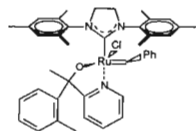
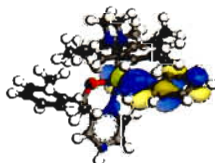
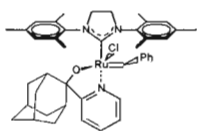
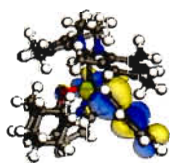


Modelling and synthesis of Grubbs-type complexes with hemilabile ligands

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Year : 2009



Modelling and synthesis of Grubbs-type complexes with hemilabile ligands

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Summary

Metathesis is a valuable method for the production of new alkenes and in the last 50 years a lot of catalytic systems for alkene metathesis were developed. In an earlier study, a Grubbs 2-type of catalyst was developed, which contained a N⁺O hemilabile ligand with two aromatic R groups. This catalyst, which is called the Puk-Grubbs 2 pre-catalyst, showed an increase in stability, activity, selectivity and a longer lifetime in a 1-octene self-metathesis reaction in comparison to Grubbs 2. In order to improve these properties even further, variation in R groups of these ligands were investigated by theoretical and experimental means.

By using the molecular modelling program Material Studio, 202 possible hemilabile ligands were investigated. During the first screening the HOMO, LUMO and electron density with electrophilic Fukui function of the ligands were compared to the diphenyl alcohol of the Puk-Grubbs 2 catalyst and 42 ligands showed similar electronic and steric properties. In the second screening, the HOMO, LUMO and electron density with nucleophilic Fukui function of these ligands, when coordinated to a simplified Grubbs 2 pre-catalyst, were again compared to the simplified Puk-Grubbs 2. From these results, 5 ligands were chosen to investigate experimentally from which 3 ligands showed similar electronic properties to the Puk-Grubbs 2 catalyst. The other two ligands were chosen to see what influence their bulky R groups have on the coordination of the ligand to Grubbs 2 as well as on the activity during a metathesis reaction.

All five ligands could be synthesized according to methods from literature. One was obtained in a very low yield (16%). They were characterized by MS, IR and NMR. Due to the bulkiness and steric hindrance, two ligands could not be coordinated to Grubbs 2 catalyst, but the other three complexes were synthesized in a relatively good yield. Because the three synthesized complexes were sensitive to air, these were only characterized by MS and NMR. These results correlated well with the modelling results.

The three synthesized complexes were found to be active for 1-octene metathesis reactions. Only one synthesized complex showed a similar selectivity to that of the Puk-Grubbs 2 catalyst. However, a much longer lifetime and higher turnover number was observed for all three complexes. An increase in temperature and higher catalyst load showed an increase in activity. It was also found that with a higher activity, the selectivity of the synthesized complexes decreased.

Samevatting

Metatese is 'n waardevolle metode vir die bereiding van nuwe alkene en in die laaste 50 jaar is baie katalitiese sisteme vir alkeen metatese ontwikkel. In 'n vroeër studie is 'n Grubbs 2-tipe katalisator ontwikkel, wat 'n hemilabiele N^+O ligand met twee aromatiese R groepe bevat. Hierdie katalisator, Puk-Grubbs 2 pre-katalisator, het in vergelyking met Grubbs 2 'n toename in stabiliteit, aktiwiteit, selektiwiteit en 'n langer lewensduur gewys in 'n 1-okteen self-metatese reaksie. In 'n poging om hierdie eienskappe verder te verbeter is verskeie R groepe van hierdie ligande ondersoek op teoreties en eksperimentele vlak.

Deur gebruik te maak van die molekulemodelleringsprogram Material Studio, is 202 moontlike hemilabiele ligande ondersoek. Tydens die eerste sifting is die HOMO, LUMO en elektrondigtheid met elektrofiliese Fukui funksie van die ligande met die difenielalkohol van die Puk-Grubbs 2 katalisator vergelyk en 42 ligande het vergelykbare elektroniese en steriese eienskappe vertoon. Tydens die tweede sifting is die HOMO, LUMO en elektrondigtheid met nukleofiliese Fukui funksie van hierdie ligande na koördinering met vereenvoudigde Grubbs 2 katalisator met 'n vereenvoudigde Puk-Grubbs 2 katalisator vergelyk. Uit hierdie resultate is 5 ligande, waarvan 3 ligande soortgelyke elektroniese eienskappe as Puk-Grubbs 2 katalisator vertoon, gekies om eksperimenteel ondersoek te word. Die ander twee ligande is gekies om die invloed van hulle groot R groepe te ondersoek op die koördinasie van die ligande aan Grubbs 2 asook die aktiwiteit in 'n metatesereaksie.

