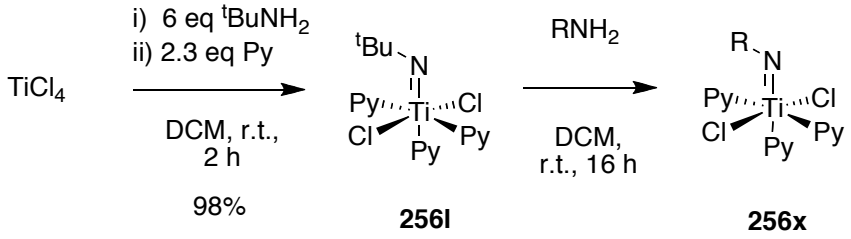


Scheme 4.68: Unsuccessful formation of Ti=N complex.

These last *in situ* experiments aimed at completing the reaction cycle, concluded our studies concerning the reactivity of titanium-imido complexes with carbon dioxide.

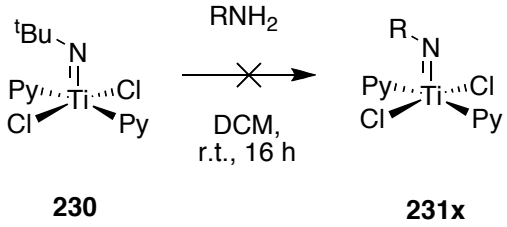
4.3 Conclusions

Concerning the generation of titanium-imido complexes, our research has shown the successful formation of 14-electron imido titanium complexes **256** and their ligand exchange derivatives (**256**) (Scheme 4.69). It has also been shown that non-aromatic amines can be used, however these are limited due to problems with purification.



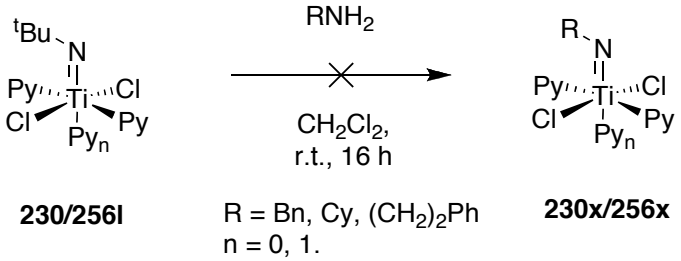
Scheme 4.69: Successful formation of 14-electron titanium-imido complexes.

Transimination of the parent ^{t}butylimido complexes did not occur with 12-electron titanium-imido complexes (Scheme 4.70). However, it was successful with the 14-electron complexes (Scheme 4.69).



Scheme 4.70: Unsuccessful transimination of 12-electron titanium-imido complexes.

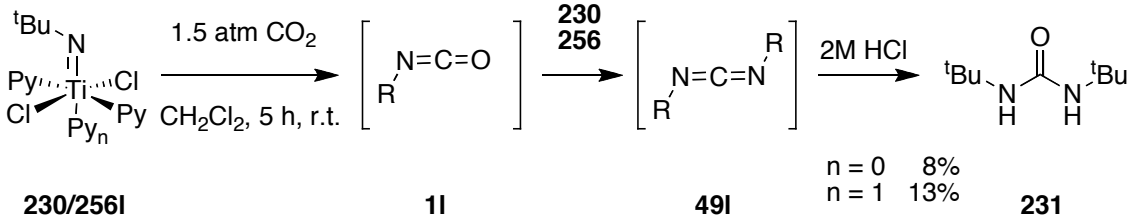
Anilines proceeded in high conversions, with the exceptions of sterically hindered substrates (Scheme 4.17). In the case of aliphatic amines pure compounds were not produced, due to the formation of an equilibrium, and an inseparable mixture of starting material and product being isolated (Scheme 4.71).



Scheme 4.71: Unsuccessful transimination with aliphatic amines.

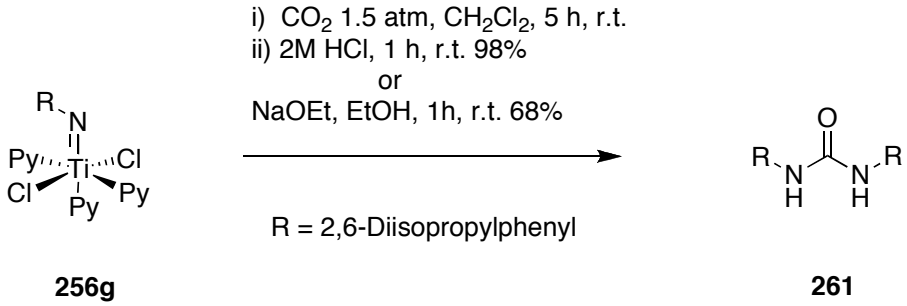
On the development of these findings, it was shown that non-aromatic 12- and 14-electron titanium-imido complexes could be generated *in situ*, all with impurities.

Three of the synthesised complexes (**230**, **232** and **256**) successfully reacted with carbon dioxide. Both 12- and 14-electron ^{t}butylimido titanium complexes **230** and **256**, reacted with carbon dioxide to form urea **231l** (Scheme 4.72). The mechanism for the reaction is believed to proceed *via* formation of an isocyanate, followed by a carbodiimide which upon hydrolysis gave the subsequent urea **231l**.



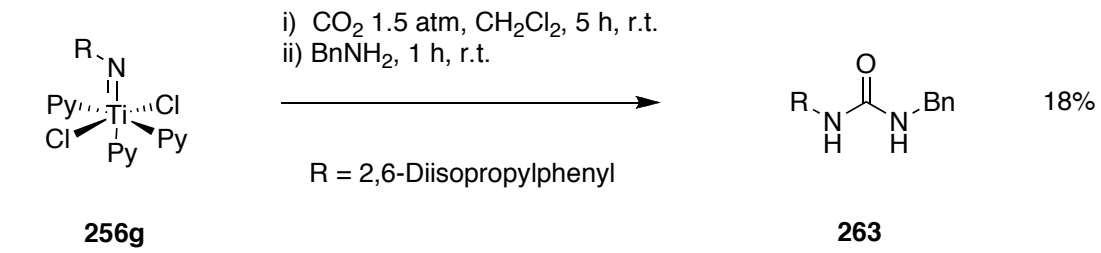
Scheme 4.72: Mechanism for the formation of symmetrical urea.

Following a similar pattern, 2,6-diisopropylphenylimido titanium complex **256g** also reacted with carbon dioxide, however, this time the reaction produced a high yield of symmetrical urea **261** when quenched in acid or with NaOEt (Scheme 4.73).



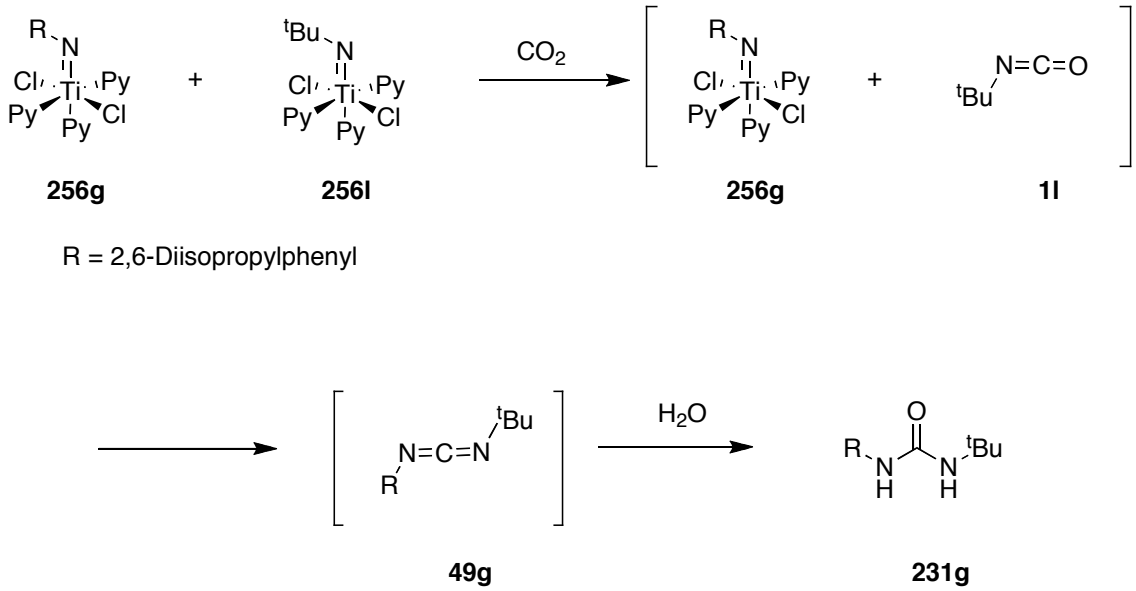
Scheme 4.73: Formation of symmetrical urea.

When the reaction was quenched with benzylamine, unsymmetrical urea **263** was obtained in moderate to low yield (Scheme 4.74). There are evidences to suggest the same four-membered metallocycle for Scheme 4.73 and 4.74.



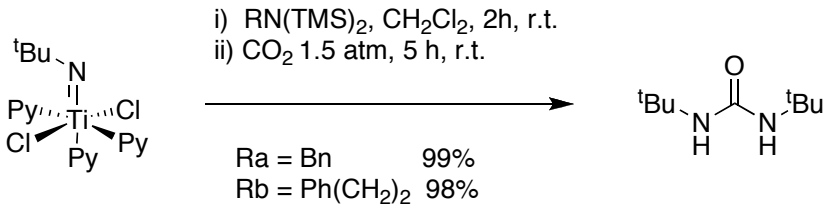
Scheme 4.74: Formation of unsymmetrical urea.

Experiments performed with a mixture of complex **256g** and complex **256l**, showed that carbon dioxide prefers to undergo heterocumulene metathesis with complex **256l**. A second heterocumulene metathesis between complex **256g** and isocyanate **1l** generated urea **231g** after hydrolysis of the corresponding carbodiimide (Scheme 4.75).



Scheme 4.75: Formation of unsymmetrical urea from carbon dioxide and mixture of complexes.

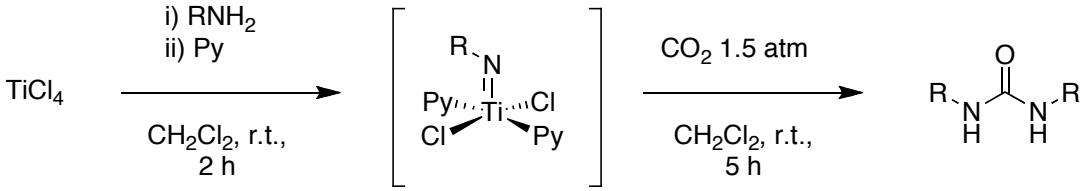
In situ formation of complexes **256l** by transimination and reaction with carbon dioxide generated ureas in poor yield and low selectivity. However, the reaction was activated to synthesise only urea **231l** in excellent yield when performed using bis-silyl amines (Scheme 4.76). Tertiary amines also showed activation of the reaction, but were not as efficient as bis-silyl amines.



256l **231l**

Scheme 4.76: Formation of urea from carbon dioxide using additives.

In situ generation of titanium-imido complexes from $TiCl_4$ and reaction with carbon dioxide has also been shown to produce symmetrical ureas **231** in moderate yield (Scheme 4.77). The reaction could be pushed to completion by using an enormous excess of amine (300 equivalents).



230 **231**

Scheme 4.77: One pot formation of Ti=N complex and reaction with carbon dioxide.

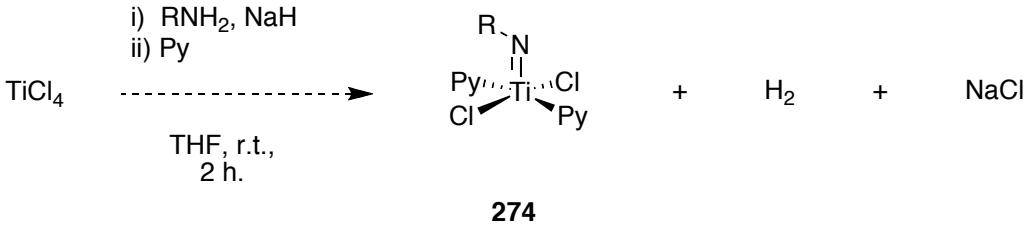
The activation of titanium-imido complexes to react with carbon dioxide has been partially achieved. When the imine substituent is an aromatic group, the activation reaction does not occur. However, when using non-aromatic amines, the reaction showed success, which could be increased by the addition of tertiary amines or silyl amines. Unfortunately, the intermediate generated (isocyanate) is more reactive than the starting material (carbon dioxide) and therefore reacts further to generate carbodiimide and urea.

The synthesised titanium-imido complexes were unstable to air or moisture. In addition, when the complexes were mixed with alcohols they carried out unwanted reactions and, in some of the cases they degraded. For this reason, alcohols were not added to the reaction mixture or used as solvent. As the only additives used in the reactions were

amines, ureas were obtained. In order to form carbamates, a complex compatible with alcohols would need to be synthesised.

4.4 Future Work

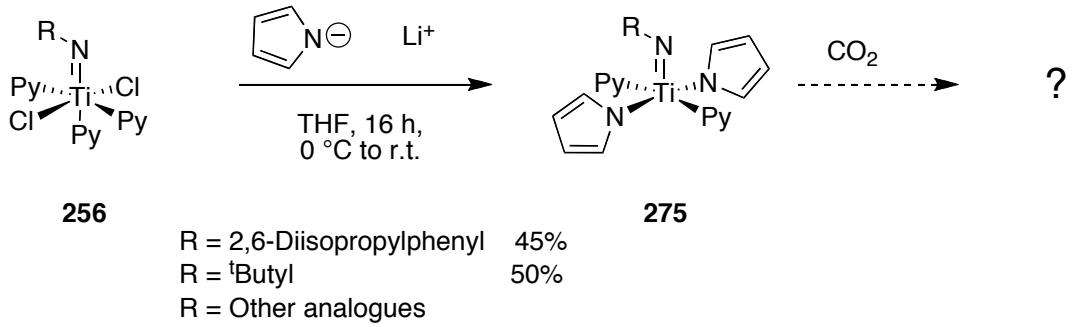
The formation of 12-electron titanium-imido complexes using either aromatic or non-aromatic amines and 14-electron titanium-imido complexes using non-aromatic amines has been problematic due to isolation and reactivity problems. A solution for the formation of the complex could be the use of strong inorganic bases such as sodium hydride (Scheme 4.78).[134] The non-nucleophilic base would be strong enough to remove HCl, and the most important feature would be the by-products formed. One of them should be hydrogen gas and the other sodium chloride. These should not affect the reaction and could be removed quickly from the reaction mixture.



274

Scheme 4.78: Proposed formation of Ti=N using added base.

The reactivity of the 14-electron titanium-imido complexes showed a wider scope than the 12-electron complexes. Successful chloride ligand exchange with phenoxides and subsequent transimination were shown. However, the use of pyrrolate anions may also be possible (Scheme 4.79). The steric effect in this case would be lower (despite the generation of 12-electron complexes), but the electronic effect would be difficult to predict. Some preliminary experiments have been developed showing the successful generation of the complex **275**, although no experiments with carbon dioxide were performed. These complexes **275** were synthesised in moderate yield, showing 12-electron titanium-imido complexes by ^{1}H NMR. These experiments could not be completed and further characterisation data is necessary. These are a new family of complexes may could be synthesised and investigated in the future.



256 **275**

R = 2,6-Diisopropylphenyl 45%
R = ^{t}Butyl 50%
R = Other analogues

Scheme 4.79: Alternative ligand modification.

The reactivity of complexes with carbon dioxide was shown to be increased in the presence of bis-silyl amines, however, this characteristic has only been applied to 12-electron non-aromatic titanium-imido complexes. The addition of these compounds could also be expanded to the rest of the 12- and 14-electron aromatic titanium-imido complexes. The aim of this study would be the activation of the titanium-imido complexes to react with carbon dioxide.

The final proposed studies concern the activation of titanium-oxo complexes to react with amines and form titanium-imido complexes. Some preliminary studies have shown unsuccessful reactivity, however, other Lewis acids could also be applied. At the final stage of the project, the most important feature would be the activation of the titanium-imido complexes in order to achieve high reactivity with carbon dioxide.

CHAPTER 5:

EXPERIMENTAL

CHAPTER 5: EXPERIMENTAL

5.1 General Experimental Details

All experimental procedures unless otherwise stated were carried out under an atmosphere of dry, oxygen free nitrogen. Those involving metal complexes were performed using standard Schlenk techniques. All glassware was rigourously flame-dried prior to use and a nitrogen atmosphere was maintained throughout the process. Handling of air / moisture sensitive compounds was performed in a M-BRAUN Uni Lab glove box under argon atmosphere. All reactions involving carbon dioxide were performed using a freshly prepared saturated solution of carbon dioxide. Degassed solutions and solvents were prepared by repeating a cycle of solidifying with a liquid nitrogen bath, applying *vacuum* (30 seconds) and melting three times. All carbon dioxide pressures were measured with a manometer at the head of the cylinder and performed in Schlenk flasks (NOTE: Pressurised glass flasks could susceptible to explosion under pressure conditions). NMR experiments were prepared using a glove box and pre-dried Youngs Tap NMR tubes. Reactions at room temperature imply temperatures in the range 20 - 25 °C. Reactions at low temperatures refer to values recorded for an external bath: 0 °C (ice bath), -40 °C and -78 (dry-ice/acetone bath). Column chromatography was performed using BDH 60 silica gel in the indicated solvent. Column chromatography was monitored by thin layer chromatography (tlc) performed on Polgram SIL G/UV_{254} plastic backed plates in the indicated solvent and were visualised by combination of ultraviolet light (254 nm) and a visualising dip of potassium permanganate.

5.2 Characterisation

Melting point are uncorrected and were recorded on a Stuart Scientific SMP3 apparatus. Melting points of complexes were measured in a sealed capillary tube. Infrared spectra were recorded on either a Perkin-Elmer 1600 FTIR instrument as solutions in chloroform, or an Avatar 320 FTIR as solids, and reported in cm^{-1}. ^{1}H NMR and ^{13}C

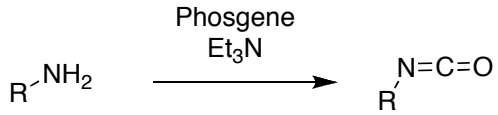
NMR spectra were recorded using Bruker DPX400, AV400, AV(II)400 and AV500 spectrometers at 400 and 500 MHz for ^{1}H and 100 and 125 MHz for ^{13}C respectively, at 298 K in $CDCl_3$, unless otherwise stated. Chemical shifts are reported in parts per million (ppm) downfield from tetramethylsilane, using residual protic solvent as internal standard (δ 7.27 ppm ($CDCl_3$) and δ 77.1 ppm ($CDCl_3$)). Coupling constants (*J*) are recorded in Hertz (Hz), rounded to the nearest 0.1 Hz and are uncorrected. The multiplicity of each signal is described by the following abbreviations: (app) apparent, (br) broad, (s) singlet, (d) doublet, (t) triplet, (q) quartet, (sept) septet, (m) multiplet, (dt) double triplet *etc*. Mass spectrometry data was recorded using a VG Micromass 70E spectrometer with electrospray ionisation (ESI) and results are quoted to four decimal places. Elemental analysis was acquired on a Hewlett Packard 1100 series system.
Note: In novel compounds and complexes, the missing data could not be obtained.

5.3 Purification of Solvents and Reagents

Solvents. Chromatography solvents were used as supplied without further purification. Reaction solvents were purchased as HPLC grade and dried by passing them through activated alumina towers (dichloromethane, hexanes and toluene) or activated alumina and CaO towers (THF and Et_2O).

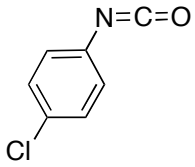
Reagents. All reagents were purchased and used without further purification unless otherwise stated. Sodium molybdate was dried prior use at 2.5 mmHg at r.t. for 24 h. All amines, anilines, pyridines and phenols were redistilled or recrystalised according to literature procedures.[135] Titanium tetrachloride was purchased in an argon atmosphere and used without further purification. 4-Methylphenyl isocyanate, 2,6-dimethylphenyl isocyanate, 2,6-diisopropylphenyl isocyanate and ^{t}butyl isocyanate were purchased under a nitrogen atmosphere, stored in the glove box and used without further purification. Diphenyl ketene was synthesised in two steps from recrystallised commercially available diphenyl acetic acid according to the literature procedure.[136] Carbon dioxide was purchased as a 99.8% <5 ppm O_2 and <2 ppm H_2O gas and used without further purification.

5.4 Preparation of Isocyanates



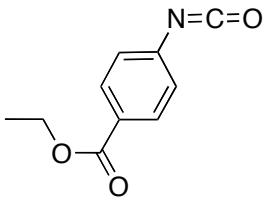
General Procedure A. To a vigourously stirred white suspension of 20% v/v solution of phosgene in toluene (8 mmol) and Et_3N (20 mmol) in dry Et_2O (100 mL) at 0 °C under a N_2 atmosphere was added a solution of amine (2 mmol) in dry Et_2O (30 mL). The white mixture was stirred for a further 1 h before being filtered and volatiles removed *in vacuo*, repeating the process until no by-products were detected by ^1H NMR. Isocyanates were characterised by ^1H NMR, ^{13}C NMR and IR spectra, which were compared with literature data or that of an authentic sample.

4-Chlorophenyl isocyanate (1a)



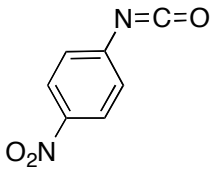
Synthesised by **General Procedure A**. 4-Chloroaniline (255 mg, 2.00 mmol) afforded **1a** (278 mg, 91%) as a yellow oil. ^1H NMR δ 7.03 (2H, m, *o*-C*H*), 7.30 (2H, m, *m*-C*H*). ^{13}C NMR δ 125.9 (*o*-*C*H), 129.7 (*m*-C*H*), 131.1 (*ipso*-*C*), 132.0 (*p*-*C*). Missing quaternary carbon (N=*C*=O). IR ν_{max} (solution in $CHCl_3$) 2268.8 (N=*C*=O), 1598.3, 1511.7, 1263.3, 1091.9, 1015.2, 829.4 cm^{-1}. Spectroscopic data in agreement with commercially available sample.