Al vyf ligande kon volgens literatuurmetodes gesintetiseer word. Een is in 'n baie lae opbrengs verkry (16%). Hulle is met behulp van MS, IR en KMR gekarakteriseer. As gevolg van grootheid en steriese hindering kon twee van die ligande nie aan die Grubbs 2 katalisator gekoördineer word nie, maar die ander drie komplekse is verkry in 'n relatiewe goeie opbrengs. Die drie gesintetiseerde komplekse is gevoelig vir lug, daarom is hulle net met MS en KMR gekarakteriseer. Hierdie resultate stem goed ooreen met die modelleringsresultate.

Al drie die gesintetiseerde komplekse is aktief vir 'n 1-okteen metatese reaksie. Net een gesintetiseerde kompleks het 'n soortgelyke selektiwiteit as die Puk-Grubbs 2 katalisator getoon. Alhoewel, 'n baie langer leeftyd asook 'n hoër omskakelingsgetal (TON) vir al drie komplekse is verkry. Met toename in reaksietemperatuur en katalisator lading is 'n toename in aktiwiteit getoon. Daar is ook gevind dat met 'n hoër aktiwiteit, die selektiwiteit van die gesintetiseerde komplekse afneem.

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List of abbreviations and numbering of structures

General abbreviations

ACM	:	Acyclic cross metathesis
ADMET	:	Acyclic diene metathesis
DFT	:	Density functional theory
G	:	Gaussian functions
GGA	:	Generalized gradient application
HOMO	:	Highest occupied molecular orbital
IP	:	Isomerisation product
L	:	Ligand
LCMO	:	Linear combination of molecular orbitals
LDA	:	Local density approximation
LUMO	:	Lowest unoccupied molecular orbital
M	:	Transition metal M
MME	:	Molecular mechanics energy
O [^] N	:	Bidentate ligand coordinated to a metal at O and N
PMP	:	Primary metathesis product
R ¹ R ² C=	:	Carbene group
RCM	:	Ring-closing metathesis
ROM	:	Ring-opening metathesis
ROMP	:	Ring-opening metathesis polymerization
S	:	Selectivity
SMP	:	Secondary metathesis product
STO	:	Slater type of orbitals
TON	:	Turnover number
X	:	Halogen atom
Ψ	:	Wavefunction

Abbreviations of chemicals

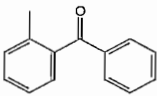
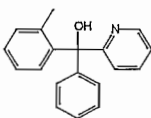
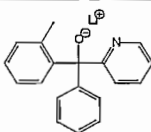
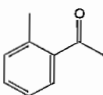
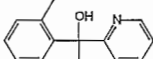
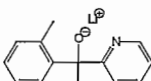
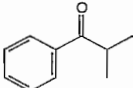
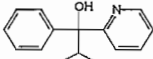
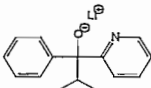
C _x	:	X indicates the carbon chain length
Cy	:	Cyclohexyl
H ₂ IMES:	:	1,3-bis-(2,4,6-trimethylphenyl)-2-imidazolindinylidene
Me	:	Methyl
NHC	:	N-heterocyclic carbene
OTs	:	Toluene sulphonate

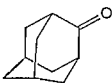
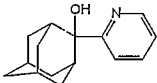
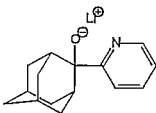
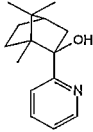
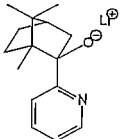
PCy ₃	:	Tricyclohexyl phosphine
Ph	:	Phenyl
THF	:	Tetrahydrofuran

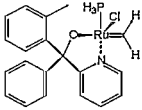
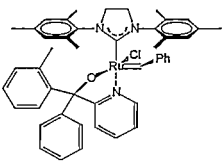
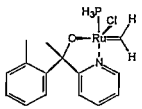
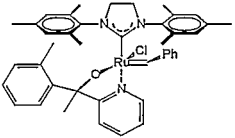
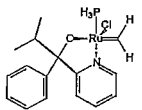
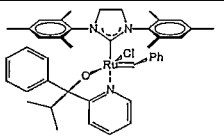
Abbreviations of characterization methods

GC	:	Gas chromatography
IR	:	Infrared spectroscopy
MS	:	Mass spectroscopy
TLC	:	Thin layer chromatography
X NMR	:	Nuclear magnetic resonance of X where X = H (Proton), C (Carbon) or P (Phosphorus)

Numbering of structures related to the 5 investigated complexes

Ketones	Alcohols	Lithium salts
 10	 15	 20
 11	 16	 21
 12	 17	 22

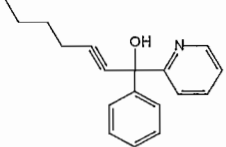
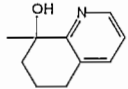
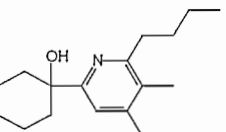
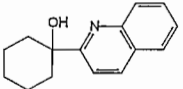
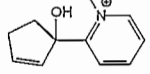
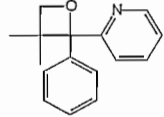
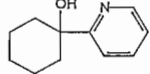
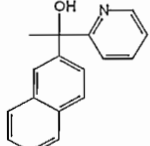
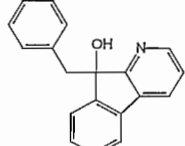
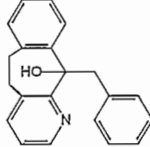
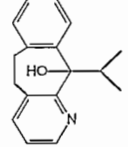
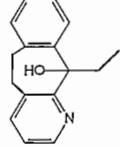
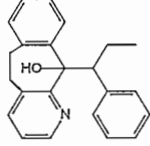
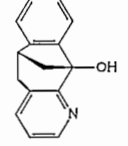
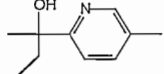
Ketones	Alcohols	Lithium salts
 13	 18	 23
 14	 19	 24

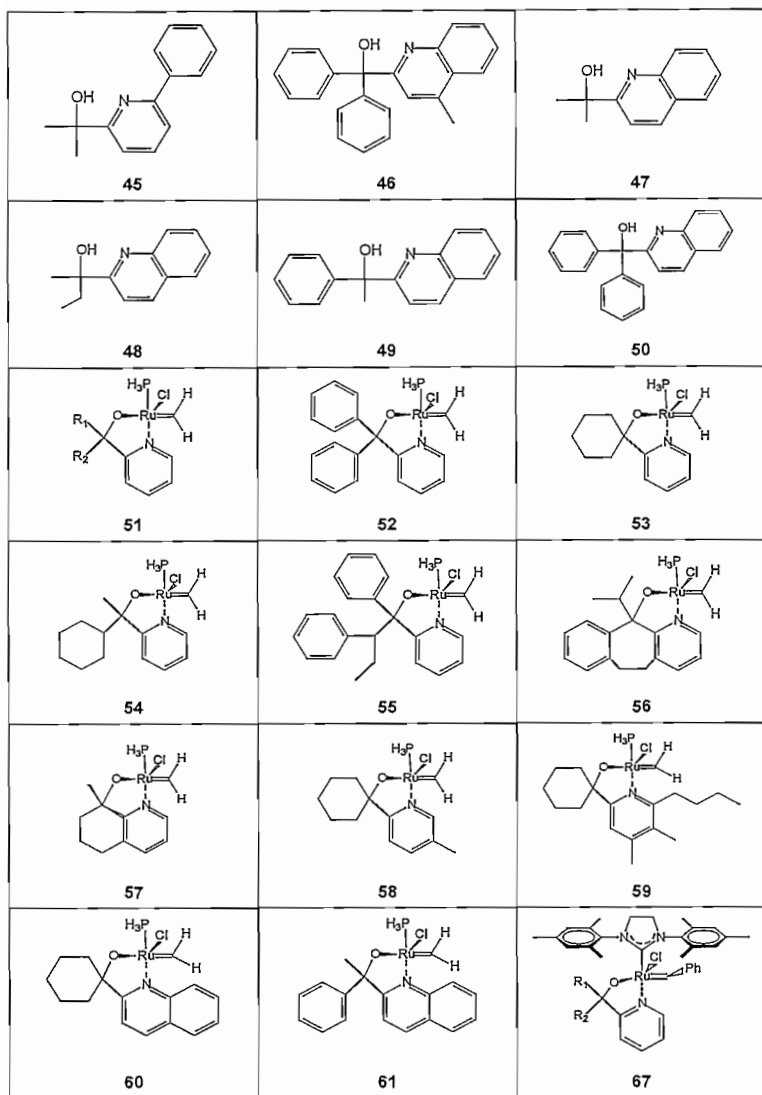
Simplified complexes	Complexes
 62	 25
 63	 26
 64	 27

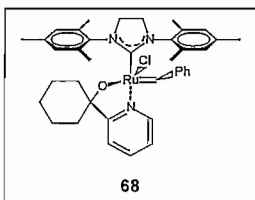
Simplified complexes	complexes
65	28
66	29

Numbering of other structures

1	2	3
4	5	6
7	8	9

 30	 31	 32
 33	 34	 35
 36	 37	 38
 39	 40	 41
 42	 43	 44





Chapter 1: Introduction and project aims

1.1 Introduction

Metathesis, which comes from the Greek words Meta (μετά), which means change, and Thesis (θέσις), which means position^{[1][2]}, describes an interchange of atoms between two molecules. Since Eleuterio^{[3][4]} obtained a low yield propene-ethene copolymer from propene using a molybdenum catalytic system, a growing interest in the field of alkene metathesis was observed.