4-Ethoxycarbonylphenyl isocyanate (1b)



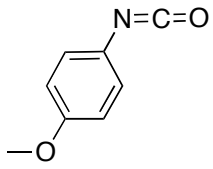
Synthesised by **General Procedure A**. 4-Ethoxycarbonylaniline (330 mg, 2.00 mmol) afforded **1b** (377 mg, 99%) as a yellow oil. ^{1}H NMR δ 1.40 (3H, t, *J* = 7.2, C*H*$_3$CH$_2$O), 4.38 (2H, q, *J* = 7.2, CH$_3$C*H*$_2$O), 7.14 (2H, m, *o*-C*H*), 8.02 (2H, m, *m*-C*H*). ^{13}C NMR δ 14.3 (*C*H$_3$CH$_2$O), 61.2 (CH$_3$*C*H$_2$O), 124.7 (*o*-C*H*), 125.4 (N=*C*=O), 127.9 (*ipso*-*C*), 131.1 (*m*-C*H*), 137.8 (*p*-*C*), 165.7 (*C*=O). IR ν_{max} (solution in CHCl$_3$) 2985.4, 2265.1 (N=*C*=O), 1714.4, 1606.9, 1278.9, 1110.0 cm^{-1}. Spectroscopic data in agreement with commercially available sample.

4-Nitrophenyl isocyanate (1c)



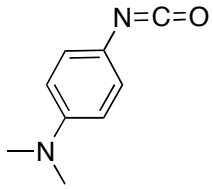
Synthesised by **General Procedure A**. 4-Nitroaniline (276 mg, 2.00 mmol) afforded **1c** (138 mg, 42%) as a yellow low melting solid. ^{1}H NMR δ 7.24 (2H, m, *o*-C*H*), 8.23 (2H, m, *m*-C*H*). ^{13}C NMR δ 125.3 (*o*-C*H*), 125.4 (*m*-C*H*), 139.9 (*p*-*C*). Missing 2 quaternary carbons (ipso-*C*, N=*C*=O). Spectroscopic data in agreement with commercially available sample.

4-Methoxyphenyl isocyanate (1d)



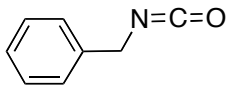
Synthesised by **General Procedure A**. 4-Methoxyaniline (272 mg, 2.45 mmol) afforded **1d** (295 mg, 88%) as a yellow oil. ^{1}H NMR δ 3.80 (3H, s, OC*H*$_3$), 6.84 (2H, m, *o*-C*H*), 7.03 (2H, m, *m*-C*H*). ^{13}C NMR δ 55.5 (O*C*H$_3$), 114.8 (*o*-*C*H), 125.6 (*m*-*C*H), 125.9 (*ipso*-*C*), 157.4 (*p*-*C*). Missing quaternary carbon of isocyanate. IR ν_{max} (solution in CHCl$_3$) 2939.2, 2838.5, 2277.9 (N=*C*=O), 1525.5, 1438.4, 1290.8, 1247.1, 1106.3, 1033.8, 831.3 cm^{-1}. Spectroscopic data in agreement with commercially available sample.

4-(*N*,*N*-Dimethylamino)phenyl isocyanate (1e)



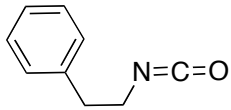
Synthesised by **General Procedure A**. 4-(*N'*,*N'*-Dimethylamino)phenylaniline (272 mg, 2.00 mmol) afforded **1e** (291 mg, 90%) as a yellow low melting solid. ^{1}H NMR δ 2.94 (6H, s, N(C*H*$_3$)$_2$), 6.65 (2H, m, *o*-C*H*), 6.98 (2H, m, *m*-C*H*). ^{13}C NMR δ 40.7 (N(*C*H$_3$)$_2$), 113.1 (*o*-*C*H), 121.8 (*p*-*C*), 125.3 (*m*-*C*H), 148.6 (*ipso*-*C*). Missing quaternary carbon (N=*C*=O). IR ν_{max} (solution in CHCl$_3$) 2891.1, 2807.3, 2274.6 (N=*C*=O), 1613.9, 1534.1, 1483.0, 1441.0, 1354.2, 1192.6, 946.5 cm^{-1}. Spectroscopic data in agreement with literature.[137]

Benzyl isocyanate (1f)



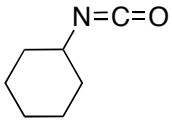
Synthesised by **General Procedure A**. benzylamine (0.20 mL, 2.00 mmol) afforded **1f** (241 mg, 91%) as a yellow oil. ^{1}H NMR δ 4.51 (2H, s, C*H*$_2$), 7.31 - 7.42 (5H, m, C*H*$_{Ar}$). ^{13}C NMR δ 46.5 (*C*H$_2$), 126.7 (*C*H$_{Ar}$), 128.0 (*C*H$_{Ar}$), 128.8 (*C*H$_{Ar}$), 136.9 (*ipso*-*C*). Missing quaternary carbon (N=*C*=O). IR ν_{max} (solution in $CHCl_3$) 3068.9, 2270.2 (N=*C*=O), 1731.2, 1605.4, 1497.4, 1455.2, 1354.2, 865.4 cm^{-1}. Spectroscopic data in agreement with literature.[138]

2-Phenylethyl isocyanate (1g)



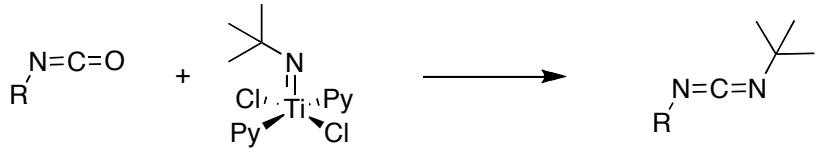
Synthesised by **General Procedure A**. 2-Phenylethylamine (0.25 mL, 2.00 mmol) afforded **1g** (270 mg, 92%) as a yellow oil. ^{1}H NMR δ 2.95 (2H, t, *J* = 6.9, C*H*$_2$Ph), 3.57 (2H, t, *J* = 6.9, C*H*$_2$N), 7.24 - 7.27 (2H, m, *m*-C*H*), 7.31 (1H, tt, *J* = 7.3, 1.4, *p*-C*H*), 7.38 (2H, tt, *J* = 6.9, 1.6, *o*-C*H*). ^{13}C NMR δ 37.7 (C*H*$_2$Ph), 44.2 (C*H*$_2$N), 123.2 (N=*C*=O), 127.0 (*C*H$_{Ar}$), 128.7 (*C*H$_{Ar}$), 128.8 (*C*H$_{Ar}$), 137.7 (*ipso*-*C*). Missing quaternary carbon (N=*C*=O). IR ν_{max} (solution in $CHCl_3$) 2924.0, 2280.5 (N=*C*=O), 1732.4, 1604.1, 1497.3, 1354.3, 1082.4, 1031.0, 944.8, 875.7 cm^{-1}. Spectroscopic data in agreement with literature.[139]

Cyclohexyl isocyanate (1j)



Synthesised by **General Procedure A**. Cyclohexylamine (0.23 mL, 2.00 mmol) afforded **1j** (115 mg, 46%) as a yellow oil. ^{1}H NMR δ 1.15 - 1.40 (3H, m, C*H*$_2$), 1.42 - 1.58 (3H, m, C*H*$_2$), 1.65 - 1.78 (2H, m, C*H*$_2$), 1.86 - 1.94 (2H, m, C*H*$_2$), 3.40 - 3.50 (1H, m, C*H*N). ^{13}C NMR δ 23.8 (*C*H$_2$), 25.2 (*C*H$_2$), 34.8 (*C*H$_2$), 53.4 (*C*HN). IR ν_{max} (solution in $CHCl_3$) 2255.2 (N=*C*=O), 1278.9, 895.8 cm^{-1}. Spectroscopic data in agreement with literature.[140]

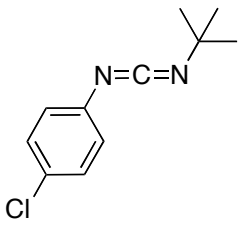
5.5 Preparation of Carbodiimides



General Procedure B. To a bright orange solution of dichloro ^{t}butylimido bispyridine titanium(IV) (1 mmol) in dry dichloromethane (15 mL) at r.t. under a N_2 atmosphere, a solution of freshly prepared isocyanate (1 mmol) in dry dichloromethane (5 mL) was added dropwise over approximately 30 seconds. The bright orange solution immediately turned to a black mixture. After stirring for 16 h the solvent was reduced to approximately 3 mL *in vacuo* and triturated with dry toluene (20 mL). The solvent was again reduced to approximately 3 mL and triturated with dry hexanes (20 mL). All volatiles were removed *in vacuo* to leave crude carbodiimide as a yellow oil. Purification by flash column chromatography produced pure carbodiimide. To minimise degradation of the carbodiimide to urea due to acidity of silica gel, chromatography was performed quickly using a short column of silica.

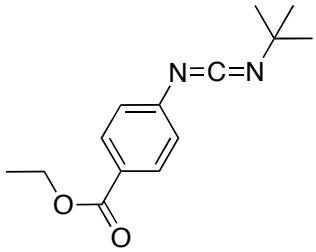
Note: MS data could not be obtained.

N'-^{t}Butyl-*N*-4-chlorophenyl carbodiimide (49a)



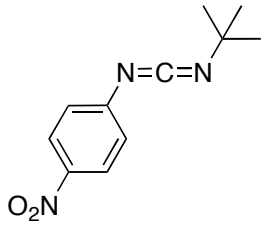
Synthesised using **General Procedure B**. 4-Chlorophenyl isocyanate **1a** (133 mg, 1.00 mmol) afforded crude carbodiimide. Purification by flash column chromatography (hexanes, 10% Et_2O:hexanes) afforded pure **49a** (117 mg, 46%) as a yellow oil. Rf 0.80 (50%, Et_2O:hexanes). ^1H NMR δ 1.41 (9H, s, C(C*H*$_3$)$_3$), 7.02 (2H, m, *m*-C*H*), 7.25 (2H, m, *o*-C*H*). ^{13}C NMR δ 31.6 (C(*C*H$_3$)$_3$), 57.7 (*C*(CH$_3$)$_3$), 124.3 (*m*-*C*H), 129.4 (*o*-*C*H), 129.7 (C_{Ar}), 135.7 (C_{Ar}), 139.7 (C_{Ar}). IR ν_{max} (solution in $CHCl_3$) 2965.4, 2929.7, 2857.2, 2129.6 (N=*C*=N), 1498.4, 1263.5 cm^{-1}.

N'-^{t}Butyl-*N*-4-ethoxycarbonylphenyl carbodiimide (49b)



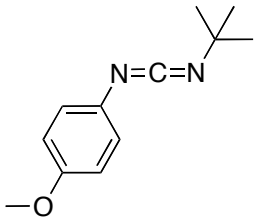
Synthesised using **General Procedure B**. 4-Ethoxycarbonylphenyl isocyanate **1b** (191 mg, 1.00 mmol) afforded carbodiimide. Purification by flash column chromatography (hexanes, 10% Et_2O:hexanes) afforded pure **49b** (121 mg, 49%) as a white low melting point. Rf 0.75 (50%, Et_2O:hexanes). ^1H NMR δ 1.38 (3H, t, *J* = 7.2, C*H*$_3$CH$_2$), 1.43 (9H, s, C(C*H*$_3$)$_3$), 4.36 (2H, q, *J* = 7.2, CH$_3$C*H*$_2$O), 7.10 (2H, d, *J* = 8.4, *o*-C*H*), 7.97 (2H, d, *J* = 8.4, *m*-C*H*). ^{13}C NMR δ 14.3 (*C*H$_3$CH$_2$O), 31.6 (C(*C*H$_3$)$_3$), 58.0 (*C*(CH$_3$)$_3$), 60.9 (CH$_3$*C*H$_2$O), 123.0 (*C*H$_{Ar}$), 126.5 (*C*$_{Ar}$), 131.1 (*C*H$_{Ar}$), 134.5 (*C*), 146.0 (*C*), 166.2 (*C*=O). IR ν_{max} (solution in $CHCl_3$) 2979.1, 2931.7, 2127.9 (N=*C*=N), 1709.1, 1602.4, 1278.2 cm^{-1}. Anal. Found (calcd for $C_{13}H_{18}N_2$): C 68.3 (68.5), H 7.4 (7.5), N 11.4 (11.1).

N'-^{t}Butyl-*N*-4-nitrophenyl carbodiimide (49c)



Synthesised using **General Procedure B**. 4-Nitrophenyl isocyanate **1c** (164 mg, 1.00 mmol) afforded carbodiimide. Purification by flash column chromatography (hexanes, 10% Et_2O:hexanes) afforded pure **49c** (140 mg, 64%) as a pale brown low melting point. Rf 0.81 (50%, Et_2O:hexanes). ^{1}H NMR δ 1.46 (9H, s, C(C*H*$_3$)$_3$), 7.15 (2H, m, *o*-C*H*), 8.17 (2H, m, *m*-C*H*). ^{13}C NMR δ 31.6 (C(*C*H$_3$)$_3$), 58.6 (*C*(CH$_3$)$_3$), 123.5 (*o*-*C*H), 125.3 (*m*-*C*H), 148.8 (*C*), 191.8 (*C*). Missing quaternary carbon. IR ν_{max} (solution in $CHCl_3$) 2963.8, 2928.1, 2859.9, 2131.7 (N=*C*=N), 1602.2, 1516.2, 1341.5, 1261.4 cm^{-1}.

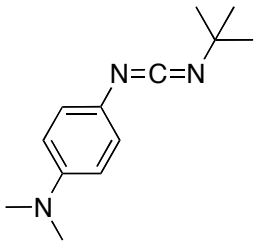
N'-^{t}Butyl-*N*-4-methoxyphenyl carbodiimide (49d)



Synthesised using **General Procedure B**. 4-Methoxyphenyl isocyanate **1d** (149 mg, 1.00 mmol) afforded carbodiimide. Purification by flash column chromatography (hexanes, 10% Et_2O:hexanes) afforded pure **49d** (163 mg, 80%) as a yellow low melting point. Rf 0.73 (50%, Et_2O:hexanes). ^{1}H NMR δ 1.40 (9H, s, C(C*H*$_3$)$_3$), 3.79 (3H, s, OC*H*$_3$), 6.83 (2H, m, *o*-C*H*), 7.03 (2H, m, *m*-C*H*). ^{13}C NMR δ 31.6 (C(*C*H$_3$)$_3$), 55.5 (O*C*H$_3$), 57.2 (*C*(CH$_3$)$_3$), 114.6 (*o*-*C*H), 124.1 (*m*-*C*H), 133.7 (ipso*C*), 137.3 (*p*-*C*), 156.8 (N=*C*=N). IR ν_{max} (solution in $CHCl_3$) 2973.4, 2933.1, 2109.7 (N=*C*=N), 1669.2,

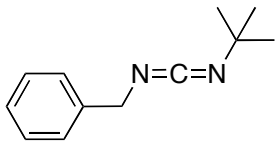
1511.0, 1290.4, 1261.0, 1181.6, 1103.7, 1034.2 cm^{-1}. Spectroscopic data in agreement with literature.[141]

N'-^{t}Butyl-*N*-4-(*N*''-dimethylamino)phenyl carbodiimide (49e)



Synthesised using **General Procedure B**. 4-(*N*'-Dimethylamino)phenyl isocyanate **1e** (162 mg, 1.00 mmol) afforded carbodiimide. Purification by flash column chromatography (hexanes, 10% Et_2O:hexanes) afforded pure **49e** (104 mg, 48%) as a yellow low melting point. Rf 0.51 (66%, Et_2O:hexanes). ^{1}H NMR δ 1.39 (9H, s, $C(CH_3)_3$), 2.93 (6H, s, $N(CH_3)_2$), 6.68 (2H, m, *m*-C*H*), 7.01(2H, m, *o*-C*H*). ^{13}C NMR δ 31.6 ($C(CH_3)_3$), 41.0 ($N(CH_3)_2$), 57.0 ($C(CH_3)_3$), 113.6 (*m*-*C*H), 123.9 (*o*-*C*H), 129.4 (*ipso*-*C*), 138.2 (N=*C*=N), 148.3 (*p*-*C*). IR ν_{max} (solution in $CHCl_3$) 2973.9, 2361.1, 2113.0 (N=*C*=N), 1603.0, 1519.0, 1367.1, 1261.4, 1192.3, 1098.1 cm^{-1}.

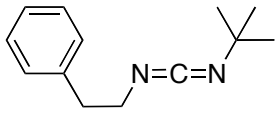
N-Benzyl-*N*'-^{t}butyl carbodiimide (49f)



Synthesised using **General Procedure B**. Benzyl isocyanate **1f** (133 mg, 1.00 mmol) afforded carbodiimide. Purification by flash column chromatography (hexanes, 10% Et_2O:hexanes) afforded pure **49f** (143 mg, 76%) as a yellow oil. Rf 0.87 (50%, Et_2O:hexanes). ^{1}H NMR δ 1.16 (9H, s, $C(CH_3)_3$), 4.35 (2H, s, CH_2Ph), 7.28 - 7.41 (5H, m, CH_{Ar}). ^{13}C NMR δ 31.2 ($C(CH_3)_3$), 50.9 (CH_2Ph), 55.3 ($C(CH_3)_3$), 127.5 (CH_{Ar}), 127.9 (CH_{Ar}), 128.6 (CH_{Ar}), 138.8 (*ipso*-*C*), 140.8 (N=*C*=N). IR ν_{max} (solution in

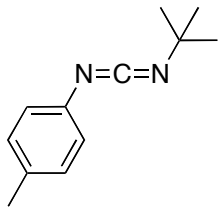
$CHCl_3$) 2974.2, 2116.6 (N=*C*=N), 1367.4, 1261.4, 1182.3, 1097.2, 1028.5, 908.7 cm^{-1}. Spectroscopic data in agreement with literature.[142]

N'-^{t}Butyl-*N*-2-phenylethyl carbodiimide (49g)



Synthesised using **General Procedure B**. 2-Phenylethyl isocyanate **1g** (147 mg, 1.00 mmol) afforded carbodiimide. Purification by flash column chromatography (hexanes, 10% Et_2O:hexanes) afforded pure **49g** (138 mg, 68%) as a colourless oil. Rf 0.83 (50%, Et_2O:hexanes). ^{1}H NMR δ 1.21 (9H, s, C(C*H*$_3$)$_3$), 2.89 (2H, t, *J* = 7.3, C*H*$_2$Ph), 3.47 (2H, t, *J* = 7.3, C*H*$_2$N), 7.20 - 7.34 (5H, m, C*H*$_{Ar}$). ^{13}C NMR δ 31.2 (C(*C*H$_3$)$_3$), 37.8 (*C*H$_2$Ph), 48.2 (*C*H$_2$N), 55.1 (*C*(CH$_3$)$_3$), 126.5 (*C*H$_{Ar}$), 128.5 (*C*H$_{Ar}$), 128.8 (*C*H$_{Ar}$), 138.9 (ipso-C$_{Ar}$), 139.9 (N=*C*=N). IR ν_{max} (solution in $CHCl_3$) 2927.0, 2869.9, 2108.3 (N=*C*=N), 1678.5, 1366.1, 1185.0, 1082.9, 1031.9 cm^{-1}. Anal. Found (calcd for $C_{13}H_{18}N_2$): C 76.9 (77.2), H 9.0 (9.0), N 13.4 (13.8).

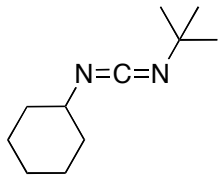
N'-^{t}Butyl-*N*-4-methylphenyl carbodiimide (49h)



Synthesised using **General Procedure B**. 4-Methylphenyl isocyanate **1h** (133 mg, 1.00 mmol) afforded carbodiimide. Purification by flash column chromatography (hexanes, 10% Et_2O:hexanes) afforded pure **49h** (71 mg, 68%) as a yellow oil. Rf 0.84 (50%, Et_2O:hexanes). ^{1}H NMR δ 1.40 (9H, s, C(C*H*$_3$)$_3$), 2.32 (3H, s, C*H*$_3$Ph), 6.99 (2H, m, *o*-C*H*), 7.10 (2H, m, *m*-C*H*). ^{13}C NMR δ 20.9 (*C*H$_3$Ph), 31.6 (C(*C*H$_3$)$_3$), 57.3 (*C*(CH$_3$)$_3$), 123.1 (*o*-*C*H), 130.0 (*m*-*C*H), 134.3 (*p*-*C*H), 138.0 (ipso-C), 136.9 (N=*C*=N). IR ν_{max}

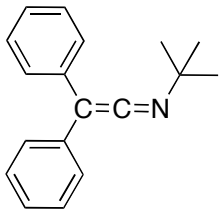
(solution in $CHCl_3$) 2974.1, 2110.2 (N=*C*=N), 1513.3, 1368.1, 1261.3, 1096.0, 1018.5 cm^{-1}. Spectroscopic data in agreement with literature.[143]

N'-^{t}Butyl-*N*-cyclohexyl carbodiimide (49i)



Synthesised using **General Procedure B**. Cyclohexyl isocyanate **1i** (125 mg, 1.00 mmol) afforded carbodiimide. Purification by flash column chromatography (hexanes, 10% Et_2O:hexanes) afforded pure **49i** (153 mg, 80%) as a yellow oil. Rf 0.83 (50%, Et_2O:hexanes). ^{1}H NMR δ 1.19 - 1.40 (13H, m, C*H*$_3$, C*H*$_2$), 1.54 - 1.62 (2H, m, C*H*$_2$), 1.70 - 1.76 (2H, m, C*H*$_2$), 1.90 - 1.98 (2H, m, C*H*$_2$), 3.15 - 3.24 (1H, m, C*H*N). ^{13}C NMR δ 24.7 (*C*H$_2$), 25.5 (*C*H$_2$), 31.3 (C(*C*H$_3$)$_3$), 35.0 (*C*H$_2$), 54.9 (*C*(CH$_3$)$_3$), 55.8 (*C*HN). Missing N=*C*=N. IR ν_{max} (solution in $CHCl_3$) 3011.4, 2933.9, 2857.3, 2109.4 (N=*C*=N), 1653.4, 1521.3, 1451.1, 1366.2, 1261.2, 1188.0, 1096.0, 1015.0 cm^{-1}. Spectroscopic data in agreement with literature.[144]

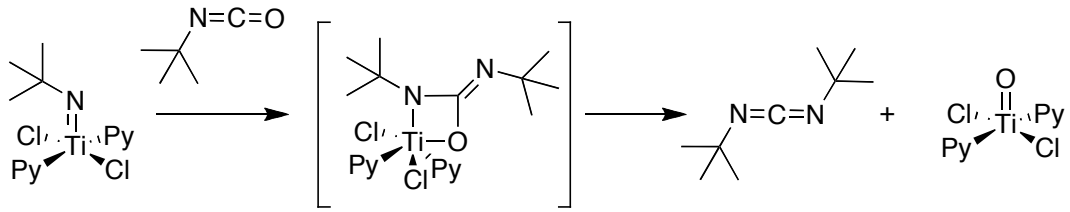
N-^{t}Butyl diphenyl ketenimine (246)



Synthesised using **General Procedure B**. Diphenyl ketene **245** (220 mg, 1.00 mmol) afforded ketenimine. Purification by flash column chromatography (50% Et_2O:hexanes) afforded pure **246** (233 mg, 94%) as a colourless low melting point. Rf 0.75 (50%, Et_2O:hexanes). ^{1}H NMR δ 1.46 (9H, s, C(C*H*$_3$)$_3$), 7.00 - 7.30 (10H, m, C*H*$_{Ar}$). ^{13}C NMR δ 30.5 (C(*C*H$_3$)$_3$), 56.4 (*C*(CH$_3$)$_3$), 125.6 (C=*C*=N), 127.5 (*C*H$_{Ar}$), 128.6 (*C*H$_{Ar}$), 129.4

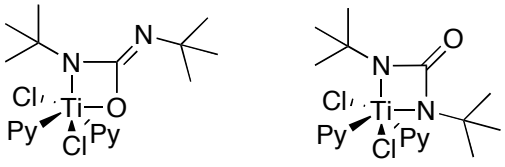
(*C*H$_{Ar}$), 169.0 (*C*=C=N). IR ν_{max} (solution in $CHCl_3$) 3069.6, 2855.3, 2006.5 (C=*C*=N), 1773.2, 1599.2, 1495.8, 1261.5 cm^{-1}. Spectroscopic data in agreement with literature.[145]

Reaction of ^{t}Butylimido Dichloro Bispyridine Titanium(IV) (230) with ^{t}Butyl Isocyanate (1l)



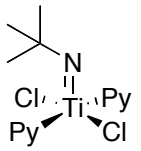
To a clear bright orange solution of ^{t}butylimido dichloro bispyridine titanium(IV) (230) (25.0 mg, 0.0072 mmol) in $CDCl_3$ (0.4 mL) in a Young Tap NMR tube was aded a solution of ^{t}butyl isocyanate (1l) (7.00 mg, 0.007 mmol) in $CDCl_3$ (0.35 mL) was added. The clear solution immediately turned to a black suspension and NMR spectra were recorded. A mixture of 9 (**236**) : 13 (**230**) : 7 (**49l**) : 1 (**235**).