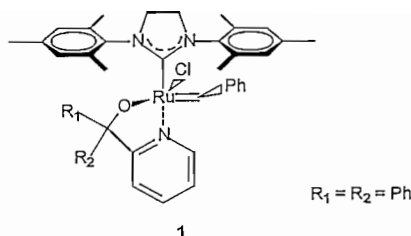
In the last decade several investigations were conducted, which led to a better understanding of catalytic systems and the metal carbene mechanism, which is named after its inventor Yves Chauvin.^[5] After Schrock^[6] discovered a tantalum catalytic system, which catalyzed the metathesis of *cis*-2-pentene, the validity of the Chauvin mechanism was confirmed. Encouraged by this, Grubbs^{[7][8][9]} developed several ruthenium based carbene pre-catalysts which showed increased catalytic activity and stability.

In order to improve the lifetime and stability of the pre-catalyst, Grubbs^[10] and Verpoort^{[11][12]} introduced the concept of hemilability by coordination of a ligand to the Grubbs 2 catalyst by a tightly bound atom and a softly bound atom. During a metathesis reaction, the softly bound atom dissociates, leaving a vacant coordination site on the metal and allows the substrate, the incoming alkene, to coordinate to the metal centre. This inspired Hermann and coworkers^[13] to develop a pre-catalyst with a hemilabile pyridinyl alcoholate ligand. This pre-catalyst showed an increase in activity at higher reaction temperatures during the alkene metathesis reactions.^[13]

In an attempt to improve the thermal stability, activity and lifetime of Grubbs 1 and Grubbs 2, Jordaan^[14] synthesized various new Grubbs-type pre-catalysts with hemilabile bidentate ligands for 1-octene metathesis. The "Puk-Grubbs 2 pre-catalyst" (1), was the most successful. It showed a major increase in lifetime, stability, activity and selectivity during the metathesis reactions.^{[14][15]}

Chauvin, Schrock and Grubbs were awarded with the Nobel Prize (Chemistry) in 2005 as a reward for their great work in the field of alkene metathesis^[16], which the committee emphasized in the following statement:

"This represents a great step forward for green chemistry, reducing potentially hazardous waste through smarter production. Metathesis is an example of how important basic science has been applied for the benefit of man, society and the environment."^[14]



1.2 Project aims and objectives

In the last decade several studies^{[13][14][17][18]} were done on organometallic carbenes. During a recent study^[14], it was proven that even with a catalyst with high selectivity, side-reactions still occur. These side reactions will increase with an increase in activity of the catalytic system.^[19] The solution was found in the synthesis of catalysts with a longer lifetime than that of Grubbs 2.^[20] So along with activity and selectivity, it is also important to improve the lifetime of the catalyst. On industrial scale, lifetime, selectivity, activity as well as stability are seen as the most important properties for the development of a catalyst.^[21]

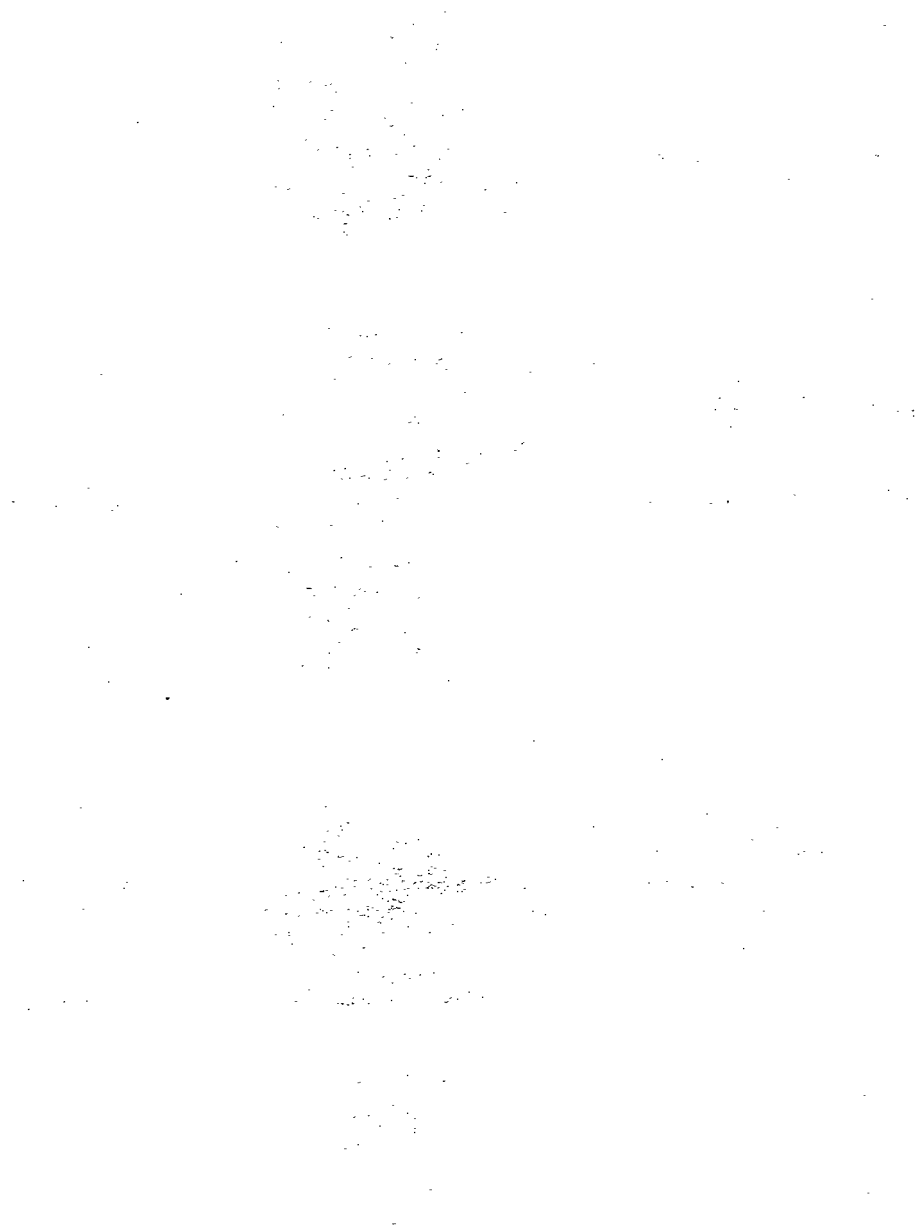
After Jordaan^[14] developed 1, it was found that the aromatic R groups of the N⁺O hemilabile ligand had a great influence on the activity and lifetime of the Grubbs pre-catalysts. In an attempt to improve the activity, selectivity and lifetime of this group of pre-catalysts, this study was performed. A number of hemilabile ligands with various R groups on the N⁺O hemilabile ligand, their Grubbs derivatives and the metathesis behaviour of these Grubbs-type pre-catalysts were investigated by molecular modelling and experimental means.

To reach the aim of the study, the following objectives are stated:

1. Extensive literature study on pre-catalysts for alkene metathesis as well as molecular modelling.
2. Molecular modelling of the structures of potential hemilabile ligands and their Grubbs derivatives for the development of new catalysts.
3. Synthesis of a series of hemilabile ligands and their Grubbs derivatives with different electronic and steric properties.
4. Characterisation of the ligands and Grubbs pre-catalysts.
5. Testing the synthesized Grubbs pre-catalysts for activity in a 1-octene metathesis reaction.

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Chapter 2: Theoretical background of Alkene Metathesis

2.1 Introduction

In chemistry, an alkene metathesis reaction can be defined as a reaction where the carbon-carbon double bonds of a molecule cleave to form two new molecules where one half of the one molecule is reattached with a double bond to one half of the other molecule (Figure 2.1).^[1]

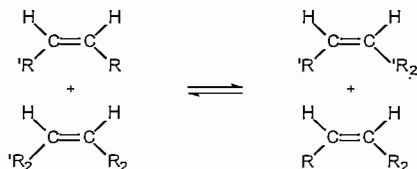


Figure 2.1: General alkene metathesis reaction

Alkene metathesis reactions can be subdivided into different categories: exchange reactions which is also called acyclic cross metathesis (ACM) or cross metathesis (CM), acyclic diene metathesis (ADMET), ring closing and ring opening metathesis reactions (ROM/RCM) and metathesis polymerization (ROMP) reactions.^{[2][3][4][5]}

In ACM (or CM), two different alkene substrates react (Figure 2.1) to form new alkene substrates. Since these newly formed alkene substrates can again undergo a metathesis reaction, this reaction is reversible. When the same alkene substrates react it is called self metathesis which can be productive or non-productive (Figure 2.2).^[2]