Metallocycle (236)



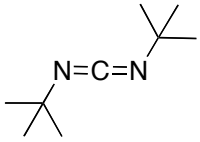
^{1}H NMR δ 1.44 (18H, s, C(C*H*$_3$)$_3$), 7.40-7.47 (4H, m, 3-C*H*), 7.80-7.90 (2H, m, 4-C*H*), 9.07 (4H, app. dd, *J* = 6.4, 1.6, 2-C*H*). ^{13}C NMR δ 31.1 (C(*C*H$_3$)$_3$), 62.9 (*C*(CH$_3$)$_3$), 124.4 (3-*C*H), 139.5 (4-*C*H), 151.8 (2-*C*H), 165.5 (*C*=N or *C*=O).

^{t}Butylimido dichloro bispyridine titanium(IV) (230)



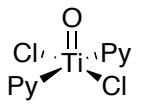
^{1}H NMR δ 0.95 (9H, s, C(C*H*$_3$)$_3$), 7.40-7.47 (4H, m, 3-C*H*), 7.80-7.90 (2H, m, 4-C*H*), 9.29 (4H, d, *J* = 5.2, 2-C*H*). ^{13}C NMR δ 30.3 (C(*C*H$_3$)$_3$), 72.7 (*C*(CH$_3$)$_3$), 124.0 (3-*C*H), 138.5 (4-*C*H), 151.8 (2-*C*H).

Bis-*N*,*N*'-^{t}Butyl carbodiimide (49l)



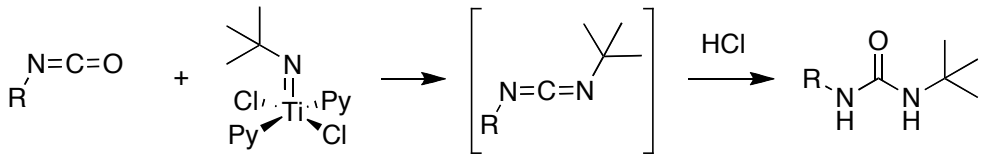
^{1}H NMR δ 1.36 (18H, s, C(C*H*$_3$)$_3$). ^{13}C NMR δ 31.8 (C(*C*H$_3$)$_3$), 55.5 (*C*(CH$_3$)$_3$). Missing Quaternary carbon (N=*C*=N).

Dichloro bispyridine oxo-titanium(IV) (235)



^{1}H NMR δ 7.10 - 720 (4H, $_{br}$, 3-C*H*), 7.55-7.65 (2H, $_{br}$, 4-C*H*), 8.60-8.70 (4H, $_{br}$, 2-C*H*). ^{13}C NMR δ 123.4 (3-*C*H), 136.7 (4-*C*H), 150.6 (2-*C*H).

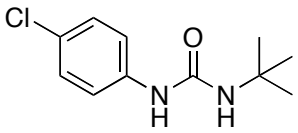
5.6 Preparation of Ureas



General Procedure C. To a bright orange solution of dichloro ^{t}butylimido bispyridine titanium(IV) (1 mmol) in dry dichloromethane (15 mL) at r.t. under a N_2 atmosphere, a solution of freshly prepared isocyanate (1 mmol) in dry dichloromethane (5 mL) was added dropwise over approximately 30 seconds. The bright orange solution turned immediately to a black mixture. After stirring the black mixture for 16 h 2M HCl (aq) (20 mL) and acetone (20 mL) were added. The clear byphasic mixture was stirred vigorously for other 16 h before being neutralised with $NaHCO_3$. The two phases were separated and the aqueous layer was extracted with dichloromethane (2x20 mL). The combined organic layers were dried over $MgSO_4$ and concentrated *in vacuo*. Purification by flash column chromatography produced pure urea.

General Procedure D. To a colorless solution crbodiimide in dichloromethane (20 mL) and acetone (20 mL), 2M HCl (aq) (20 mL) was added. The clear byphasic mixture was stirred vigorously for other 16 h before being neutralised with $NaHCO_3$. The two phases were separated and the aqueous layer was extracted with dichloromethane (2x20 mL). The combined organic layers were dried over $MgSO_4$ and concentrated *in vacuo*. Purification by flash column chromatography produced pure urea.

N'-^{t}Butyl-*N*-4-chlorophenyl urea (231a)

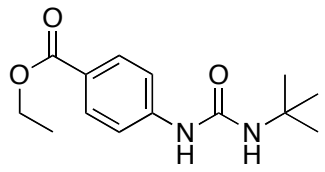


Synthesised using **General Procedure C**. 4-Chlorophenyl isocyanate **1a** (133 mg, 1.00 mmol) afforded urea. Purification by flash column chromatography (Et_2O:hexanes, 10% to 20% to 50%) afforded pure **231a** (126 mg, 63%) as a white solid.

Synthesised using **General Procedure D**. 4-Chlorophenyl carbodiimide **49a** (76 mg, 0.35 mmol) afforded urea. Purification by flash column chromatography (Et_2O:hexanes, 10% to 20% to 50%) afforded pure **231a** (76 mg,%) as a white solid.

mp 190 - 193 °C (lit. mp not recorded). Rf 0.28 (50%, Et_2O:hexanes). ^{1}H NMR δ 1.38 (9H, s, C(CH_3)$_3$), 4.60 (1H, s_{br}, N*H*), 6.22 (1H, s_{br}, N*H*), 7.24 (4H, s, CH_{Ar}). ^{13}C NMR δ 29.3 (C(*C*H$_3$)$_3$), 51.0 (*C*(CH$_3$)$_3$), 121.4 (*o*-*C*H), 128.2 (*ipso*-*C*), 129.1 (*m*-*C*H), 137.6 (*p*-*C*), 154.3 (*C*=O). Spectroscopic data in agreement with literature.[146]

N'-^{t}Butyl-*N*-4-ethoxycarbonyphenyl urea (231b)



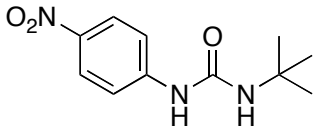
Synthesised using **General Procedure C**. 4-Ethoxycarbonylphenyl isocyanate **1b** (191 mg, 1.00 mmol) afforded urea. Purification by flash column chromatography (Et_2O:hexanes, 20% to 50%) afforded pure **231b** (246 mg, 93%) as a white solid.

Synthesised using **General Procedure D**. 4-Ethoxycarbonylphenyl carbodiimide **49b** (117 mg, 0.48 mmol) afforded urea. Purification by flash column chromatography (Et_2O:hexanes, 20% to 50%) afforded pure **231b** (121 mg,%) as a white solid.

mp 134 - 136 °C. Rf 0.10 (50%, Et_2O:hexanes). ^{1}H NMR δ 1.35 (9H, s, C(CH_3)$_3$), 1.37 (3H, t, *J* = 7.1, CH_3CH$_2$O), 4.34 (2H, q, *J* = 7.1, CH$_3$CH_2O), 5.47 (1H, s_{br}, N*H*), 7.37 (2H, m, *o*-C*H*), 7.58 (1H, s_{br}, N*H*), 7.90 (2H, m, *m*-C*H*). ^{13}C NMR δ 14.4 (*C*H$_3$CH$_2$O), 29.3 (C(*C*H$_3$)$_3$), 50.8 (*C*(CH$_3$)$_3$), 60.9 (CH$_3$*C*H$_2$O), 117.8 (*o*-*C*H), 123.6 (*ipso*-*C*), 130.9

(*m*-*C*H), 144.1 (*p*-*C*), 154.6 (*C*=O, urea), 166.9 (*C*=O, ester). IR ν_{max} (solution in $CHCl_3$) 3440.1, 3012.5, 2970.0, 1707.5 (C=O), 1505.9, 1282.8, 1176.1 cm^{-1}. ESI/MS: *m/z* 265.1547 (M+H, 4%), 287.1357 (M+Na, 100%). HRMS: found (calcd for $C_{14}H_{21}N_2O_3$) m/z 265.1547 (265.1547). Anal. Found (calcd for $C_{14}H_{20}N_2O_3$): C 63.2 (63.6), H 7.7 (7.6), N 10.2 (10.6).

N-^{t}Butyl-*N*-4-nitrophenyl urea (231c)

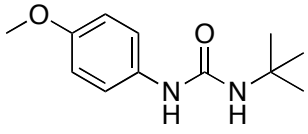


Synthesised using **General Procedure C**. 4-Nitrophenyl isocyanate **1c** (164 mg, 1.00 mmol) afforded urea. Purification by flash column chromatography (Et_2O:hexanes, 20% to 50%) afforded pure **231c** (201 mg, 85%) as a pale yellow solid.

Synthesised using **General Procedure D**. 4-Nitrophenyl carbodiimide **49c** (48 mg, 0.22 mmol) afforded urea. Purification by flash column chromatography (Et_2O:hexanes, 20% to 50%) afforded pure **231c** (51 mg,%) as a white solid.

mp 142 - 143 °C (lit. mp not recorded). Rf 0.10 (50%, Et_2O:hexanes). ^{1}H NMR δ 1.41 (9H, s, C(C*H*$_3$)$_3$), 4.78 (1H, s_{br}, N*H*), 6.73 (1H, s_{br}, N*H*), 7.50 (2H, m, *o*-C*H*), 8.16 (2H, m, *m*-C*H*). ^{13}C NMR δ 29.2 (C(*C*H$_3$)$_3$), 51.4 (*C*(CH$_3$)$_3$), 117.6 (*o*-*C*H), 125.3 (*m*-*C*H), 142.8 (*ipso*-*C*), 145.6 (*p*-*C*), 159.2 (*C*=O). IR ν_{max} (solution in $CHCl_3$) 3437.6, 2967.0, 1710.4 (C=O), 1602.0, 1533.2, 1504.3, 1341.9, 1301.8, 1245.7, 1178.3, 1113.0, 909.2 cm^{-1}. ESI/MS: *m/z* 260.0991 (M+Na, 76%). HRMS: found (calcd for $C_{11}H_{15}N_3O_3Na$) m/z 260.0991 (260.1006). Spectroscopic data in agreement with literature.[147]

N'-^{t}Butyl-*N*-4-methoxyphenyl urea (231d)

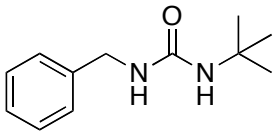


Synthesised using **General Procedure C**. 4-Methoxyphenyl isocyanate **1d** (149 mg, 1.00 mmol) afforded urea. Purification by flash column chromatography (Et_2O:hexanes, 20% to 50%) afforded pure **231d** (171 mg, 77%) as a white solid.

Synthesised using **General Procedure D**. 4-mathoxyphenyl carbodiimide **49d** (100 mg, 0.49 mmol) afforded urea. Purification by flash column chromatography (Et_2O:hexanes, 20% to 50%) afforded pure **231d** (70 mg,%) as a white solid.

mp 140 - 143 °C (lit. 142 - 145 °C). Rf 0.40 (66%, Et_2O:hexanes). ^{1}H NMR δ 1.34 (9H, s, C(CH_3)$_3$), 3.77 (3H, s, OCH_3), 4.88 (1H, s_{br}, NH), 6.53 (1H, s_{br}, NH), 6.83 (2H, m, *o*-CH), 7.17 (2H, m, *m*-CH). ^{13}C NMR δ 29.4 (C(*C*H$_3$)$_3$), 50.5 (*C*(CH$_3$)$_3$), 55.5 (O*C*H$_3$), 114.5 (*o*-*C*H), 123.8 (*m*-*C*H), 131.7 (*ipso*-*C*), 155.9 (*p*-*C*), 156.4 (*C*=O). Spectroscopic data in agreement with literature.[148]

N-Benzyl-*N*'-^{t}butyl urea (231f)



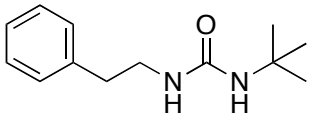
Synthesised using **General Procedure C**. Benzyl isocyanate **1f** (133 mg, 1.00 mmol) afforded crude urea. Purification by flash column chromatography (Et_2O:hexanes, 20% to 50%) afforded pure **231f** (182 mg, 82%) as a white solid.

Synthesised using **General Procedure D**. 4-Banzyl carbodiimide **49f** (74 mg, 0.39 mmol) afforded urea. Purification by flash column chromatography (Et_2O:hexanes, 20% to 50%) afforded pure **231f** (78 mg,%) as a white solid.

mp 109 - 112 °C (lit. 110 - 112 °C). Rf 0.25 (66%, Et_2O:hexanes). ^{1}H NMR δ 1.33 (9H, s, C(CH_3)$_3$), 4.30 (2H, d, J = 5.6, CH_2Ph), 4.45 (1H, s_{br}, NH), 4.73 (1H, m, NH), 7.23 - 7.36 (5H, m, CH_{Ar}). ^{13}C NMR δ 29.5 (C(*C*H$_3$)$_3$), 44.4 (CH_2), 50.4 (*C*(CH$_3$)$_3$), 127.2

(CH_{Ar}), 127.5 (CH_{Ar}), 128.6 (CH_{Ar}), 139.5 (*ipso*-*C*), 157.5 (*C*=O). Spectroscopic data in agreement with literature.[149]

N'-^{t}Butyl-*N*-2-phenylethyl urea (231g)

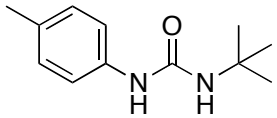


Synthesised using **General Procedure C**. 2-Phenylethyl isocyanate **1g** (147 mg, 1.00 mmol) afforded crude urea. Purification by flash column chromatography (Et_2O:hexanes, 20% to 50%) afforded pure **231g** (147 mg, 67%) as a white solid.

Synthesised using **General Procedure D**. 2-Phenylethyl carbodiimide **49g** (80 mg, 0.40 mmol) afforded urea. Purification by flash column chromatography (Et_2O:hexanes, 20% to 50%) afforded pure **231g** (67 mg,%) as a white solid.

mp 73 - 74 °C (lit. 70 - 71 °C). Rf 0.20 (66%, Et_2O:hexanes). ^{1}H NMR δ 1.33 (9H, s, $C(CH_3)_3$), 2.82 (2H, t, *J* = 6.9, CH_2Ph), 3.41 (2H, q, *J* = 6.9, CH_2N), 4.30 (1H, s_{br}, N*H*), 4.37 (1H, m, N*H*), 7.19 - 7.36 (5H, m, CH_{Ar}). ^{13}C NMR δ 29.6 ($C(CH_3)_3$), 36.5 (CH_2Ph), 41.5 (CH_2N), 50.3 ($C(CH_3)_3$), 126.4 (CH_{Ar}), 128.6 (CH_{Ar}), 128.9 (CH_{Ar}), 139.4 (*ipso*-*C*), 157.5 (*C*=O). Spectroscopic data in agreement with literature.[150]

N'-^{t}Butyl-*N*-4-methylphenyl urea (231h)

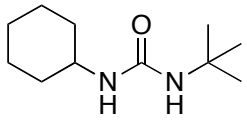


Synthesised using **General Procedure C**. 4-Methylphenyl isocyanate **1h** (133 mg, 1.00 mmol) afforded crude urea. Purification by flash column chromatography (Et_2O:hexanes, 20% to 50%) afforded pure **231h** (161 mg, 78%) as a white solid.

Synthesised using **General Procedure D**. 4-Methylphenyl carbodiimide **49h** (55 mg, 0.29 mmol) afforded urea. Purification by flash column chromatography (Et_2O:hexanes, 20% to 50%) afforded pure **231h** (53 mg,%) as a white solid.

mp 184 - 186 °C. Rf 0.20 (66%, Et_2O:hexanes). ^1H NMR δ 1.36 (9H, s, $C(CH_3)_3$), 2.31 (3H, s, CH_3Ph), 4.74 (1H, s_{br}, N*H*), 6.25 (1H, s_{br}, N*H*), 7.08 - 7.16 (4H, m, CH_{Ar}). ^{13}C NMR δ 20.8 ($PhCH_3$), 29.4 ($C(CH_3)_3$), 50.7 ($C(CH_3)_3$), 121.7 (*m*-*C*H), 129.9 (*o*-*C*H), 133.6 (*p*-*C*H), 136.1 (*ipso*-*C*), 155.2 (*C*=O). IR ν_{max} (solution in $CHCl_3$) 3428.9, 3010.8, 1668.7 (C=O), 1514.1, 1452.8, 1393.2, 1311.3 cm^{-1}. ESI/MS: *m/z* 229.1316 (M+Na, 11%). HRMS: found (calcd for $C_{12}H_{18}N_2ONa$) m/z 229.1316 (229.1311). Anal. Found (Calcd for $C_{12}H_{18}N_2O$): C 69.4 (69.8), H 8.8 (8.8), N 13.4 (13.6).

N'-^{t}Butyl-*N*-cyclohexyl urea (231i)

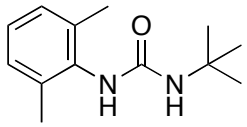


Synthesised using **General Procedure C**. Cyclohexyl isocyanate **1i** (125 mg, 1.00 mmol) afforded crude urea. Purification by flash column chromatography (Et_2O:hexanes, 20% to 50%) afforded pure **231i** (172 mg, 87%) as a white solid.

Synthesised using **General Procedure D**. Cyclohexyl carbodiimide **49i** (50 mg,0.28 mmol) afforded urea. Purification by flash column chromatography (Et_2O:hexanes, 20% to 50%) afforded pure **231i** (55 mg,%) as a white solid.

mp 223 - 224 °C (lit. 226 °C). Rf 0.33 (66%, Et_2O:hexanes). ^1H NMR δ 1.00 - 1.50 (14H, m, CH_2, CH_3), 1.55 - 1.61 (1H, m, CH_2), 1.65 - 1.72 (2H, m, CH_2), 1.87 - 1.96 (2H, m, CH_2), 3.40 - 3.53 (1H, m, C*H*N), 4.15 - 4.45 (2H, s_{br}, N*H*). ^{13}C NMR δ 25.1 (CH_2), 25.7 (CH_2), 29.6 ($C(CH_3)_3$), 34.1 (CH_2), 48.9 ($C(CH_3)_3$), 50.3 (*C*HN), 157.2 (*C*=O). Spectroscopic data in agreement with literature.[151]

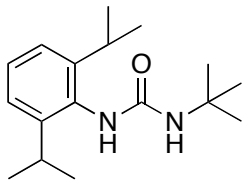
N'-^{t}Butyl-*N*-2,6-dimethylphenyl urea (231j)



Synthesised using **General Procedure C**. 2,6-Dimethylphenyl isocyanate **1j** (147 mg, 1.00 mmol) afforded crude urea. Purification by flash column chromatography (Et_2O:hexanes, 20% to 50%) afforded pure **231j** (132 mg, 60%) as a white solid.

mp 169 - 171 °C. Rf 0.13 (50%, Et_2O:hexanes). ^{1}H NMR δ 1.29 (9H, s, C(C*H*$_3$)$_3$), 2.30 (6H, s, C*H*$_3$Ph), 4.08 (1H, s_{br}, N*H*), 5.45 (1H, s_{br}, N*H*), 7.09 - 7.14 (3H, m, C*H*$_{Ar}$). ^{13}C NMR δ 18.3 (*C*H$_3$Ph), 29.3 (C(*C*H$_3$)$_3$), 50.4 (*C*(CH$_3$)$_3$), 127.7 (*p*-*C*H), 128.8 (*m*-*C*H), 134.3 (*ipso*-*C*), 137.1 (*o*-*C*), 155.8 (*C*=O). IR ν_{max} (solution in $CHCl_3$) 3343.7, 3289.2, 2963.0, 2921.8, 1635.2 (C=O), 1556.7, 1449.9, 1361.7, 1278.0, 1215.4, 767.2 cm^{-1}. ESI/MS: *m/z* 221.1667 (M+H, 7%), 243.1480 (M+Na, 50%). HRMS: found (calcd for $C_{13}H_{21}N_2O$) m/z 221.1667 (221.1648). HRMS: found (calcd for $C_{13}H_{20}N_2ONa$) m/z 243.1480 (243.1468).