Productive :



Non-productive :

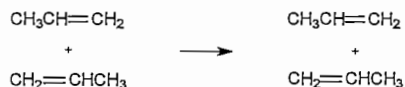


Figure 2.2: Productive and non-productive self metathesis ^[2]

Ring-opening metathesis (ROM) and ring-closing metathesis (RCM) can also be distinguished (Figure 2.3).^[2]



Figure 2.3: Ring-opening (ROM) and ring closing (RCM) metathesis reactions

Metathesis polymerization reactions take place using ring-opening metathesis polymerization (ROMP) which result in the formation of linear polymers as well as cyclic oligomers (Figure 2.4).^{[2][5]}

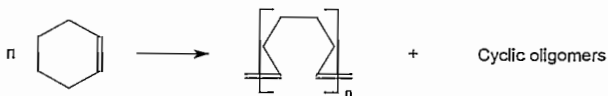


Figure 2.4: Ring-opening metathesis polymerization (ROMP)

When dialkenes are used in ACM reactions, also polymers will be obtained (Figure 2.5). This reaction is called acyclic diene metathesis (ADMET).^{[5][6]}

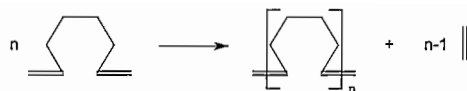


Figure 2.5: Acyclic diene metathesis (ADMET)

To obtain the desired metathesis product and to reduce side reactions (e.g. alkylation, isomerization, cyclization and addition across the double bond) it is important to choose the correct solvent (to reduce alkylation side reactions) and temperature during a metathesis reaction. But also the order of mixing chemicals and the type of catalytic system are of great importance during the reaction.^[4] In order to control the production of new chemicals, these factors were investigated for several decades. During these investigations, many catalytic systems were developed (§2.2) and a deeper insight in the function of catalytic systems (§2.3) as well as the metathesis mechanism (§2.4) was gained. This great work leads us, the chemists of nowadays, to new challenges and opportunities to explore the field of alkene metathesis even more.

2.2 The development of the alkene metathesis catalysts

Although Calderon^[6] was the first to use the expression 'alkene metathesis' in 1967, the first alkene metathesis reaction was performed by Schneider and Fröhlich in 1931.^[9] They discovered a reaction where the double bonds of the propene molecules undergo a reaction forming ethene and butene at high temperatures without any catalytic system. In 1957 Eleuterio^{[10][11]} used a $\text{MoO}_3/\text{Al}_2\text{O}_3/\text{LiAlH}_4$ catalytic system to produce low yields of a propene-ethene copolymer from propene. Truett^[12] was the first to publish the ROMP of norbornene in 1960.

At about the same time catalytic systems were discovered for metathesis reactions where atoms were exchanged to form non-polymeric organic compounds.^[4] After Peters and Evering^{[13][14]} discovered a catalytic system for the transformation of propene molecules into 2-butene and ethene in 1960, Banks and Bailey^[15] found an Al_2O_3 supported $\text{Mo}(\text{CO})_6$ catalytic system for the same type of reaction. They called this type of reaction "olefin disproportionation".^[2] When the Phillips group developed the commercial triolefin process for the production of butane and ethylene in 1964, this type of reaction gained a lot of attention.^[16]

However, at first the exchange reactions and polymerization reactions were not recognized as one type of reaction, because of the differences in catalytic systems and reaction conditions. For the production of polymers using ROMP, mainly Ziegler-Natta type catalysts were used in

combination with low reaction temperatures (room temperature or even lower) where exchange reactions were carried out using supported oxide catalysts at high temperatures (160°C). In 1967 Calderon^[8] discovered that the metathesis reaction of propene, as showed by Banks and Bailey^[15], could also take place in the presence of the homogeneous $WCl_6/EtAlCl_2/EtOH$ catalytic system instead of the heterogeneous supported catalyst which was normally used for this type of exchange reactions. After testing several other alkene substrates, it was found that the same type of reaction was responsible for exchange reactions as well as polymerization reactions.^[4] From this moment on, this type of reactions was called metathesis reactions.

In 1964 Fischer prepared the first catalytic systems where carbene ligands were coordinated to the metal. These can be represented with the general formula: $R^1R^2C=ML$ where $R^1R^2C=$ represents the carbene group and ML the transition metal with coordinated ligand L attached.^{[4][6]} Fischer's $Me(MeO)=W(CO)_5$ metal carbene catalyst showed to be electrophilic, where catalytic systems with nucleophilic carbene ligands resulted in nucleophilic reactivity of the carbene group. The reason why the metal in Fischer-type carbenes are more electron rich is because of the type of ligands (L) attached to the metal (M) and substituents (R) coordinated to the carbene group. The ligands L are σ -(primary bonding) and π -(secondary bonding) acceptors and the R substituents are π -donors, such as $-OMe$ and $-NMe_2$.^[17] The carbon atom of the carbene group forms a σ -bond to the metal atom, and a degenerative π -back bond from the metal to the carbon (Figure 2.6). The more electron donating these carbene group ligands are, the more electron rich the metal becomes and the larger the metal to carbon back bond will be, which will result in a stronger bond between the carbon and metal.^[18]

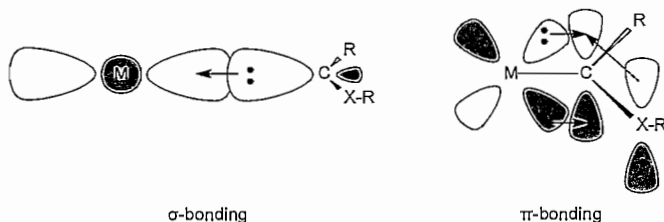


Figure 2.6: σ and π bonds bond between metal and a Fischer-type carbene ($X=O, N$ or S).^{[18][19]}

After Schrock's^[20] discovery of the $Ta(=CH-tBu)Cl(PMe_3)(O-tBu)_2$ catalytic system in 1980, which catalyzed the metathesis of *cis*-2-pentene, the transition metal carbene complexes can be divided into two different classes, i.e. Fischer-type carbenes in which the carbene carbon atom is electrophilic and Schrock-type carbenes where the carbene carbon is nucleophilic.^[21]

In Schrock-type carbenes, the electrons are spread between the carbon and metal atoms due to the fact that they have no π -acceptor ligands (L) on the transition metal and no π -donor substituents (R) on the carbene group. This makes them nucleophilic and forms a triplet metal-carbon bond which consists of a σ bond and a strong π -back bond between the metal and carbon atom (Figure 2.7).

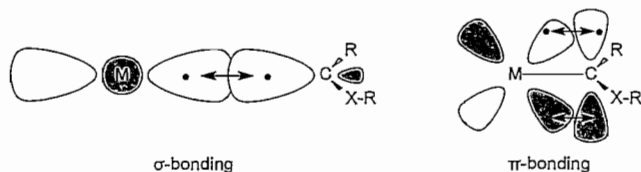
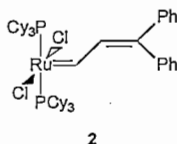


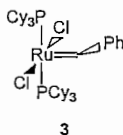
Figure 2.7: σ and π bonds between the metal and a Schrock-type carbene (X=O, N or S)^{[18][19]}

Grubbs, who was interested in methylene intermediates for the Fischer-Tropsch process, investigated Schrock-type carbenes and discovered that catalytic systems where ruthenium was used as carbene metal, preferred to react with alkenes (§2.3.1).^[22] His first ruthenium based complex was publicized in 1988.^{[23][24]} He synthesized a high molecular weight monodisperse polymer after a ROMP of 7-oxanorbornene by using a $\text{Ru}(\text{H}_2\text{O})_6(\text{OTs})_2$ catalyst system (OTs is a toluene sulphate group). In this study, the importance of a strained alkene and ruthenium(II) was emphasized.^{[24][16]}

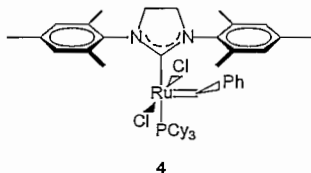
After he used the knowledge and methodology he had obtained for the synthesis of the tungsten catalytic systems for the preparation of ruthenium catalytic systems, he synthesized a ruthenium-type complex from tris(triphenylphosphine)ruthenium(II)chloride and 3,3-diphenylcyclopropene.^{[25][26]} This catalyst was shown to be active in ROMP of strained and electron rich cyclo-alkenes^{[27][16]}, but it also showed stability in the presence of protic solvents.^[25] After the triphenylphosphine groups of this catalyst system were replaced by bulkier tricyclohexyl phosphine (PCy_3) it was shown to be very active for metathesis of less strained cyclic alkenes as well as acyclic alkenes.^[28] Grubbs reported this first molecular well-defined ruthenium-type complex as Grubbs 0 (2) in 1992.^[16]