N'-^{t}Butyl-*N*-2,6-diisopropylphenyl urea (231k)



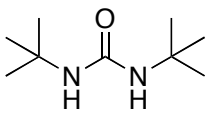
Method A: Synthesised using **General Procedure C**. 2,6-Diisopropylphenyl isocyanate **1k** (203 mg, 1.00 mmol) afforded crude urea. Purification by flash column chromatography (Et_2O:hexanes, 20% to 50%) afforded pure **231k** (71 mg, 35%) as a white solid.

Method B: To an orange solution of ^{t}butylimido dichloro trispyridine titanium(IV) (2.14 g, 5 mmol) in dry dichloromethane (60 mL) at r.t., a solution of aniline (0.94 mL, 5 mmol) in dry dichloromethane (5 mL) was added. After stirring for 3 h., volatile solvents were removed *in vacuo*. The brown solid was dissolved in dichloromethane (3 mL) and washed with hexanes (60 mL) to give a dark brown solid (876 mg). ^{1}H NMR showed a 7 : 3 mixture (starting material : product). A solution of the brown solid (800 mg, 1.28 mmol of starting material, 0.54 mmol product) was degassed before carbon dioxide (1.5 atmospheres) was added. The brown solution was stirred for 5 h before it was quenched with 2M HCl (20 mL) and stirred for a further 1 h. The biphasic mixture was neutralised with $NaHCO_3$. The two phases were separated and the aqueous layer was extracted with dichloromethane (2x20 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated *in vacuo*. Purification by flash column chromatography (Et_2O:hexanes, 20% to 50%) afforded **231k** (118 mg, 36%) as a white solid.

Method C: This compound was also synthesised by the **Method B**, stirring the initial solution for 4 h to isolate a brown solid (1.26 g). ^{1}H NMR showed a 36 : 64 starting material : product mixture. A solution of the brown solid (1.20 mg, 0.96 mmol of starting material, 1.71 mmol product). Workup as above yielded **231k** (55 mg, 21%) as a white solid.

mp 178 - 179 °C. Rf 0.39 (50%, Et_2O:hexanes). ^{1}H NMR δ 1.15 - 1.25 (12H, s_{br}, $CH(CH_3)_2$), 1.27 (9H, s, $C(CH_3)_3$), 3.32 (2H, sept, J = 6.9, $CH(CH_3)_2$), 7.20 (2H, d, J = 7.7, *m*-C*H*), 7.33 (1H, t, J = 7.7, *p*-C*H*). ^{13}C NMR δ 23.6 ($C(CH_3)_3$), 28.2 ($CH(CH_3)_2$), 29.2 ($CH(CH_3)_2$), 50.4 ($C(CH_3)_3$), 124.2 (*m*-*C*H), 128.9 (*p*-*C*H), 131.1 (*o*-*C*H), 148.0 (*ipso*-*C*), 156.7 (*C*=O). IR ν_{max} (solution in $CHCl_3$) 3421.3, 3011.5, 2967.0, 1662.5 (C=O), 1522.5, 1458.0, 1392.8, 1365.1, 1317.0 cm^{-1}. ESI/MS: *m/z* 277.2291 (M+H, 16%), 299.2320 (M+Na, 32%). HRMS: found (calcd for $C_{17}H_{29}N_2O$) m/z 277.2291 (277.2274). Spectroscopic data in agreement with literature.[152]

Bis-*N*,*N*'-^{t}butyl Urea (231l)



Method A: Synthesised using **General Procedure C**. To a solution of dichloro ^{t}butylimido bispyridine titanium(IV) (350 mg, 1.00 mmol) in dichloromethane (15 mL), a solution of ^{t}butyl isocyanate **1l** (99 mg, 1.00 mmol) in dichloromethane (5 mL) was added to afford crude urea. Purification by flash column chromatography (Et_2O:hexanes, 20% to 50%) afforded **231l** (98 mg, 62%) as a white solid.

Method B: To a degassed solution of dichloro ^{t}butylimido bispyridine titanium(IV) (349 mg, 1.00 mmol) in dichloromethane (20 mL), was added carbon dioxide (1.5 atmospheres). After stirring for 5 h, the brown solution was quenched with 2M HCl (20 mL) and stirred for a further 1 h. The biphasic mixture was neutralised with $NaHCO_3$. The two phases were separated and the aqueous layer was extracted with dichloromethane (2x20 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated *in vacuo*. Purification by flash column chromatography (Et_2O:hexanes, 20% to 50%) afforded **231l** (4 mg, 8%) as a white solid.

Method B: To a degassed solution of dichloro ^{t}butylimido trispyridine titanium(IV) (427 mg, 1.00 mmol) in dichloromethane (20 mL), was added carbon dioxide (1.5 atmospheres), to afford **231l** (7 mg, 14%) as a white solid.

Method C: To a solution of dichloro ^{t}butylimido trispyridine titanium(IV) (427 mg, 1.00 mmol) in dichloromethane (20 mL), a solution of *N*,*N*-bis(trimethylsily) benzylamine (251 mg, 1.00 mmol) in dichloromethane (2 mL) was added. The solution was then degassed three times before applying carbon dioxide (1.5 atmospheres). The solution was stirred for 5 h before being quenched with 2M HCl (20 mL) and stirred for a further one h. The biphasic mixture was neutralised with $NaHCO_3$. The two phases were separated and the aqueous layer was extracted with dichloromethane (2x20 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated *in*

vacuo. Purification by flash column chromatography (Et_2O:hexanes, 20% to 50%) afforded **231l** (49 mg, 99%) as a white solid.

This compounds was also synthesised by **Method C** with the difference of using bis(trimethylsilyl) 2-phenylethylamine (275 mg, 1 mmol) to afford **231l** (48 mg, 97%) as a white solid.

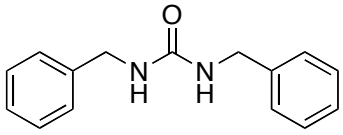
This compounds was also synthesised by **Method C** with the difference of using triethylamine (0.14 mL, 1 mmol) to afford **231l** (32 mg, 37%) as a white solid.

Method D: To a clear yellow solution of titanium tetrachloride (0.50 mL, 4.65 mmol) in dry dichloromethane (20 mL) at 0°C, ^{t}butyl amine (X mmol) was added drop-wise over a period of 5 min. After stirring the orange mixture for a period of 0.5 h, the solid was removed by filtration to give a bright orange solution, pyridine (X mmol) was added and the mixture was stirred for further 0.5 h. The dark red suspension was then filtered to give a dark orange solution. The solution was degassed three times before applying carbon dioxide (1.5 atmospheres). After stirring for five hours, the brown solution was quenched with 2M HCl (20 mL) and stirred for a further 1 h. The byphasic mixture was neutralised with $NaHCO_3$. The two phases were separated and the aqueous layer was extracted with dichloromethane (2x20 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated *in vacuo*. Purification by flash column chromatography (Et_2O:hexanes, 20% to 50%) afforded **231l** (X%) as a white solid.

Entry	^{t}BuNH$_2$ mL	^{t}BuNH$_2$ mmol	Py mL	Py mmol	**231l** mg	**231l** yield %
231la	0.48	4.65	1.50	18.6	24	2
231lb	1.47	13.9	0.87	10.7	28	7
231lc	2.93	27.9	0.87	10.7	208	26
231ld	0.1	0.91	1.70	21.0	149	95

mp 238 - 240 °C (lit. 238 - 239 °C). Rf 0.14 (50%, Et_2O:hexanes). ^1H NMR δ 1.32 (9H, s, $C(CH_3)_3$), 4.05 (1H, s_{br}, N*H*). ^{13}C NMR δ 29.7 ($C(CH_3)_3$), 50.3 ($C(CH_3)_3$), 157.0 (*C*=O). Spectroscopic data in agreement with literature.[153]

Bis-*N*,*N*'-benzyl urea (233)



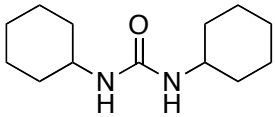
Method A: To a degassed solution of dichloro benzylimido bispyridine titanium(IV) (381 mg, 095 mmol) in dichloromethane (20 mL), was added carbon dioxide (1.5 atmospheres). After stirring for five hours, the pale orange mixture was quenched with 2M HCl (20 mL) and stirred for a further one h. The biphasic mixture was neutralised with $NaHCO_3$. The two phases were separated and the aqueous layer was extracted with dichloromethane (2x20 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated *in vacuo*. Purification by flash column chromatography (Et_2O:hexanes, 20% to 50%) afforded **233** (40 mg, 18%) as a white solid.

Method B: Synthesised by **General Procedure G**. To a clear yellow solution of titanium tetrachloride (X mmol) in dry dichloromethane (20 mL) at 0 °C, was added benzyl amine (X mmol) dropwise over a period of 5 min. After stirring the orange mixture for a period of 0.5 h, the solid was removed by filtration to give a bright orange solution, pyridine (X mmol) was then added and the mixture was stirred for further 0.5 h. The dark red suspension was then filtered to give a dark orange solution (in entry **233e**, TMSCl (4.63 mL, 36.5 mmol) was added). The solution was degassed before applying carbon dioxide (1.5 atmospheres). After stirring for five hours, the brown solution was quenched with 2M HCl (20 mL) and stirred for a further one h. The by-phasic mixture was neutralised with $NaHCO_3$. The two phases were separated and the aqueous layer was extracted with dichloromethane (2x20 mL). The combined organic layers were dried over $MgSO_4$ and concentrated *in vacuo*. Purification by flash column chromatography (Et_2O:hexanes, 20% to 50%) afforded **233** (X%) as a white solid.

Entry	$TiCl_4$ mL	$TiCl_4$ mmol	$BnNH_2$ mL	$BnNH_2$ mmol	Py mL	Py mmol	**233** mg	**233** yield %
233a	0.50	4.65	0.50	4.65	1.50	18.2	91	16
233b	0.50	4.65	1.50	13.7	0.85	10.5	262	48
233c	0.50	4.65	3.06	27.9	0.87	10.7	377	34
233d	0.10	0.91	2.99	27.3	1.70	21.0	210	96
233e	0.10	0.91	2.99	27.3	1.70	21.0	217	99

mp 165 - 168 °C (Crystallised from CH_2Cl_2). ^{1}H NMR δ 4.37 (4H, d, *J* = 6.0, C*H*$_2$Ph), 4.79 (2H, s_{br}, N*H*), 7.18 - 7.35 (10H, m, C*H*$_{Ar}$). ^{13}C NMR δ 44.6 (*C*H$_2$Ph), 127.4 (*C*H$_{Ar}$), 127.5 (*C*H$_{Ar}$), 128.7 (*C*H$_{Ar}$), 138.1 (*C*$_{Ar}$), 158.0 (C=O). IR ν_{max} (solution in $CHCl_3$) 3447.0, 3007.8, 2962.6, 2927.5, 1670.2 (C=O), 1530.5, 1264.5, 1097.7, 1027.5 cm^{-1}. ESI/MS: *m/z* 241.1324 (M+H$^+$, 54%), 263.1144 (M+Na$^+$,30%). HRMS found (calcd for $C_{15}H_{16}N_2O$) m/z 241.1324 (241.1335). Spectroscopic data in agreement with literature.[154]

Bis-*N*,*N*'-cyclohexyl urea (268a)



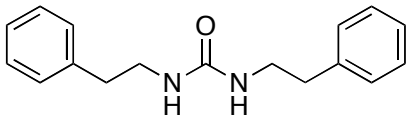
Synthesised by **General Procedure G**, using cyclohexyl amine (X mmol).

Entry	$TiCl_4$ mL	$TiCl_4$ mmol	$CyNH_2$ mL	$CyNH_2$ mmol	Py mL	Py mmol	**268a** mg	**268a** yield %
268aa	0.50	4.65	0.53	4.65	1.50	18.2	73	14
268ab	0.50	4.65	1.56	13.7	0.85	10.5	182	36
268ac	0.50	4.65	3.20	27.9	0.87	10.7	199	19

Entry	$TiCl_4$ mL	$TiCl_4$ mmol	$CyNH_2$ mL	$CyNH_2$ mmol	Py mL	Py mmol	**268a** mg	**268a** yield %
268ad	0.10	0.91	3.13	27.3	1.70	21.0	198	97
268ae	0.10	0.91	3.13	27.3	1.70	21.0	202	99

mp 225 - 228 °C (lit. 227 - 229 °C). ^{1}H NMR δ 1.05 - 1.20 (6H, m, C*H*$_2$), 1.34 (4H, qt, *J* = 11.9, 3.5, C*H*$_2$), 1.60 (2H, dt, *J* = 13.0, 3.8, C*H*$_2$), 1.69 (4H, dt, *J* = 13.8, 3.8, C*H*$_2$), 1.90 - 1.97 (4H, m, C*H*$_2$), 3.48 (2H, tt, *J* = 10.5, 3.8, C*H*N), 3.95 - 4.15 (2H, s_{br}, N*H*). ^{13}C NMR δ 25.0 (*C*H$_2$), 25.7 (*C*H$_2$), 34.0 (*C*H$_2$), 49.2 (*C*HN). Missing quaternary carbon (C=O). Spectroscopic data in agreement with literature.[155]

Bis-*N*,*N*'-(2-phenylethyl) urea (268b)

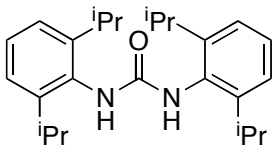


This compounds was synthesised by **General Procedure G**. Using 2-phenylethyl amine (X mmol).

Entry	$TiCl_4$ mL	$TiCl_4$ mmol	$Ph(CH_2)_2NH_2$ mL	$Ph(CH_2)_2NH_2$ mmol	Py mL	Py mmol	**268b** mg	**268b** yield %
268ba	0.50	4.65	0.59	4.65	1.50	18.2	107	17
268bb	0.50	4.65	1.73	13.7	0.85	10.5	343	56
268bc	0.50	4.65	3.50	27.9	0.87	10.7	521	42
268bd	0.10	0.91	3.46	27.3	1.70	21.0	235	96
268be	0.10	0.91	3.46	27.3	1.70	21.0	241	99

mp 139 - 140 °C (lit. 138 - 141 °C). ^{1}H NMR δ 2.73 (4H, t, *J* = 6.9, C*H*$_2$Ph), 3.39 (4H, q, *J* = 6.5, C*H*$_2$N), 4.15 (2H, s_{br}, N*H*), 7.15 - 7.32 (10H, m, C*H*$_{Ar}$). ^{13}C NMR δ 36.4 (*C*H$_2$Ph), 41.6 (*C*H$_2$N), 126.4 (*C*H$_{Ar}$), 128.6 (*C*H$_{Ar}$), 128.8 (*C*H$_{Ar}$), 139.2 (*ipso*-*C*$_{Ar}$), 157.9 (C=O). Spectroscopic data in agreement with literature.[156]

N,*N*'-Bis-2,6-diisopropylphenyl urea (261)

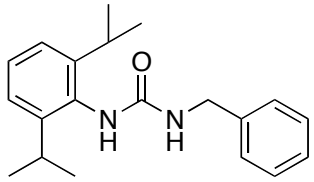


Method A: To a degassed solution of dichloro bispyridine 2,6-diisopropylphenylimido titanium(IV) (540 mg, 1.07 mmol) in dichloromethane (20 mL) was added carbon dioxide (1.5 atmospheres). After stirring for 5 hours, the brown solution was quenched with 2M HCl (20 mL) and stirred for a further one h. The biphasic mixture was neutralised with $NaHCO_3$. The two phases were separated and the aqueous layer was extracted with dichloromethane (2x20 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated *in vacuo*. Purification by flash column chromatography (Et_2O:hexanes, 20% to 50%) afforded **261** (189 mg, 98%) as a white solid.

Method B: To a degassed solution of dichloro bispyridine 2,6-diisopropylphenylimido titanium(IV) (630 mg, 1.19 mmol) in dichloromethane (20 mL), was added carbon dioxide (1.5 atmospheres). After stirring for five hours, the brown solution was quenched with NaOEt (812 mg, 12.0 mmol) and stirred for a further one h. The pale orange mixture was quenched with 2M HCl (20 mL) and stirred for a further one h. The biphasic mixture was neutralised with $NaHCO_3$. The two phases were separated and the aqueous layer was extracted with dichloromethane (2x20 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated *in vacuo*. Purification by flash column chromatography (Et_2O:hexanes, 20% to 50%) afforded **261** (306 mg, 68%) as a white solid.

mp 234 - 232 °C (lit. 230 °C). ^{1}H NMR δ 1.16 (12H, d, *J* = 5.6, CH(C*H*$_3$)$_2$), 3.07 (2H, sept, *J* = 5.6, C*H*(CH$_3$)$_2$), 6.80 - 7.25 (3H, m, C*H*$_{Ar}$), 7.72 (1H, s$_{br}$, N*H*). Spectroscopic data in agreement with literature.[157]

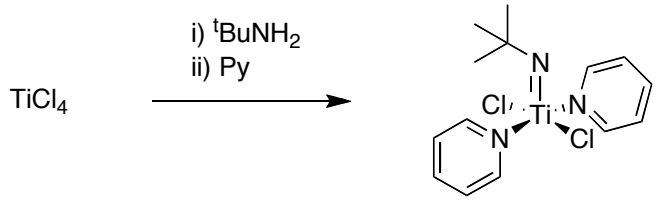
N-Benzyl-*N*'-2,6-diisopropylphenyl urea (263)



To an orange solution of ^{t}butylimido dichloro trispyridine titanium(IV) (854 mg, 2.00 mmol) in dry dichloromethane (40 mL) at r.t., a solution of 2,6-diisopropylaniline (0.38 mL, 2.00 mmol) in dry dichloromethane (3 mL) was added. After stirring for 5 h the solvent was evaporated and the solid washed with hexanes (2x20 mL). The brown solid was dissolved in dichloromethane (20 mL) and carbon dioxide (1.5 atmospheres) was added after degassing (x3). After stirring for 16 hours, the brown solution was quenched with $BnNH_2$ (0.22 mL, 2 mmol) and stirred for a further one h. The pale orange mixture was quenched with 2M HCl (20 mL) and stirred for a further one h. The biphasic mixture was neutralised with $NaHCO_3$ before the two phases were separated and the aqueous layer was extracted with dichloromethane (2x20 mL). The combined organic layers were dried over $MgSO_4$ and concentrated *in vacuo*. Purification by flash column chromatography (Et_2O:hexanes, 20% to 50%) afforded **263** (114 mg, 18%) as a white solid. mp 185 - 186 °C (lit. 186 - 188). ^{1}H NMR δ 1.16 (12H, d, *J* = 5.6, CH(C*H*$_3$)$_2$), 3.31 (2H, sept, *J* = 5.6, C*H*(CH$_3$)$_2$), 4.39 (2H, d, *J* = 4.8, C*H*$_2$Ph), 4.50 (1H, s$_{br}$, N*H*), 5.97 (1H, s$_{br}$, N*H*), 7.15 - 7.35 (8H, m, C*H*$_{Ar}$). ^{13}C NMR δ 28.4 (CH(*C*H$_3$)$_2$), 44.2 (*C*H$_2$Ph), 124.2 (*C*H$_{Ar}$), 127.3 (*C*H$_{Ar}$), 127.6 (*C*H$_{Ar}$), 128.6 (*C*H$_{Ar}$), 129.2 (*C*$_{Ar}$), 130.7 (*C*$_{Ar}$), 139.2 (*C*H$_{Ar}$), 148.1 (*C*$_{Ar}$), 157.6 (C=O). Missing primary carbon. Spectroscopic data in agreement with literature.[158]

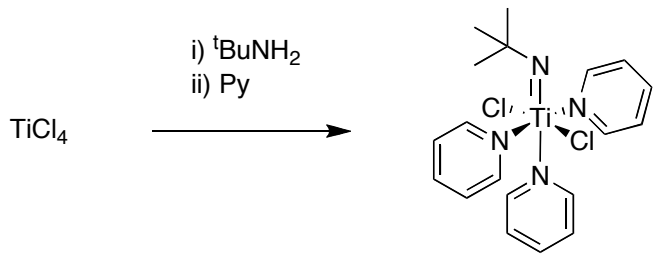
5.7 Preparation of Titanium Complexes

^{t}Butylimido dichloro bispyridine titanium(IV) (231)



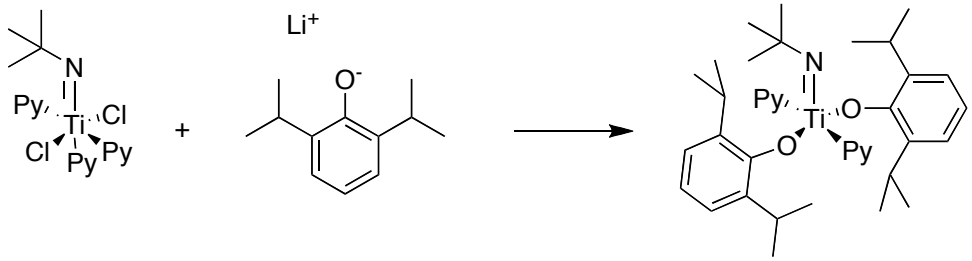
To a clear yellow solution of titanium tetrachloride (2.00 mL, 18.2 mmol) in dry dichloromethane (200 mL) at 0 °C, ^{t}butyl amine (9.5 mL, 90 mmol) was added drop-wise over a period of 5 min. After stirring the orange mixture for a period of 2 h, the solid was removed by filtration to give a bright orange solution and pyridine (3.3 mL, 41 mmol) was then added. After stirring for 2 h, the dark red suspension was filtered to get a dark orange solution. Volatile solvents were removed *in vacuo* and the solid was extracted with toluene : dichloromethane (5 : 1, 2x50 mL). Volatile solvents were removed *in vacuo* and the solid was washed with pentane (2x60 mL) to give **231** (3.85 g, 61%) as a pale orange powder. ^{1}H NMR δ 0.93 (9H, s, C(C*H*$_3$)$_3$), 7.42 (4H, t, *J* = 6.8, 3-C*H*), 7.84 (2H, t, *J* = 7.6, 4-C*H*), 9.28 (4H, d, *J* = 4.8, 2-C*H*). ^{13}C NMR δ 30.4 (C(*C*H$_3$)$_3$), 73.4 (*C*(CH$_3$)$_3$), 124.3 (3-*C*H), 138.6 (4-*C*H), 151.7 (2-*C*H). Spectroscopic data in agreement with literature.[159]

^{t}Butylimido dichloro trispyridine titanium(IV) (256)



To a clear yellow solution of titanium tetrachloride (1.00 mL, 9.12 mmol) in dry dichloromethane (200 mL) at 0°C, ^{t}butyl amine (6.10 mL, 57.5 mmol) was added dropwise over a period of 5 min. After stirring the orange mixture for a period of 2 h, the solid was removed by filtration to give a bright orange solution. Pyridine (3.00 mL, 37.4 mmol) was then added and the dark red suspension was stirred for 2 h before being filtered to give a dark orange solution. Volatile solvents were removed *in vacuo* to get **256** (3.14 g, 81%) as an orange solid. ^{1}H NMR δ 0.97 (9H, s, C(C*H*$_3$)$_3$), 7.19 (2H, sbr, 3-C*H*^{axPy}), 7.42 (4H, t, *J* = 5.2, 3-C*H*^{eqPy}), 7.61 (1H, s$_{br}$, 4-C*H*^{axPy}), 7.85 (2H, t$_{br}$, 2H, 4-C*H*^{eqPy}), 8.63 (2H, s$_{br}$, 2-C*H*^{axPy}), 9.29 (4H, d, *J* = 4.0, 2-C*H*^{eqPy}). ^{13}C NMR δ 30.2 (C(*C*H$_3$)$_3$), 72.7 (*C*(CH$_3$)$_3$), 123.5 (3-*C*H^{axPy}), 124.0 (3-*C*H^{eqPy}), 136.3 (4-*C*H^{axPy}), 138.5 (4-*C*H^{eqPy}), 150.3 (2-*C*H^{axPy}), 151.8 (2-*C*H^{eqPy}). Spectroscopic data in agreement with literature.[160]

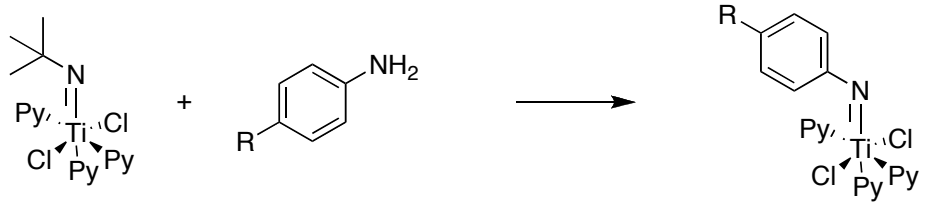
Bispyridine ^{t}butylimido bis-(2,6-diisopropylphenolate) titanium(IV) (259)



To a solution of 2,6-diisopropylphenol (4.34 mL, 23.4 mmol) in dry THF (100 mL) at -40 °C, was added *n*-butyllithium 2.5 M in hexanes (9.4 mL, 23.4 mmol) dropwise over 1 min. The solution was warmed to r.t. and stirred for 1 h. The yellow solution was added to a solution of ^{t}butylimido dichloro trispyridine titanium(IV) (5.00 g, 11.7 mmol) in THF (100 mL) at -40 °C. After stirring for 10 min, the brown solution was warmed to r.t. and stirred for further 16 h. After removing volatile solvent *in vacuo*, the yellow solid was extracted with toluene : Et_2O (2 : 1, 2x75 mL) to remove LiCl as a white solid. Volatile were removed from the yellow solution *in vacuo* and the solid was washed with cold dry Et_2O (2x20 mL), to give **259** as yellow solid (4.08 g, 56%). ^{1}H

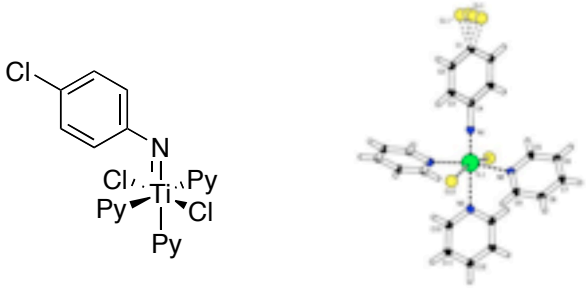
NMR δ 0.91 (9H, s, C(C*H*$_3$)$_3$), 1.02 (24H, d, *J* = 6.8, CH(C*H*$_3$)$_2$), 3.98 (4H, s$_{br}$, C*H*(CH$_3$)$_2$), 6.74 (2H, t, *J* = 7.6, *p*-C*H*^{phenol}), 7.02 (4H, d, *J* = 7.6, *m*-C*H*^{phenol}), 7.02 - 7.03 (4H, m, 3-C*H*^{py}), 7.70 (2H, tt, *J* = 7.6, 1.6, 4-C*H*^{py}), 8.87 (4H, s$_{br}$, 2-C*H*^{py}). ^{13}C NMR δ 23.8 (CH(*C*H$_3$)$_2$), 25.4 (*C*H(CH$_3$)$_2$), 31.7 (C(*C*H$_3$)$_3$), 68.8 (*C*(CH$_3$)$_3$), 117.2 (*p*-*C*H^{phenol}), 122.8 (*m*-*C*H^{phenol}), 124.0 (3-*C*H^{py}), 137.2 (4-*C*H^{py}), 137.8 (*o*-*C*^{phenol}), 150.2 (2-*C*H^{py}), 158.1 (*ipso*-*C*^{phenol}). Spectroscopic data in agreement with literature.[161]

General Procedure E.



General Procedure E. To an orange solution of ^{t}butylimido dichloro trispyridine titanium(IV) (1 equivalent) in dry dichloromethane (20 mL) at r.t., was added a solution of aniline (1 equivalent) in dry dichloromethane (5 mL). After stirring for 48 h, volatile solvents were removed *in vacuo* and the resulting brown solid was extracted with dry dichloromethane (20 mL) to give a dark brown solution. Purification by recrystallisation (dichloromethane : hexanes) (30 mL), storing at r.t. or at -25 °C if required.

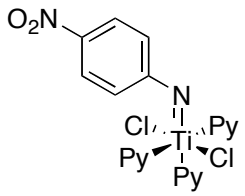
Dichloro 4-chlorophenylimido trispyridine titanium(IV) (256a)



Synthesised using **General Procedure E**. To a solution of ^{t}butylimido dichloro trispyridine titanium(IV) (2.52 g, 5.90 mmol) in dichloromethane (20 mL), was added a

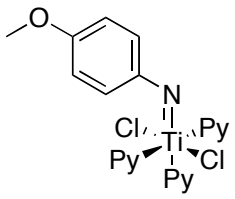
solution of 4-chloroaniline (764 mg, 5.90 mmol) in dichloromethane (5 mL) to afford **256a** (1.59 g, 56%) as a dark brown solid. ^{1}H NMR δ 6.86 (2H, d, *J* = 8.4, *o*-C*H*^{imine}), 6.99 (2H, d, *J* = 8.4, *m*-C*H*^{imine}), 7.19 - 7.30 (2H, m, 3-C*H*^{axPy}), 7.37 (4H, t, *J* = 6.8, 3-C*H*^{eqPy}), 7.69 (1H, t, *J* = 7.6, 4-C*H*^{axPy}), 7.82 (2H, t, *J* = 6.8, 4-C*H*^{eqPy}), 8.78 (2H, s_{br}, 2-C*H*^{axPy}), 9.08 (4H, d, *J* = 4.8, 2-C*H*^{eqPy}). ^{13}C NMR δ 123.7 (3-*C*H^{axPy}), 124.2 (3-*C*H^{eqPy}), 125.0 (*m*-*C*H^{imine}), 127.0 (*p*-*C*^{imine}), 128.1 (*o*-*C*H^{imine}), 137.1 (4-*C*H^{axPy}), 138.8 (4-*C*H^{eqPy}), 150.8 (2-*C*H^{axPy}), 151.1 (2-*C*H^{eqPy}), 157.5 (*ipso*-*C*^{imine}). IR ν_{max} (solution in $CHCl_3$) 3317.6, 3213.3, 3059.7, 2566.1, 1600.8, 1492.2, 1440.9, 1325.8, 1212.6, 1088.7, 1062.5, 1038.0, 011.4, 1004.5, 828.0, 757.6, 750.1 cm^{-1}. Anal. Found (Calcd for $C_{21}H_{19}N_4Cl_3Ti$): C 51.30 (52.37), H 4.02 (3.98), N 11.62 (11.63).

Dichloro 4-nitrophenylimido trispyridine titanium(IV) (256b)



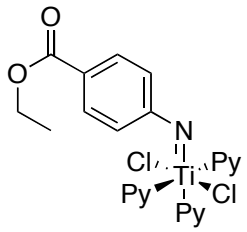
Synthesised using **General Procedure E**. To a solution of ^{t}butylimido dichloro trispyridine titanium(IV) (5.76 g, 12.6 mmol) in dichloromethane (20 mL), was added a solution of 4-nitroaniline (1.74 mg, 12.6 mmol) in dichloromethane (5 mL) to afford **256b** (4.33 g, 70%) as red crystals. mp 164 - 166 °C (lit. not recorded). ^{1}H NMR δ 6.87 (2H, d, *J* = 8.8, *o*-C*H*^{imine}), 7.26 (2H, t, *J* = 7.6, 3-C*H*^{axPy}), 7.42 (4H, t, *J* = 7.6, 3-C*H*^{eqPy}), 7.72 (1H, t, *J* = 7.6, 4-C*H*^{axPy}), 7.87 (2H, t, *J* = 7.6, 4-C*H*^{eqPy}), 7.96 (2H, d, *J* = 8.8, *m*-C*H*^{imine}), 8.78 (2H, d, *J* = 7.6, 2-C*H*^{axPy}), 9.07 (4H, d, *J* = 7.6, 2-C*H*^{eqPy}). ^{13}C NMR δ 123.7 (*o*-*C*H^{imine}), 123.9 (3-*C*H^{axPy}), 124.4 (3-*C*H^{eqPy}), 124.9 (*m*-*C*H^{imine}), 137.0 (4-*C*H^{axPy}), 139.1 (4-*C*H^{eqPy}), 141.0 (*ipso*-*C*^{imine}), 150.6 (2-*C*H^{eqPy}), 151.7 (2-*C*H^{axPy}), 162.2 (*p*-*C*^{imine}). IR ν_{max} (solid) 3305.7, 3166.8, 3086.3, 1599.5, 1573.1, 1480.9, 1439.5, 1304.6, 1210.9, 1166.8, 1100.5, 1060.1, 1043.3, 1036.6, 1011.9, 960.5, 849.5 cm^{-1}. Anal. Found (Calcd for $C_{21}H_{19}N_4Cl_3Ti$): C 47.57 (47.75), H 3.89 (4.39), N 13.34 (13.26). Spectroscopic data in agreement with literature.[162]

Dichloro 4-(methoxyphenyl)imido trispyridine titanium(IV) (256c)



Synthesised using **General Procedure E**. To a solution of ^{t}butylimido dichloro trispyridine titanium(IV) (5.00 g, 11.7 mmol) in dichloromethane (20 mL), was added a solution of 4-methoxyaniline (1.44 g, 11.7 mmol) in dichloromethane (5 mL) to afford **256c** (3.56 g, 64%) as dark green solid. mp 92 - 94 °C deg. ^{1}H NMR δ 3.67 (3H, s_{br}, C*H*$_3$O), 6.55 (2H, s_{br}, *m*-C*H*^{imine}), 6.93 (2H, s_{br}, *o*-C*H*^{imine}), 7.22 (2H, s_{br}, 3-C*H*^{axPy}), 7.33 (4H, s_{br}, 3-C*H*^{eqPy}), 7.65 (1H, s_{br}, 4-C*H*^{axPy}), 7.78 (2H, s_{br}, 4-C*H*^{eqPy}), 8.70 (2H, s_{br}, 2-C*H*^{axPy}), 9.09 (4H, s_{br}, 2-C*H*^{eqPy}). ^{13}C NMR δ 55.4 (*C*H$_3$O), 113.2 (*m*-*C*H^{imine}), 123.7 (3-*C*H^{axPy}), 124.1 (3-*C*H^{eqPy}), 124.9 (*o*-*C*H^{imine}), 136.5 (4-*C*H^{axPy}), 138.6 (4-*C*H^{eqPy}), 150.4 (2-*C*H^{axPy}), 151.7 (2-*C*H^{eqPy}), 154.6 (*ipso*-*C*^{imine}), 154.7 (*p*-*C*^{imine}). IR ν_{max} (solid) 3058.6, 3012.2, 2938.0, 2907.7, 2831.5, 2584.4, 1601.8, 1510.1, 1482.4, 1489.1, 1440.8, 1273.2, 1235.7, 1212.7, 1063.3, 1036.6, 1011.8, 827.5. cm^{-1}.

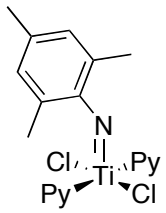
Dichloro 4-(ethoxycarbonyl)phenylimido trispyridine titanium(IV) (256e)



Synthesised using **General Procedure E**. To a solution of ^{t}butylimido dichloro trispyridine titanium(IV) (5.00 g, 11.7 mmol) in dichloromethane (20 mL), was added a solution of 4-ethoxycarbonyl aniline (1.93 mg, 11.7 mmol) in dichloromethane (5 mL) to afford **256e** (4.13 g, 68%) as red crystals. mp 118 - 120 °C (deg). ^{1}H NMR δ 1.32

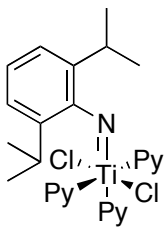
(3H, t, J = 7.1, CH_3CH$_2$O), 4.28 (2H, q, J = 7.1, CH$_3$CH_2O), 6.88 (2H, d, J = 8.4, o-CH^{imine}), 7.24 (2H, s_{br}, 3-CH^{axPy}), 7.35 (4H, t, J = 6.4, 3-CH^{eqPy}), 7.70 (1H, s_{br}, 4-CH^{axPy}), 7.75 (2H, d, J = 8.4, m-CH^{imine}), 7.81 (2H, t, J = 7.3, 4-CH^{eqPy}), 8.80 (2H, s_{br}, 2-CH^{axPy}), 9.08 (4H, s_{br}, 2-CH^{eqPy}). ^{13}C NMR δ 14.4 (CH$_3$CH$_2$O), 60.5 (CH$_3$$CH_2$O), 123.2 (*ipso*-$C^{imine}$), 123.4 ($o$-$C$H^{imine}), 123.8 (3-$C$H^{axPy}), 124.3 (3-$C$H^{eqPy}), 130.2 ($m$-$C$H^{imine}), 137.4 (4-$C$H^{axPy}), 138.9 (4-$C$H^{eqPy}), 151.0 (2-$C$H^{axPy}), 151.6 (2-$C$H^{eqPy}), 161.7 ($p$-$C^{imine}$), 166.5 ($C$=O). IR ν_{max} (solid) 3313.7, 3199.2, 3069.8, 2983.6, 2897.4, 2504.1, 1704.8, 1601.5, 1585.2, 1482.8, 1441.6, 1331.1, 1270.2, 1213.1, 1153.6, 1107.5, 1095.8, 1064.7, 1041.6, 1010.9, 1003.5, 964.9, 858.8 cm^{-1}. Anal. Found (Calcd for $C_{21}H_{19}N_4Cl_3Ti$): C 54.97 (55.52), H 4.77 (4.66), N 10.65 (10.97).

Dichloro 2,4,6-trimethylphenylimido bispyridine titanium(IV) (256f)



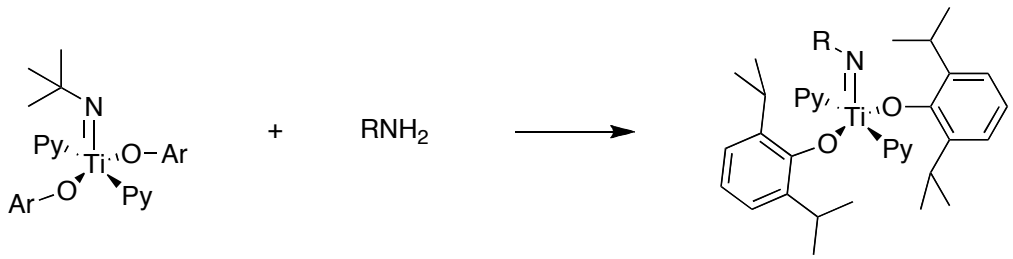
Synthesised using **General Procedure E**. To a solution of ^{t}butylimido dichloro trispyridine titanium(IV) (2.13 g, 5.00 mmol) in dichloromethane (20 mL), was added a solution of 2,4,6-trimethylaniline (0.70 mL, 5.00 mmol) in dichloromethane (5 mL) to afford **256f** (1.56 g, 76%) as pale brown solid (80% purity). ^{1}H NMR δ 2.20 (3H, s, p-PhCH_3), 2.50 (6H, s, o-Ph(CH_3)$_2$), 6.66 (2H, s, m-CH_{Ar}), 7.49 (4H, dd, J = 7.4, 6.5, 3-CH_{Py}), 7.89 (2H, t, J = 7.6, 4-CH_{Py}), 9.13 (4H, d, J = 4.9, 2-CH_{Py}).

Dichloro 2,6-diisopropylphenylimido trispyridine titanium(IV) (256g)



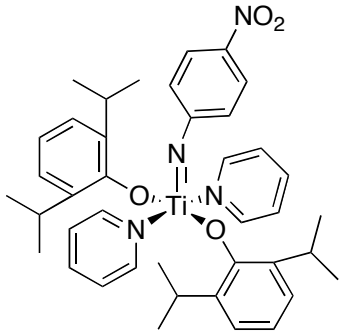
Synthesised using **General Procedure E**. To a solution of ^{t}butylimido dichloro trispyridine titanium(IV) (4.91 g, 11.5 mmol) in dichloromethane (20 mL), was added a solution of 2,6-diisopropylaniline (2.17 mL, 11.5 mmol) in dichloromethane (5 mL) the reaction was stirred for two days to afford **256g** (5.10 g, 84%) as dark yellow solid. ^{1}H NMR δ 1.11 (12H, d, *J* = 5.2, CH(C*H*$_3$)$_2$), 4.33 (2H, sept, *J* = 5.2, C*H*(CH$_3$)$_2$), 6.81 (1H, t, *J* = 6.4, *p*-C*H*^{imine}), 6.92 (2H, d, *J* = 6.4, *m*-C*H*^{imine}), 7.25 (2H, s$_{br}$, 3-C*H*^{axPy}), 7.48 (4H, t, *J* = 5.2, 3-C*H*^{eqPy}), 7.67 (1H, t, *J* = 5.6, 4-C*H*^{axPy}), 7.89 (2H, t, *J* = 5.2, 4-C*H*^{eqPy}), 8.64 (2H, s$_{br}$, 2-C*H*^{axPy}), 9.17 (4H, d, *J* = 4.9, 2-C*H*^{eqPy}). ^{13}C NMR δ 24.1 (CH(*C*H$_3$)$_2$), 27.5 (*C*H(CH$_3$)$_2$), 122.2 (*m*-*C*H^{imine}), 123.0 (3-*C*H^{axPy}), 123.7 (*p*-*C*H^{imine}), 124.6 (3-*C*H^{eqPy}), 136.3 (4-*C*H^{axPy}), 139.0 (4-*C*H^{eqPy}), 145.5 (*o*-*C*^{imine}), 150.3 (2-*C*H^{axPy}), 151.2 (2-*C*H^{eqPy}), 156.9 (*ipso*-*C*^{imine}). Spectroscopic data in agreement with literature.[163]

General Procedure F



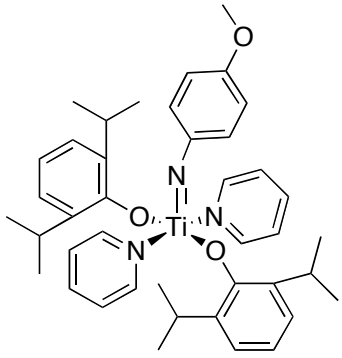
General Procedure F. To a mixture of ^{t}butylimido bispyridine bis-(2,6-diisopropylphenol) titanium(IV) (1 equivalent) in Et$_2$O (20 mL) was added aniline (1 equivalent). The bright yellow mixture was stirred for 16 h to give a brown mixture. After filtration the solid was dried and purified by recrystallisation under slow diffusion, dissolving in dichloromethane (10 mL) and layer with Et$_2$O (10 mL) or hexane (10 mL), storing at r.t. or at -25 °C if required. To give the corresponding titanium complex.

Bis-2,6-diisopropylphenol 4-nitrophenylimido bispyridine titanium(IV) (259a)



Synthesised using **General Procedure F**. To a mixture of ^{t}butylimido bispyridine bis-(2,6-diisopropylphenol) titanium(IV) (2.20 g, 3.49 mmol) was added 4-nitroaniline (481 mg, 3.49 mmol) to afford **259a** (1.96 g, 81%) as dark yellow solid. mp. 134- 136 °C. ^{1}H NMR δ 1.04 (24H, d, J = 6.9, CH(CH_3)$_2$), 3.80 (4H, sept, J = 6.9, CH(CH$_3$)$_2$), 6.21 (2H, app dt, J = 7.2, 2.1, o-CH^{imine}), 6.85 (2H, t, J = 7.6, p-CH^{phenol}), 7.05 (4H, d, J = 7.6, m-CH^{phenol}), 7.40 (4H, t, J = 6.7, 3-CH^{Py}), 7.82 (2H, t, J = 6.7, 4-CH^{Py}), 7.91 (2H, app dt, J = 7.2, 2.1, m-CH^{imine}), 8.79 (2H, m, 2-CH^{Py}). ^{13}C NMR δ 23.6 (CH(CH$_3$)$_2$), 26.3 (CH(CH$_3$)$_2$), 119.5 (o-CH^{imine}), 119.7 (p-CH^{phenol}), 123.1 (o-CH^{phenol}), 124.9 (3-CH^{Py}), 125.5 (m-CH^{imine}), 137.3 (o-C^{phenol}), 138.9 (4-CH^{Py}), 149.6 (2-CH^{Py}), 158.4 (*ipso*-C^{phenol}), 191.7 (p-C^{imine}). Missing *ipso*-C^{imine}. IR ν_{max} (solid) 2958.7, 1572.8, 1479.6, 1431.1, 1330.9, 1301.1, 1261.1, 1210.9, 1104.3, 953.0, 897.0, 875.1, 751.8, 708.9 cm^{-1}.

Bis-2,6-diisopropylphenol 4-methoxyphenylimido bispyridine titanium(IV) (259b)

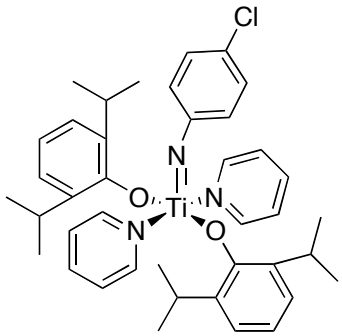


Synthesised using **General Procedure F**. To a mixture of ^{t}butylimido bispyridine bis-(2,6-diisopropylphenol) titanium(IV) (714 g, 1.13 mmol) was added 4-methoxyaniline

(139 mg, 1.13 mmol) to afford **259b** (386 g, 50%) as pale brown solid (85% purity). ^{1}H NMR δ 1.06 (24H, d, *J* = 6.9, CH(C*H*$_3$)$_2$), 3.73 (3H, s, OC*H*$_3$), 3.98 (4H, sept, *J* = 6.9, C*H*(CH$_3$)$_2$), 6.59 (4H, s, C*H*^{imine}), 6.78 (2H, t, *J* = 7.6, *p*-C*H*^{phenol}), 7.04 (4H, d, *J* = 7.6, *m*-C*H*^{phenol}), 7.31 (4H, t, *J* = 6.9, 3-C*H*^{Py}), 7.74 (2H, t$_{br}$, 4-C*H*^{Py}), 8.85 (4H, s$_{br}$, 2-C*H*^{Py}). ^{13}C NMR δ 23.7 (CH(*C*H$_3$)$_2$), 25.9 (*C*H(CH$_3$)$_2$), 55.5 (O*C*H$_3$), 113.2 (*m*-*C*H^{imine}), 118.1 (*o*-*C*H^{imine}), 122.8 (*p*-*C*H^{phenol}), 122.9 (*m*-*C*H^{phenol}), 124.5 (3-*C*H^{Py}), 137.3 (4-*C*H^{Py}), 138.1 (*o*-*C*H^{phenol}), 149.9 (2-*C*H^{Py}), 152.5 (*p*-*C*^{imine}), 155.7 (*ipso*-*C*^{imine}), 158.4 (*ipso*-*C*^{phenol}). IR ν$_{max}$ (solid) 2962.4, 1513.1, 1490.0, 1431.3, 1328.9, 1265.0 1233.5, 1213.4, 1040.9, 897.1cm^{-1}.

Note: no other data was collected as impure.

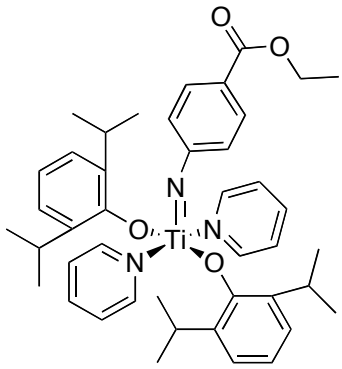
4-Chlorophenylimine bis-2,6-diisopropylphenol bispyridine titanium(IV) (259c)



Synthesised using **General Procedure F**. To a mixture of ^{t}butylimido bispyridine bis-(2,6-diisopropylphenol) titanium(IV) (2.75 g, 4.36 mmol) was added 4-chloroaniline (556 mg, 4.36 mmol) to afford **259c** (2.28 g, 76%) as orange solid. mp. 121 - 123 °C (deg). ^{1}H NMR δ 1.26 (24H, d, *J* = 6.9, CH(C*H*$_3$)$_2$), 4.21 (2H, sept, *J* = 6.9, C*H*(CH$_3$)$_2$), 6.36 (4H, t, *J* = 6.2, 3-C*H*^{Py}), 6.61 (2H, dm, *J* = 8.6, *o*-C*H*^{imine}), 6.67 (2H, t, *J* = 7.5, 4-C*H*^{Py}), 6.99 (2H, t, *J* = 7.7, *p*-C*H*^{phenol}), 7.06 (2H, dm, 8.6, *m*-C*H*^{imine}), 7.22 (4H, d, *J* = 7.7, *m*-C*H*^{phenol}), 8.87 (4H, d, *J* = 4.4, 2-C*H*^{Py}). ^{13}C NMR δ 24.1 (CH(*C*H$_3$)$_2$), 26.5 (*C*H(CH$_3$)$_2$), 119.7 (*p*-*C*H^{phenol}), 122.7 (*o*-*C*H^{imine}), 123.4 (*m*-*C*^{phenol}), 123.5 (*m*-*C*H^{imine}), 124.4 (3-*C*H^{Py}), 128.3 (*p*-*C*H^{phenol}), 137.1 (*p*-*C*^{imine}), 138.1 (4-*C*H^{Py}), 149.8 (2-*C*H^{Py}), 158.5 (*ipso*-*C*^{phenol}), 158.8 (*ipso*-*C*H^{imine}). IR ν$_{max}$ (solid) 2962.0, 2869.0, 1621.0,

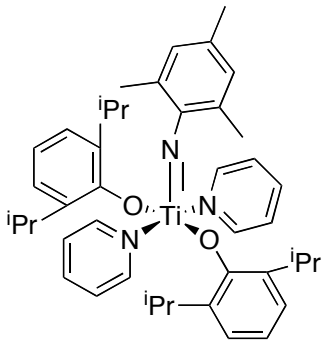
1602.7, 1494.9, 1459.1, 1433.0, 1332.1, 1259.7, 1203.9, 1093.4, 910.3 cm^{-1}. Anal. Found (Calcd for $C_{21}Cl_3H_{19}N_4Ti$): C 70.03 (70.02), H 7.03 (7.05), N 6.46 (6.12).

Bis-2,6-diisopropylphenol 4-(ethoxycarbonyl)phenylimido bispyridine titanium(IV) (259d)



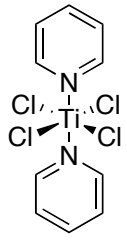
Synthesised using **General Procedure F**. To a mixture of ^{t}butylimido bispyridine bis-(2,6-diisopropylphenol) titanium(IV) (2.34 g, 3.70 mmol) was added 4-ethoxycarbonylaniline (612 mg, 3.70 mmol) to afford **259d** (1.10 g, 41%) as orange crystals. mp. 123- 124 °C. ^{1}H NMR δ 1.04 (24H, d, J = 6.8, CH(CH_3)$_2$), 1.34 (3H, t, J = 7.2, CH_3CH$_2$O), 3.88 (4H, sept, J = 6.8, CH(CH$_3$)$_2$), 4.29 (2H, q, J = 7.2, CH$_3$CH_2O), 6.35 (2H, d, J = 8.4, *o*-CH^{imine}), 6.81 (2H, t, J = 7.6, *p*-CH^{phenol}), 7.04 (4H, d, J = 7.6, *m*-CH^{phenol}), 7.36 (4H, t, J = 6.4, 3-CH^{Py}), 7.71 (2H, d, J = 6.4 , *m*-CH^{imine}), 7.79 (2H, t, J = 6.4, 4-CH^{Py}), 8.83 (4H, d_{br}, 2-CH^{Py}). ^{13}C NMR δ 14.5 (*C*H$_3$CH$_2$O), 23.7 (CH(*C*H$_3$)$_2$), 26.1 (*C*H(CH$_3$)$_2$), 60.1 (CH$_3$*C*H$_2$O), 118.8 (*p*-*C*H^{phenol}), 120.3 (*o*-*C*H^{imine}), 122.7 (*o*-*C*^{phenol}), 122.9 (*m*-*C*H^{phenol}), 124.7 (3-*C*H^{Py}), 130.4 (*m*-*C*H^{imine}), 131.6 (*ipso*-*C*^{imine}), 137.4 (4-*C*H^{Py}), 138.6 (*ipso*-*C*^{phenol}), 158.4 (2-*C*H^{Py}), 163.3 (*p*-*C*^{imine}), 167.0 (*C*=O). IR ν_{max} (solid) 2966.6, 1685.1, 1597.8, 1433.0, 1327.6, 1279.1, 1260.0, 1205.7, 900.9, 752.4, 713.2 cm^{-1}.

2,4,6-Trimethylphenylimido bis-2,6-diisopropylphenol bispyridine titanium(IV) (259c)



Synthesised using **General Procedure F**. To a mixture of ^{t}butylimido bispyridine bis-(2,6-diisopropylphenol) titanium(IV) (2.40 g, 3.80 mmol) was added 2,4-trimethylaniline (0.53 mL, 3.80 mmol) to afford **259e** (1.41 g, 53%) as pale brown solid (85% purity). ^{1}H NMR δ 0.99 (24H, d, J = 6.8, CH(CH_3)$_2$), 1.66 (6H, s, *o*-Ph(CH_3)$_2$), 2.11 (3H, s, *p*-PhCH_3), 3.83 (4H, sept, J = 6.8, CH(CH$_3$)$_2$), 6.45 (2H, s, *m*-CH^{imine}), 6.85 (2H, t, J = 7.5, *p*-CH^{phenol}), 7.09 (4H, d, J = 7.5, *m*-CH^{phenol}), 7.31 (4H, t, J = 6.5, 3-CH^{Py}), 7.77 (2H, t, J = 7.6, 4-CH^{Py}), 8.92 (4H, b$_{rs}$, 2-CH^{Py}).

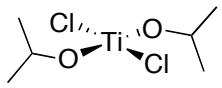
Bispyridine tetrachloro titanium(IV) (255)



To a clear solution of $TiCl_4$ (0.5 mL, 4.56 mmol) in dichloromethane (40 mL) pyridine (0.74 mL, 9.12 mmol) was added to give a pale yellow solution. After stirring for 2 h the yellow precipitate was filtered and dried *in vacuo* to afford **255** (1.23 g, 79%) as a yellow powder. ^{1}H NMR δ 7.73 - 7.79 (4H, m, 3-CH), 8.23 (2H, tt, J = 7.76, 1.7, 4-CH), 8.77 (4H, dt, J = 4.8, 1.7, *2*-CH). IR ν_{max} (solid) 3249.4, 3072.5, 1604.6, 1529.3, 1482.0,

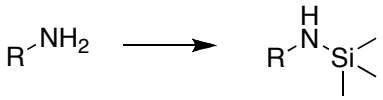
1442.5, 1352.1, 12110, 1062.7, 1041.4, 1.13.2, 752.1, 733.9. Spectroscopic data in agreement with literature.[164]

Dichloro diisopropoxide titanium(IV) (252)[131]



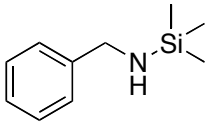
To a clear yellow solution of titanium(IV) isopropoxide (5.00 mL, 16.9 mmol) in hexane (40 mL) at 0 °C was added titanium tetrachloride (1.85 mL, 16.8 mmol) dropwise over 5 min. A white precipitate resulted after stirring for 10 min at r.t. The solid was filtered after 1 h, washed with pentane (2x20 mL) and dried under *vacuo* to afford **252** (3.89 g, 50%) as white solid. ^{1}H NMR δ 1.45 (12H, d, *J* = 6.4, CH(C*H*$_3$)$_2$), 4.88 (2H, sept, *J* = 6.4, C*H*(CH$_3$)$_2$). ^{13}C NMR δ 25.3 (CH(*C*H$_3$)$_2$), 61.0 (*C*H(CH$_3$)$_2$). Spectroscopic data in agreement with literature.

5.8 Preparation of Silyl amines



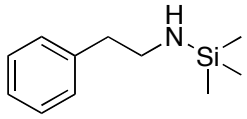
General Procedure G. To a clear solution of amine in Et$_2$O at 0 °C, was added n-butyl lithium 2.5 M in hexanes (1.5 equivalents) dropwise over 1 min to get a coloured solution. After stirring for 5 min at 0 °C and 1 h a r.t., the coloured mixture was cooled to 0 °C and TMS-Cl (2 equivalents) was added drop-wise over 1 min. After stirring for 5 min at 0 °C and 2 h at r.t. the pale brown mixture was filtered and volatile solvents were removed *in vacuo*, until a clear coloured oil was observed.

N-Trimethylsilyl benzylamine



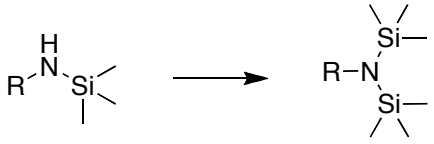
Synthesised using **General procedure G**. To a solution of benzylamine (10.0 mL, 91.3 mmol) in dry Et_2O (250 mL), was added n-BuLi 2.5 M in hexanes (54.5 mL, 137 mmol). After stirring, TMS-Cl (23.2 mL, 183 mmol) was added to afford product (12.5 g, 76%) as a yellow oil. ^{1}H NMR δ 0.11 (9H, s, Si(C*H*$_3$)$_3$), 3.95 (2H, d, *J* = 6.4, C*H*$_2$Ph), 7.15 - 7.45 (5H, m, C*H*$_{Ar}$). Spectroscopic data in agreement with literature.[165]

N-Trimethylsilyl-2-phenylethylamine



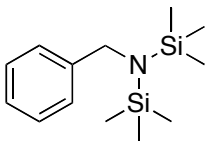
Synthesised using **General procedure G**. To a solution of 2-phenylethylamine (10.0 mL, 79.1 mmol) in dry Et_2O (250 mL), was added n-BuLi 1.6 Min hexanes (74.1 mL, 119 mmol). After stirring, TMS-Cl (20.1 mL, 158 mmol) was added to afford product (7.63 g, 44%) as a yellow oil in 88% purity. ^{1}H NMR δ 0.06 (9H, s, Si(C*H*$_3$)$_3$), 2.71 (2H, m, C*H*$_2$Ph), 2.99 (2H, m, C*H*$_2$N), 7.15 - 7.45 (5H, m, C*H*$_{Ar}$). Spectroscopic data in agreement with literature.[166]

General Procedure H.



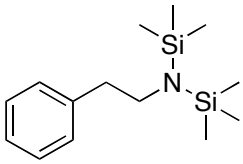
General Procedure H. To a clear solution of *N*-trimethylsilyl amine (1 equivalent) in Et_2O at 0 °C, was added n-butyllithium 2.5 M in hexanes (1.5 equivalents) dropwise over 1 min to get a coloured solution. After stirring for 5 min at 0 °C and 2 h a r.t., the coloured mixture was cooled to 0 °C and TMS-Cl (2 equivalents) was added drop-wise over 1 min. After stirring for 5 min at 0 °C and 16 h at r.t. the pale brown mixture was filtered and volatile removed *in vacuo*.

N,*N*-Bis(trimethylsilyl) benzylamine



Synthesised using **General procedure H**. To a solution of *N*-trimethlsilyl benzylamine (4.28 g, 23.9 mmol) in dry Et_2O (150 mL), was added n-BuLi 2.5 M in hexanes (16.0 mL, 35.9 mmol). After stirring, TMS-Cl (6.60 mL, 52.0 mmol) was added to afford product (3.61 g, 60%) as a brown oil. ^{1}H NMR δ 0.14 (18H, s, Si(CH_3)$_3$), 4.17 (2H, s, CH_2Ph), 7.20 - 7.35 (5H, m, CH_{Ar}). ^{13}C NMR δ 2.0 Si(*C*H$_3$)$_3$), 48.7 (*C*H$_2$Ph), 126.0 (*C*H$_{Ar}$), 126.4 (*C*H$_{Ar}$), 128.0 (*C*H$_{Ar}$), 144.4 (*ipso*-*C*$_{Ar}$). Spectroscopic data in agreement with literature.[167]

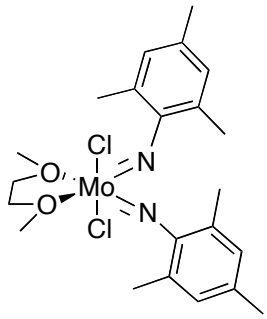
N,*N*-Bis(trimethylsilyl)-2-phenylethylamine



Synthesised using **General procedure H**. To a solution of *N*-trimethlsilyl-2-phenylethylamine (7.60 g, 39.4 mmol) in dry Et_2O (150 mL), was added n-BuLi 2.5 M in hexanes (23.6 mL, 59.1 mmol). After stirring, TMS-Cl (10.0 mL, 78.8 mmol) was added to afford product (8.34 g, 83%) as a brown oil. ^{1}H NMR δ 0.20 (18H, s, Si(CH_3)$_3$), 2.65 - 2.70 (2H, m, CH_2Ph), 2.98 - 3.04 (2H, m, CH_2N), 7.15 - 7.35 (5H, m, CH_{Ar}). ^{13}C NMR δ 2.2 (Si(*C*H$_3$)$_3$), 42.3 (*C*H$_2$Ph), 48.0 (*C*H$_2$N), 126.1 (*C*H$_{Ar}$), 128.5 (*C*H$_{Ar}$), 128.6 (*C*H$_{Ar}$), 140.4 (*ipso*-*C*$_{Ar}$). Spectroscopic data in agreement with literature.[168]

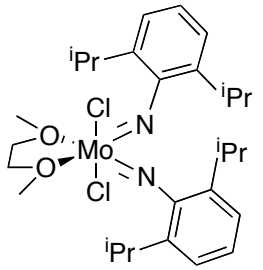
5.9 Synthesis of Molybdenum Complexes

(Bis-2,4,6-trimethylphenylimido) dichloro (1,2dimethoxyethane) molybdenum(VI) (214a)[169]



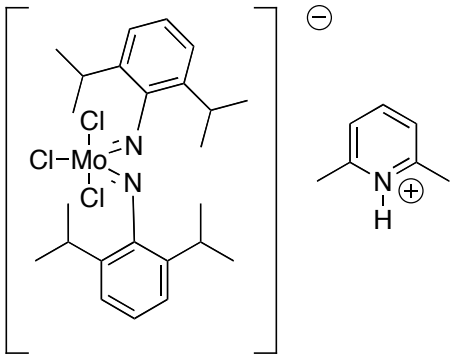
To a mixture of sodium molybdate (1.99 g, 9.69 mmol) in 1,2-dimethoxyethane (60 mL), 2,4,6-trimethylaniline (2,70 mL, 19.4 mmol) and Et_3N (3.90 mL, 38.7 mmol) were added dropwise over a period of 5 min. The mixture turned red after adding TMSCl (8.40 mL, 77.5 mmol) and was heated to reflux. A dark brown mixture appeared after refluxing for 16 h, which was cooled to r.t., filtered and washed with DME (2x20 mL). The solid was dried in *vacuo* to afford **214a** (2.23 g, 50%) as a dark red solid. mp. 179 °C. ^{1}H NMR δ 2.15 (6H, s, *p*-PhCH_3), 2.80 (12H, s, *o*-Ph(CH_3)$_2$), 3.53 (4H, s, O-CH_2), 3.57 (6H, s, O-CH_3), 6.70 (4H, s, *m*-C*H*). IR ν_{max} (solid) 1520, 1484, 1278, 1112, 1091, 1038, 949 cm^{-1}.

(Bis-2,6-diisopropylphenylimido) dichloro (1,2dimethoxyethane) molybdenum(VI) (214b)[170]



To a mixture of sodium molybdate (1.56 g, 7.60 mmol) in 1,2-dimethoxyethane (60 mL), 2,6-diisopropylaniline (2.90 mL, 15.2 mmol) and Et_3N (3.10 mL, 30.4 mmol) were added dropwise over a period of 5 min. The mixture turned red after adding TMSCl (6.60 mL, 60.8 mmol) and was then heated to reflux. A dark brown mixture appeared after refluxing for 16 h, which was cooled to r.t., filtered and washed with DME (2x20 mL). The solid was dried in *vacuo* to afford **214b** (4.53 g, 98%) as a dark red solid. mp. 191 °C. ^{1}H NMR δ 1.37 (24H, d, J = 6.5, CH(CH_3)$_2$), 3.35 (4H, s, O-CH_2), 3.50 (6H, s, O-CH_3), 4.41 (4H, sept, J = 6.5, CH(CH$_3$)$_2$), 6.98 - 7.04 (2H, m, *p*-CH_{Ar}), 7.11 - 7.16 (4H, m, *o*-CH_{Ar}). IR ν_{max} (solid) 1461, 1269, 1089, 1054, 1010, 974.

Bis-(2,6-diisopropylphenyl)imido trichloro 1-*H*-2,6-lutidine molybdenum(VI) (221)



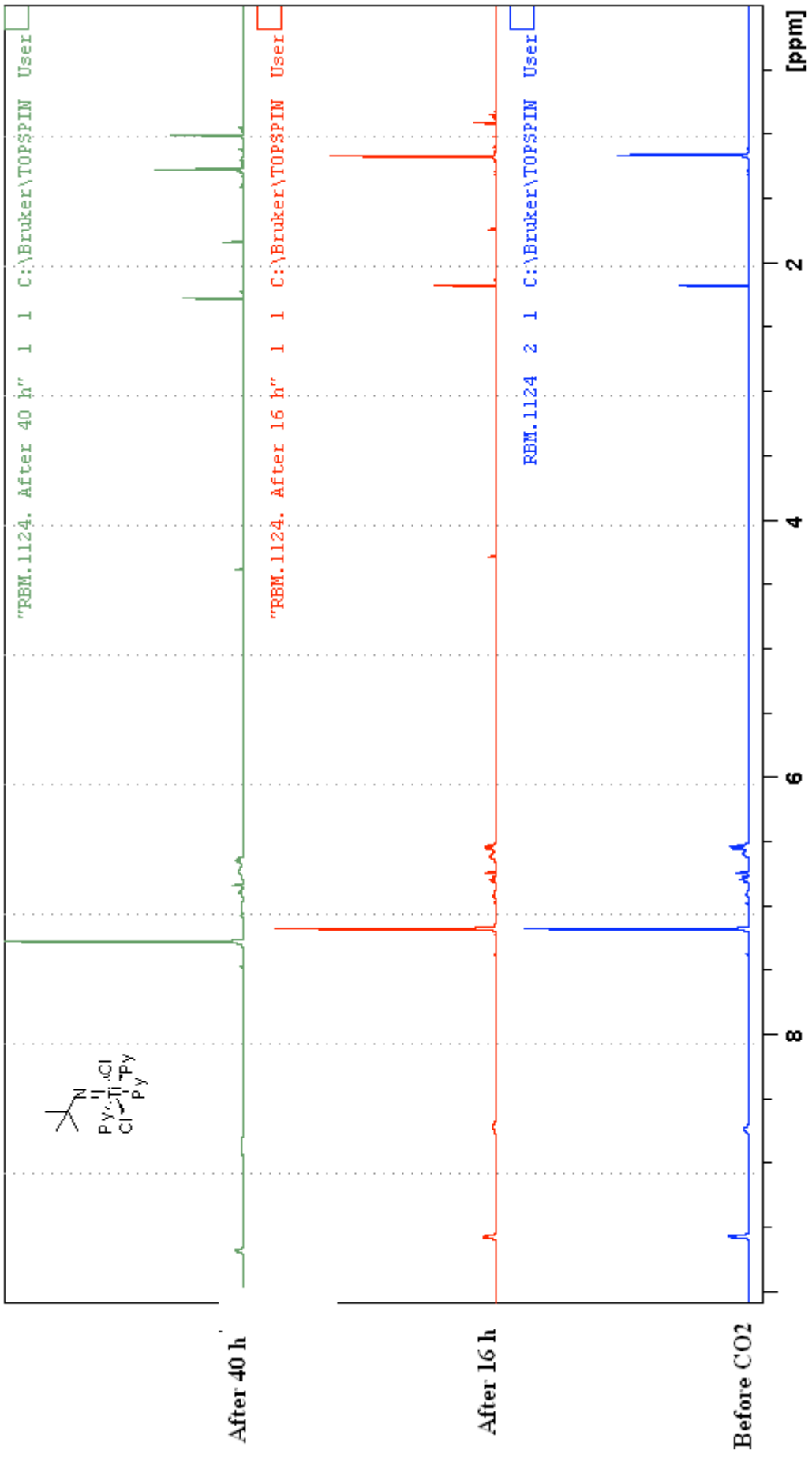
To a mixture of sodium molybdate (2.20 g, 10.7 mmol) in toluene (80 mL) at -50 °C, were added 2,6-diisopropylaniline (4.00 mL, 21.4 mmol), 2,6-lutidine (5.00 mL, 42,7 mmol) and TMSCl (6.3 mL, 50 mmol) dropwise consecutively over a period of 10 min. The dark red mixture was heated to reflux for 48 h before being filtered while still hot. The dark red solution was concentrated in *vacuo* to approximately 15 mL and pentane (40 mL) was added. The dark red solid was filtered and washed with cold toluene (40 mL) to get **221** (1.12 g, 18%) as red solid. Purification by recrystalisation from toluene afforded **221** (624 mg) a dark red crystals. mp 102 - 104 °C (deg). ^{1}H NMR δ 1.07 (24H, d, J = 6.4, CH(CH_3)$_2$), 3.00 (6H, s, *o*-CH_3^{Lut}), 3.82 (4H, sept, J = 6.4, CH(CH$_3$)$_2$), 7.01 - 7.12 (6H, m, CH_{Ar}^{imine}), 7.48 (2H, d, J = 8.0, 3-CH^{Lut}), 8.14 (1H, t, J = 8.0, 4-CH^{Lut}). ^{13}C NMR δ 24.1, 28.3, 117.4, 122.4, 124.7, 127.7, 145.1, 153.9. Missing 3 carbons. IR ν_{max} (solid) 3059.5, 2962.4, 1639.1, 1624.0, 1582.8, 1462.3, 1259.8, 1221.1,

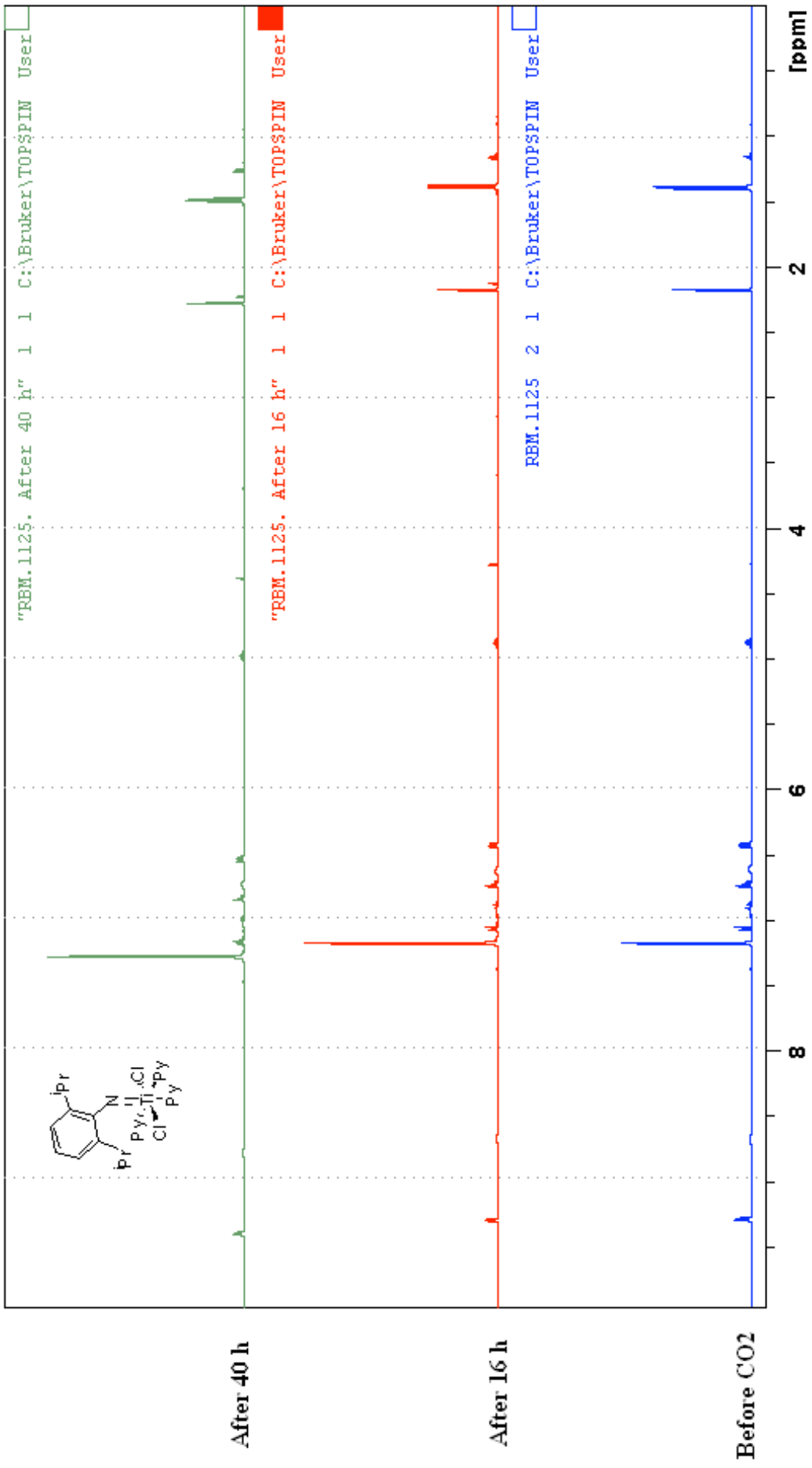
1174.2, 1097.2, 1046.0, 960.9 cm^{-1}. ESI/MS: *m/z* 662.17 (M^+, 14%). HRMS: found (calcd for $C_{31}H_{44}N_3Cl_3Mo$) m/z 662.1772 (662.1717).

5.10 Appendices

5.10.1.- NMR Experiments

In this section are shown the ^1H NMR of the experiments in section 4.2.1.2.


"RBM.1124. After 40 h" 1 1 C:\Bruker\TOPSPIN User
"RBM.1124. After 16 h" 1 1 C:\Bruker\TOPSPIN User
RBM.1124 2 1 C:\Bruker\TOPSPIN User
[ppm]
2
4
6
8
After 40 h
After 16 h
Before CO2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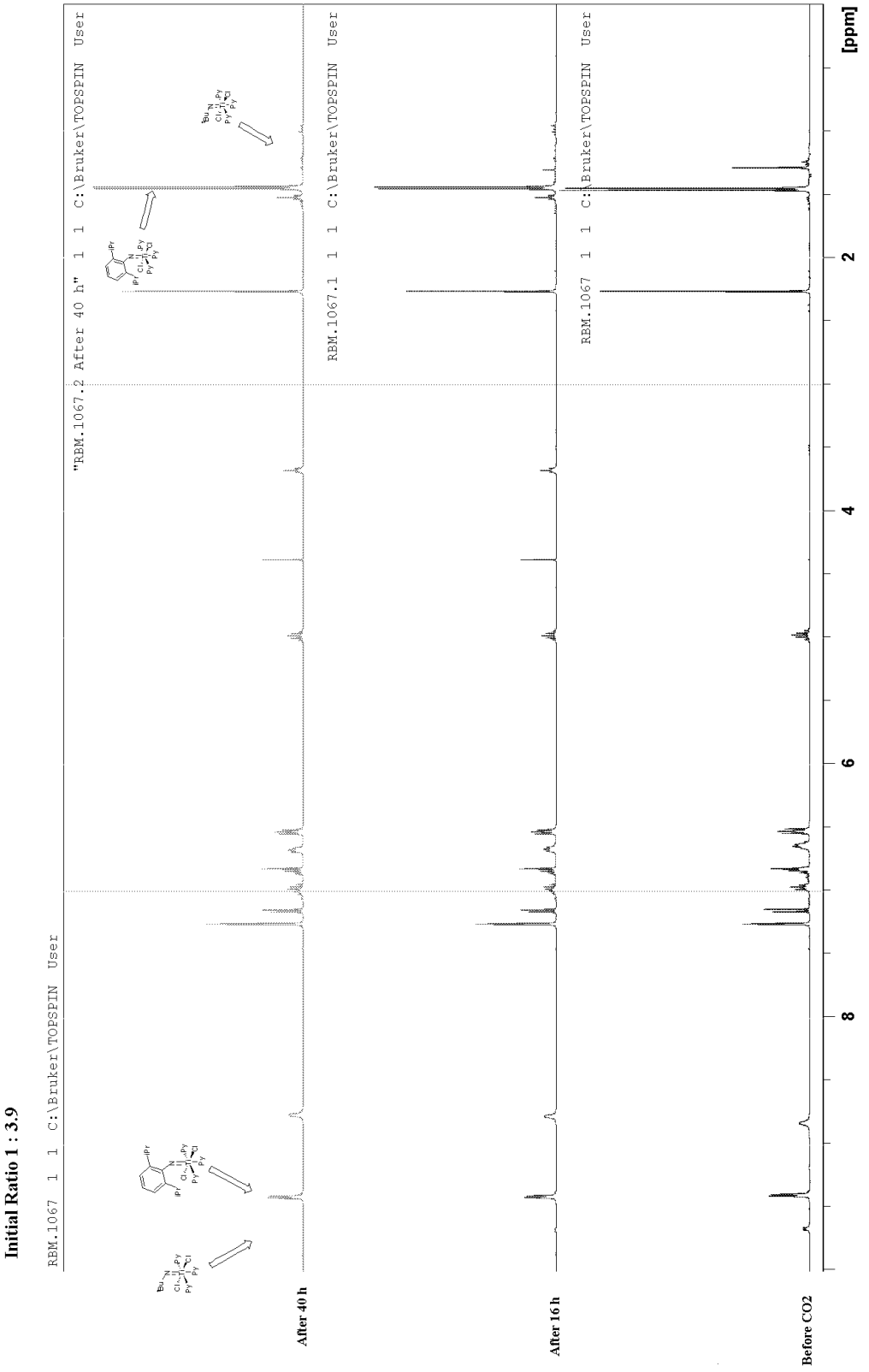
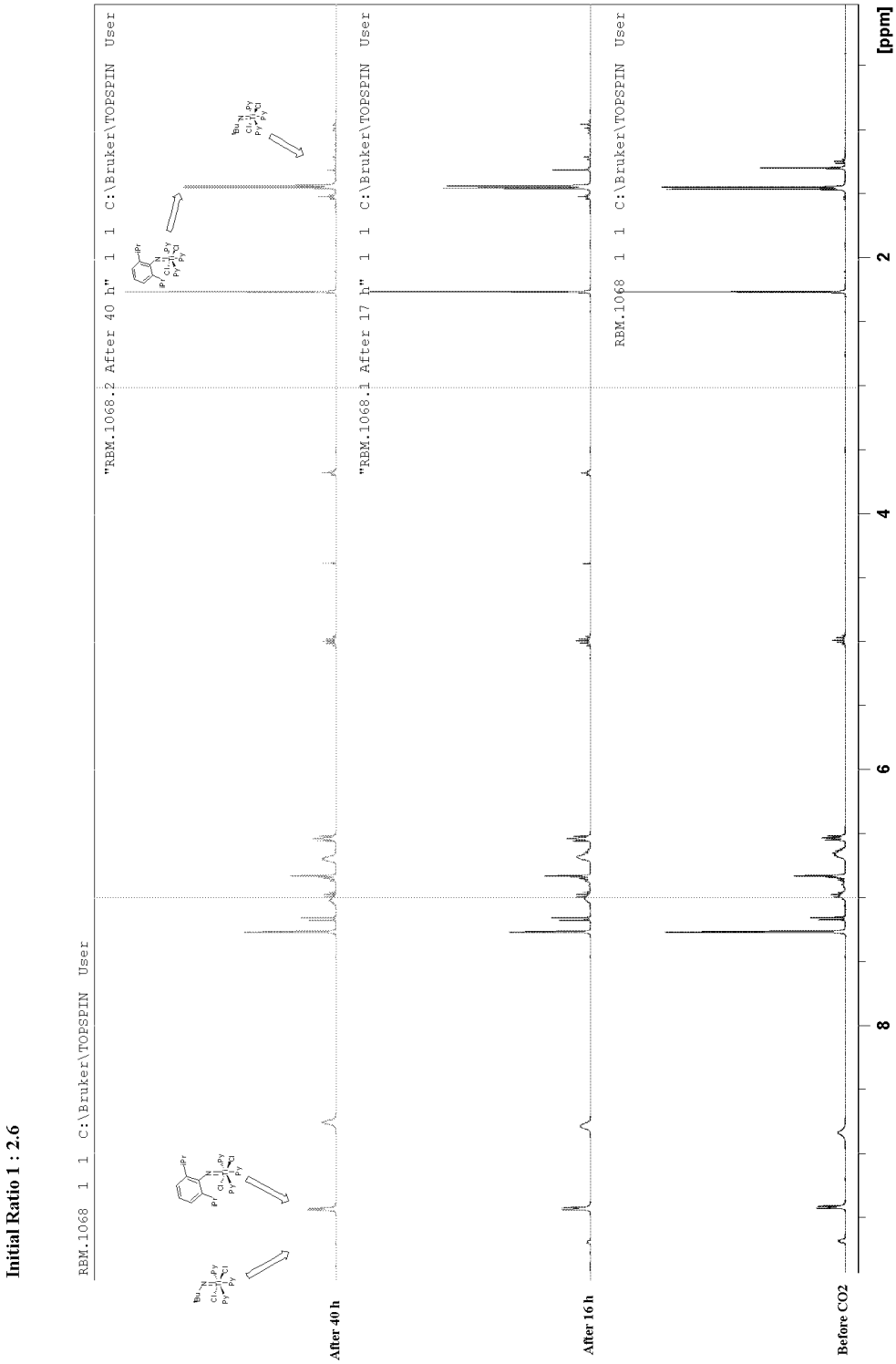
"RBM.1125. After 16 h" 1 1 C:\Bruker\TOPSPIN User
RBM.1125 2 1 C:\Bruker\TOPSPIN User
[ppm]
2
4
6
8
After 40 h
After 16 h
Before CO2


Initial Ratio 1 : 3.9
RBM.1067 1 1 C:\Bruker\TOPSPIN User
"RBM.1067.2 After 40 h" 1 1 C:\Bruker\TOPSPIN User
RBM.1067.1 1 1 C:\Bruker\TOPSPIN User
RBM.1067 1 1 C:\Bruker\TOPSPIN User
After 40 h
After 16 h
Before CO2
8
6
4
2
[ppm]


Initial Ratio 1 : 2.6
RBM.1068 1 1 C:\Bruker\TOPSPIN User
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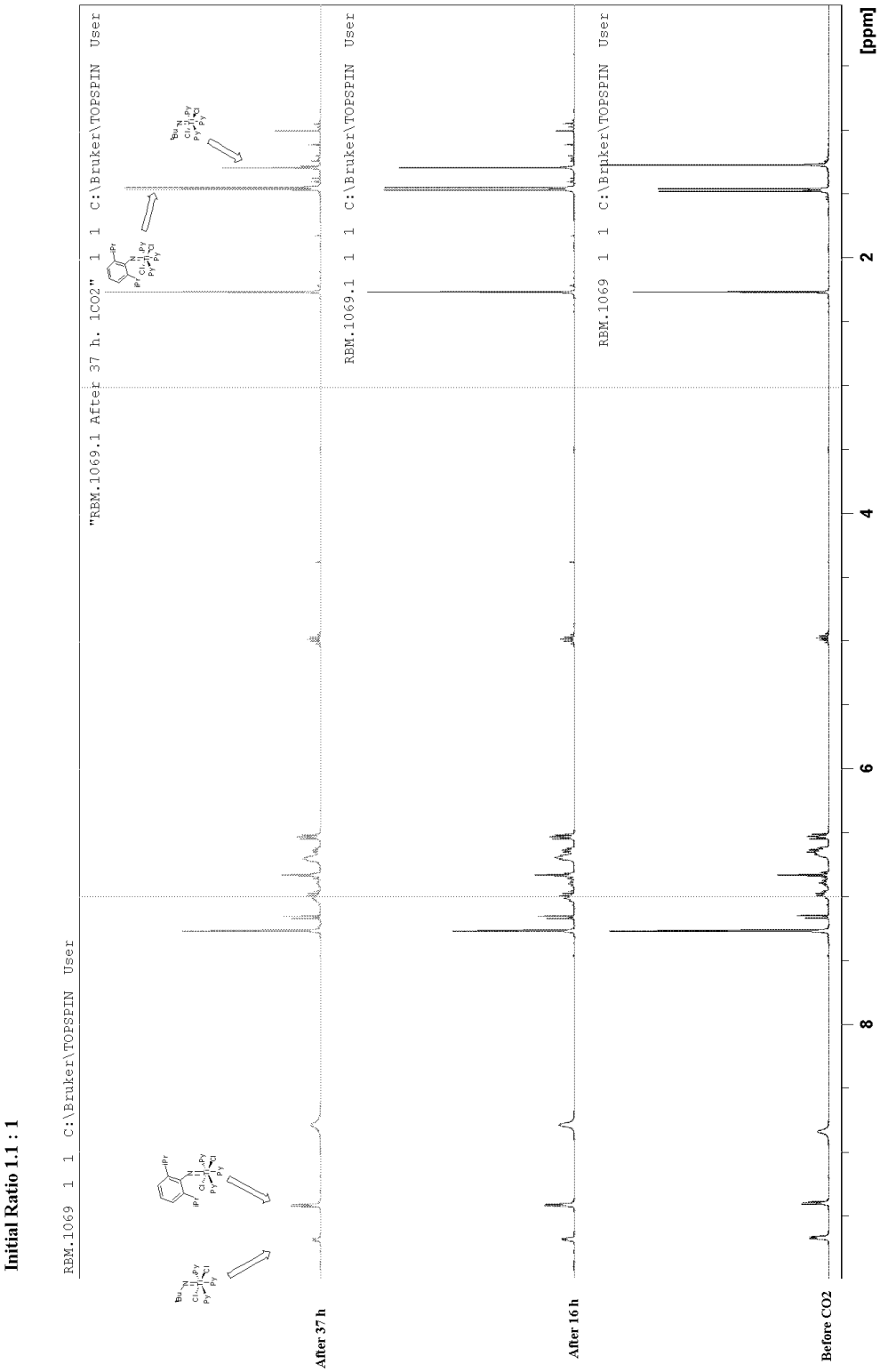
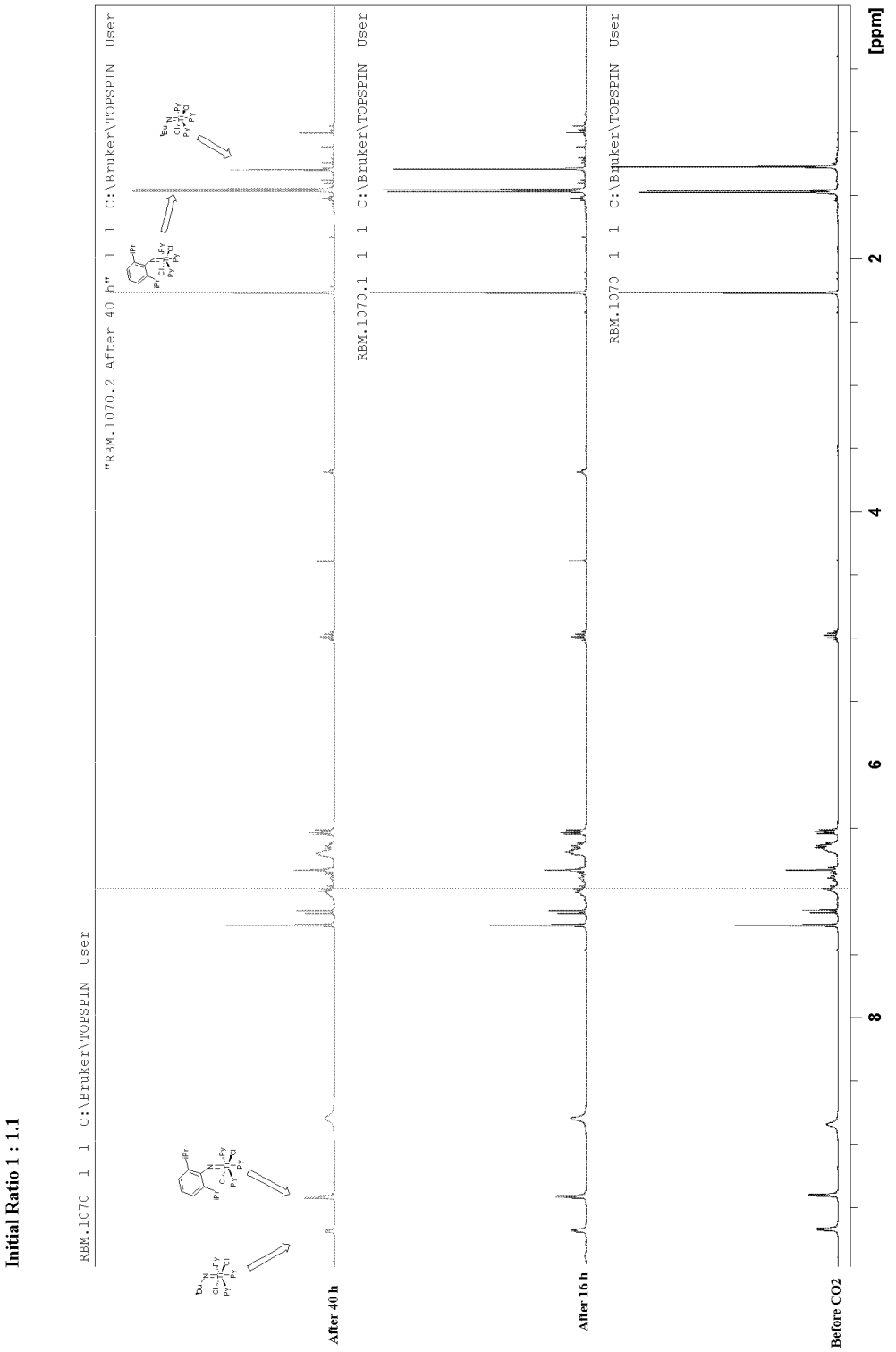
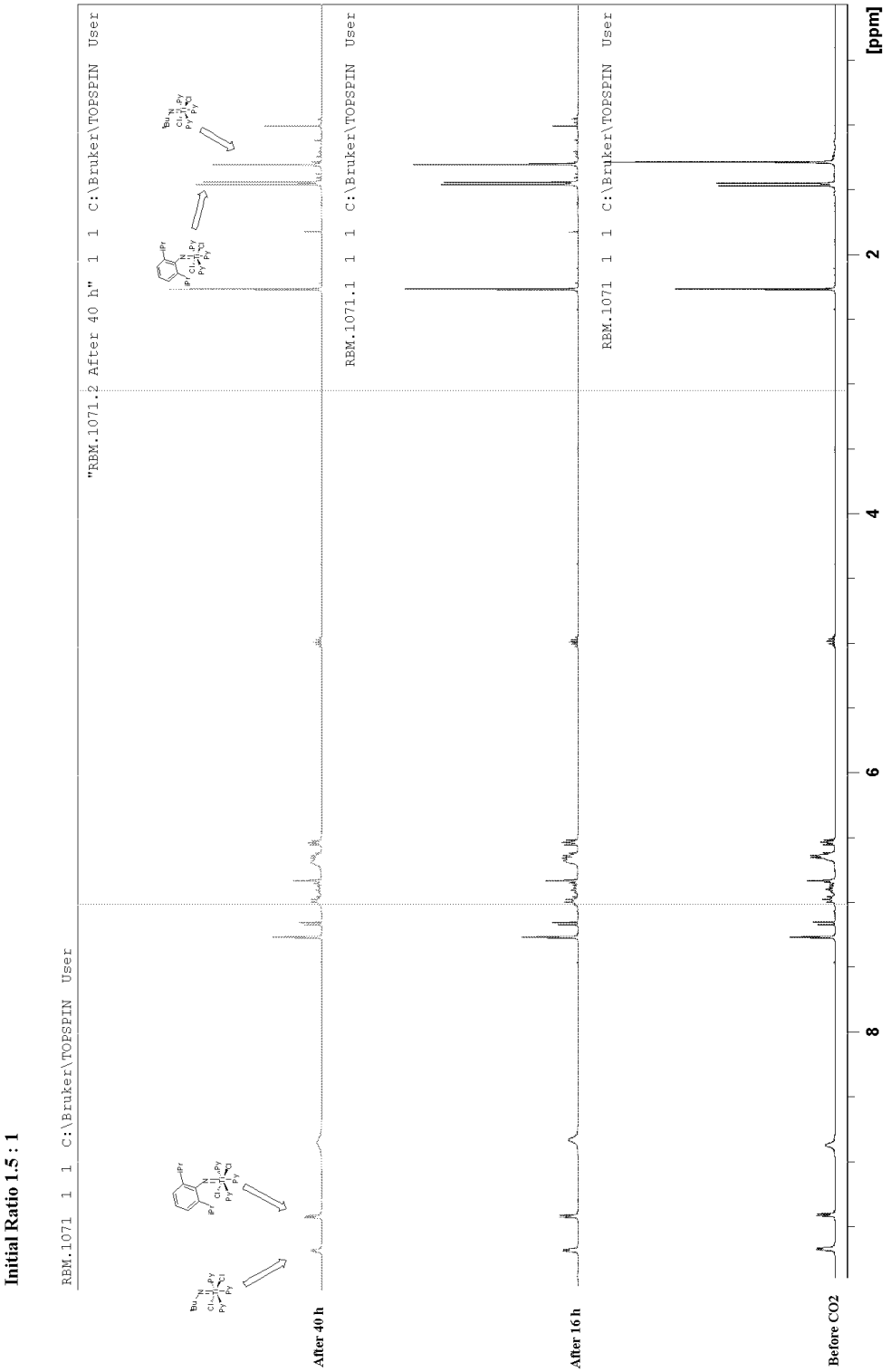
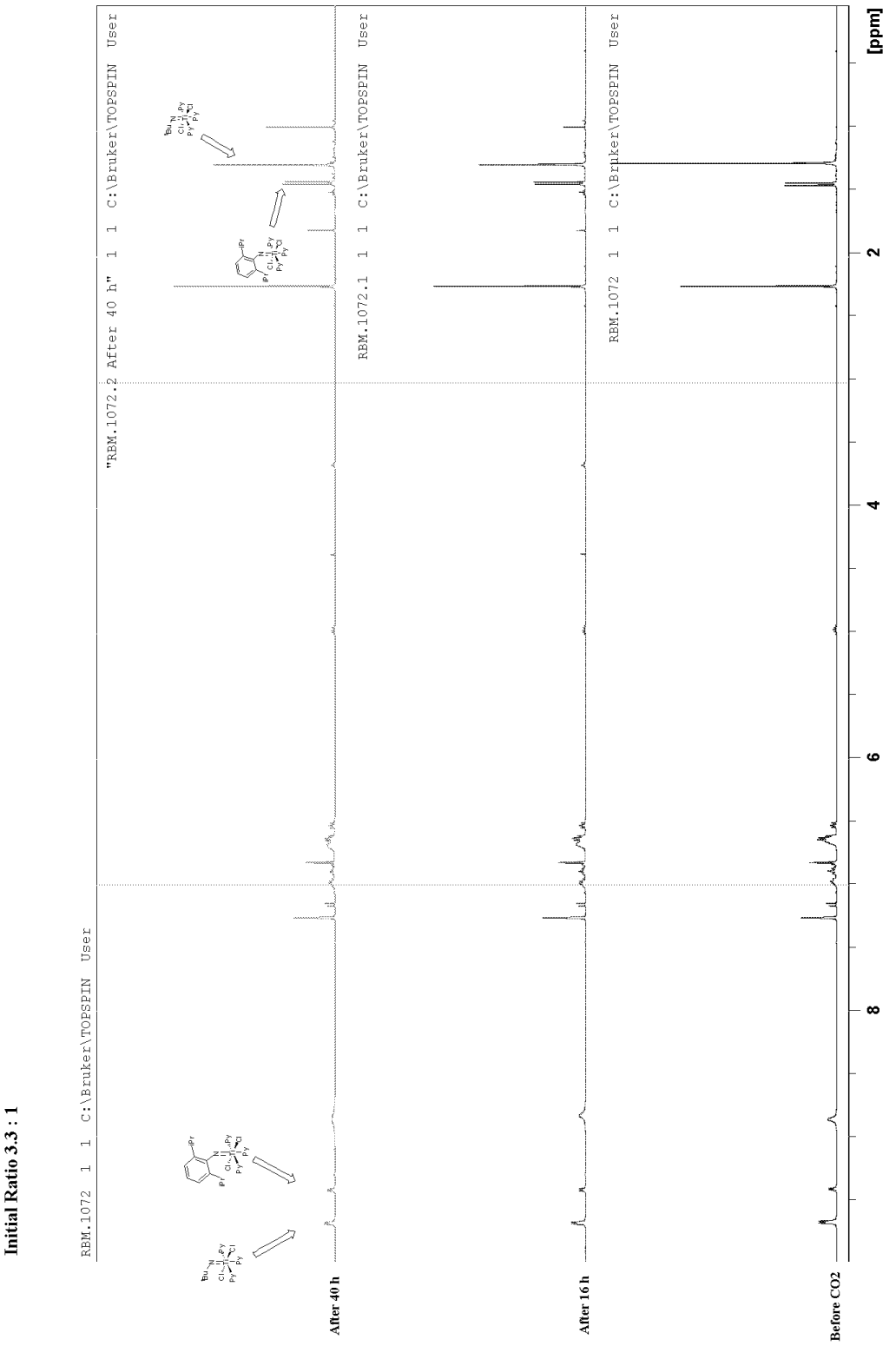
"RBM.1068.1 After 17 h" 1 1 C:\Bruker\TOPSPIN User
RBM.1068 1 1 C:\Bruker\TOPSPIN User
After 40 h
After 16 h
Before CO2
8
6
4
2
[ppm]


Initial Ratio 1.1 : 1
RBM.1069 1 1 C:\Bruker\TOPSPIN User
"RBM.1069.1 After 37 h. 1CO2" 1 1 C:\Bruker\TOPSPIN User
RBM.1069.1 1 1 C:\Bruker\TOPSPIN User
RBM.1069 1 1 C:\Bruker\TOPSPIN User
After 37 h
After 16 h
Before CO2
8
6
4
2
[ppm]


Initial Ratio 1 : 1.1
RBM.1070 1 1 C:\Bruker\TOPSPIN User
"RBM.1070.2 After 40 h" 1 1 C:\Bruker\TOPSPIN User
RBM.1070.1 1 1 C:\Bruker\TOPSPIN User
RBM.1070 1 1 C:\Bruker\TOPSPIN User
After 40 h
After 16 h
Before CO2
8
6
4
2
[ppm]


Initial Ratio 1.5 : 1
RBM.1071 1 1 C:\Bruker\TOPSPIN User
"RBM.1071.2 After 40 h" 1 1 C:\Bruker\TOPSPIN User
RBM.1071.1 1 1 C:\Bruker\TOPSPIN User
RBM.1071 1 1 C:\Bruker\TOPSPIN User
After 40 h
After 16 h
Before CO2
8
6
4
2
[ppm]


Initial Ratio 3.3 : 1
RBM.1072 1 1 C:\Bruker\TOPSPIN User
"RBM.1072.2 After 40 h" 1 1 C:\Bruker\TOPSPIN User
RBM.1072.1 1 1 C:\Bruker\TOPSPIN User
RBM.1072 1 1 C:\Bruker\TOPSPIN User
After 40 h
After 16 h
Before CO2
8
6
4
2
[ppm]

5.10.2.- X-ray Crystallographic Data

4-Chlorophenylimine bis-2,6-diisopropylphenol bispyridine titanium(IV) (259c)

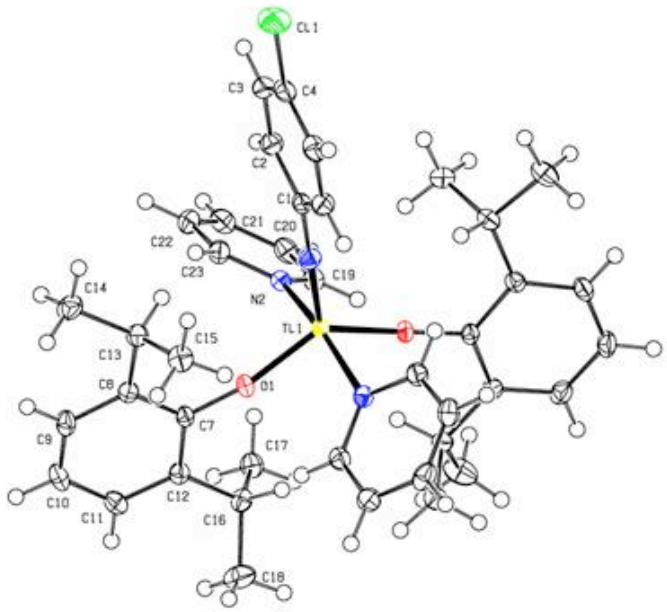


Table 5.1: Crystal data and structure refinement at 90(2)K.

Empirical formula	C40 H48 Cl N3 O2 Ti
Formula weight	686.16
Crystal description	ORANGE BLOCK
Crystal size	0.53 x 0.52 x 0.46 mm
Crystal system	Monoclinic
Space group	C 2/c
Unit cell dimensions	a = 13.4745(7) A alpha = 90 deg.
	b = 15.0657(8) A beta = 106.602(1) deg.
	c = 18.5721(10) A gamma = 90 deg.
Volume	3613.0(3) A^3
Reflections for cell refinement	10392
Range in theta	2.58 to 27.54 deg.

Z 4

Density (calculated) 1.261 Mg/m^3

Absorption coefficient 0.349 mm^-1

F(000) 1456

Diffractometer type Bruker SMART APEX CCD area detector

Wavelength 0.71073 A

Scan type \w

Reflections collected 12924

Theta range for data collection 2.29 to 27.55 deg.

Index ranges -17<=h<=17, -19<=k<=19, -22<=l<=24

Independent reflections 4159 [R(int) = 0.0190]

Observed reflections 3874 [I>2I\s(I)]

Absorption correction Semi-empirical from equivalents (Tmin = 0.678, Tmax = 0.746)

Decay correction 0%

Structure solution by direct and difmap methods

Hydrogen atom location geom, Me from diffmap

Hydrogen atom treatment constr

Data / restraints / parameters 4159/0/219 (least-squares on F^2)

Final R indices [I>2sigma(I)] R1 = 0.0321, wR2 = 0.0850

Final R indices (all data) R1 = 0.0344, wR2 = 0.0865

Goodness-of-fit on F^2 1.021

Final maximum delta/sigma 0.000

Weighting scheme

calc w=1/[\s^2^(Fo^2^)+(0.0430P)^2^+3.5639P] where P=(Fo^2^+2Fc^2^)/3

Largest diff. peak and hole 0.331 and -0.285 e.A^-3

Table 5.2: Relevant bond lengths [A] and angles for tipyno.

Ti1-N1 1.7268(14)

Ti1-O1 1.8717(8)

Ti1-O1#1 1.8717(8)

Ti1-N2 2.2309(10)

Ti1-N2#1 2.2309(10)

C1-N1	1.370(2)
O1-C7	1.3428(13)
N2-C19	1.3461(15)
N2-C23	1.3463(15)

N1-Ti1-O1	113.84(3)
N1-Ti1-O1#1	113.84(3)
O1-Ti1-O1#1	132.33(5)
N1-Ti1-N2	96.67(3)
O1-Ti1-N2	87.54(4)
O1#1-Ti1-N2	87.08(4)
N1-Ti1-N2#1	96.67(3)
O1-Ti1-N2#1	87.08(4)
O1#1-Ti1-N2#1	87.54(4)
N2-Ti1-N2#1	166.66(5)
N1-C1-C2#1	121.10(8)
N1-C1-C2	121.10(8)
C1-N1-Ti1	180.0
C7-O1-Ti1	168.94(8)
O1-C7-C12	118.74(10)
O1-C7-C8	120.23(10)
C19-N2-C23	117.50(11)
C19-N2-Ti1	124.84(8)
C23-N2-Ti1	117.66(8)
N2-C19-C20	122.77(11)
N2-C19-H19A	118.6
N2-C23-C22	122.99(12)
N2-C23-H23A	118.5

Trichloro bis-(2,6-diisopropylphenyl)imido 1-*H*-2,6-lutidine molybdenum (VI) (221)

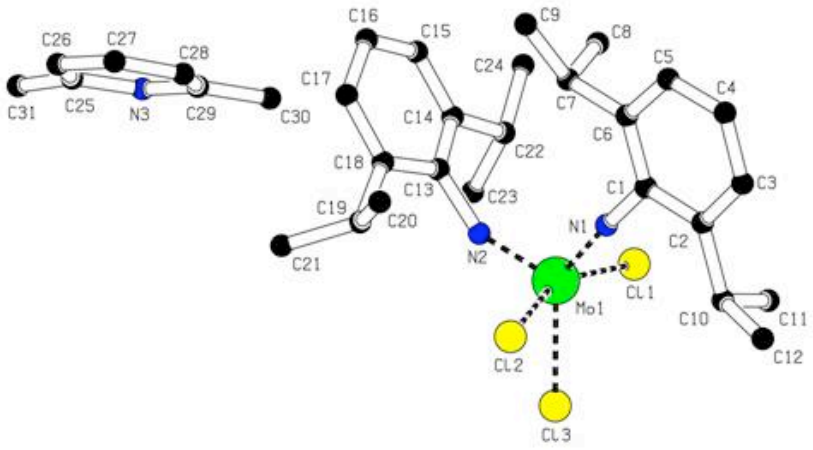


Table 5.3: Crystal data and structure refinement for MOIMCL at 150(2)K.

Empirical formula	C31 H43 Cl3 Mo N3
Formula weight	659.97
Crystal description	red column
Crystal size	0.32 x 0.11 x 0.10 mm
Crystal system	Monoclinic
Space group	P 21
Unit cell dimensions	a = 10.1461(13) A alpha = 90 deg.
	b = 15.959(2) A beta = 92.619(2) deg.
	c = 10.1550(13) A gamma = 90 deg.
Volume	1642.6(6) A^3
Reflections for cell refinement	8184
Range in theta	2.4 to 27.3 deg.
Z	2
Density (calculated)	1.334 Mg/m^3

Absorption coefficient 0.667 mm^-1

F(000) 686

Diffractometer type Bruker SMART1000 CCD area detector

Wavelength 0.71073 A

Scan type omega

Reflections collected 19240

Theta range for data collection 2.01 to 26.41 deg.

Index ranges -13<=h<=13, -20<=k<=20, -13<=l<=13

Independent reflections 6709 [R(int) = 0.033]

Observed reflections 6202 [I>2sigma(I)]

Absorption correction Semi-empirical from equivalents (Tmin = 0.858, Tmax = 1.000)

Decay correction none

Structure solution by direct and difference Fourier methods

Hydrogen atom location sp2-bound Me H from delta-F; others placed geometrically

Hydrogen atom treatment rigid rotor; riding model

Data / restraints / parameters 6673/3/345 (least-squares on F^2)

Final R indices [I>2sigma(I)] R1 = 0.0702, wR2 = 0.189

Final R indices (all data) R1 = 0.0752, wR2 = 0.195

Goodness-of-fit on F^2 1.04

Absolute structure parameter 0.08(8)

Final maximum delta/sigma 0.001

Weighting scheme

calc w=1/[\s^2^(Fo^2^)+(0.138P)^2^+5.384P] where P=(Fo^2^+2Fc^2^)/3

Largest diff. peak and hole 5.49 and -0.91 e.A^-3

Table 5.4: relevant bond lengths [A], angles and torsions [deg] for MOIMCL.

Mo1-N1 1.748(5)

Mo1-N2 1.763(6)

Mo1-Cl1 2.3886(19)

Mo1-Cl3 2.4522(18)

Mo1-Cl2 2.4538(19)

N1-C1 1.381(8)

N2-C13	1.414(10)
N1-Mo1-N2	109.2(3)
N1-Mo1-Cl1	93.8(2)
N2-Mo1-Cl1	100.7(2)
N1-Mo1-Cl3	138.8(2)
N2-Mo1-Cl3	111.7(2)
Cl1-Mo1-Cl3	83.09(7)
N1-Mo1-Cl2	86.2(3)
N2-Mo1-Cl2	101.2(2)
Cl1-Mo1-Cl2	156.88(7)
Cl3-Mo1-Cl2	81.84(6)
C1-N1-Mo1	173.7(8)
N1-C1-C2	118.2(7)
N1-C1-C6	119.5(7)
C13-N2-Mo1	149.5(5)
C29-N3-C25	124.1(7)
C14-C13-N2	120.1(7)
C18-C13-N2	117.4(7)
N3-C25-C31	115.9(8)
N3-C29-C28	118.0(8)
N3-C29-C30	116.6(8)
N2-Mo1-N1-C1	125(4)
Cl1-Mo1-N1-C1	-132(4)
Cl3-Mo1-N1-C1	-49(5)
Cl2-Mo1-N1-C1	24(4)
Mo1-N1-C1-C2	49(5)
Mo1-N1-C1-C6	-130(4)
N1-Mo1-N2-C13	3.1(11)
Cl1-Mo1-N2-C13	-94.8(10)
Cl3-Mo1-N2-C13	178.5(10)
Cl2-Mo1-N2-C13	92.9(11)

N1-C1-C2-C3	179.6(8)
N1-C1-C2-C10	2.5(12)
N1-C1-C6-C5	179.9(8)
N1-C1-C6-C7	-3.7(13)
Mo1-N2-C13-C14	87.3(12)
Mo1-N2-C13-C18	-94.7(12)
N2-C13-C14-C15	-172.3(7)
N2-C13-C14-C22	8.7(11)
N2-C13-C18-C17	174.0(8)
N2-C13-C18-C19	-6.9(13)
C29-N3-C25-C26	0.2(13)
C29-N3-C25-C31	-177.8(9)
N3-C25-C26-C27	-0.5(14)
C25-N3-C29-C28	1.4(13)
C25-N3-C29-C30	-179.0(8)
C27-C28-C29-N3	-2.7(14)

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