Because it was very difficult to synthesize **2**, further investigations were done. In the 90's, Schwab^[29] found an alternative synthetic route for this complex.^[30] Grubbs then discovered a catalyst that was synthesized from $\text{RuCl}_2(\text{PPh}_3)_3$, phenyldiazomethane and tricyclohexylphosphine^[22] which was shown to be very active for metathesis with a higher tolerance towards functional groups than the Schrock-type carbenes. This catalyst was easier to handle because of its relative stability to air and moisture.^[5] This catalyst was called the first generation Grubbs catalyst (Grubbs 1) (**3**).^{[7][22]}



After more investigation on **3**^[31], it was found that the PCy_3 ligands suffered from P-C degradation at higher temperatures.^{[32][33][34]} Imidazolylidene ligands were investigated which can mimic the phosphine behaviour with an improved stability at higher temperatures. In 1999 Grubbs, Nolan, Furstner and Herrmann replaced the PCy_3 group with an N-heterocyclic carbene (NHC)-ligand^{[32][35][36]} which led to the synthesis of a new type of catalyst, the second generation Grubbs catalyst (Grubbs 2) (**4**).



This NHC-ligand which was developed by Arduengo^[37] in 1991, has two bulky substituents attached to the NHC-heterocyclic part. The sterical hindrance of these ligands slowed down the decomposition step of the catalyst which made it more stable. The NHC ring which is a stronger σ -donor than PCy_3 promotes the dissociation in the activation step of the alkene metathesis mechanism (Figure 2.13).^{[35][38][39]} This NHC-ligand makes it possible for Grubbs 2 to form π -stacking between the phenyl group on the NHC-ligand and the phenyl of the carbene. π -Stacking takes place when two phenyl rings are orientated parallel in the same direction. The orbitals of both rings will be coordinated to each other and the electrons of both rings will be delocalized over the two phenyl rings. This leads to a more stable catalyst.^{[40][41]} It was found that Grubbs 2 improved not only the thermal stability of Grubbs 1, but also showed an increased activity and a longer lifetime.^{[16][42]} There were some misconceptions around the

structure of the second generation Grubbs catalyst^{[43][44][45]} but the catalyst as shown above is the commercially available Grubbs 2 catalyst (4).

Since the development of these well-defined Grubbs catalysts, a large amount of research was done on the Grubbs 1 and 2 catalysts trying to find more active and more stable catalysts for alkene metathesis.

Several research groups started to investigate chelating ligands^{[46][47][48][49]}, since they seem to increase the stability when coordinated to a catalyst. These ligands also seemed to give unique reactivities to complexes due to the mixed functionalities these catalysts can contain.^[50] Chelating ligands are ligands that can be attached very close to the metal with two or more bonds. These ligands can also exhibit the property of hemilability (Figure 2.8). A hemilabile ligand is a kind of chelating ligand that is attached to the metal by both a tightly bound atom and a softly bound atom. In a reaction the labile group A will open up and allow the substrate to coordinate to the metal centre. So by breaking the soft bond of the labile group A a free coordination site is obtained which leads to higher activity.^{[48][49][51]}

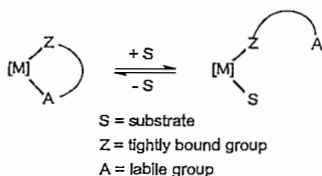
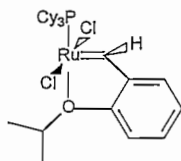
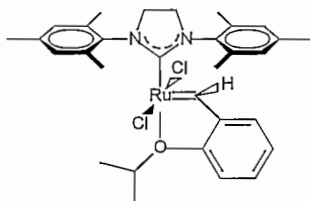


Figure 2.8: The concept of hemilability ^{[3][52]}

In 1999 Hoveyda^[46] replaced a PCy_3 group of Grubbs 1 by a chelating ligand which was also attached to the phenyl of the carbene group of the catalyst. This catalyst was found to be extremely stable in air and moisture. It was called the first generation Hoveyda-Grubbs catalyst (HGR1) (5). Together with Blechert^{[53][54]}, Hoveyda introduced the second generation Hoveyda catalyst in 2000 (6). The PCy_3 ligand of the first generation Hoveyda-Grubbs catalyst was replaced by a NHC-ligand just as for Grubbs 2. Although this catalyst showed a lower initiation activity than Grubbs 1 and 2, it showed a higher activity towards electron-deficient substrates (e.g. acrylonitrile) and was fully recyclable.^[55]

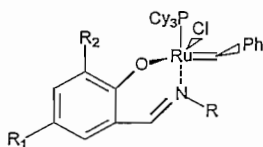


5 (HGr1)



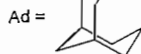
6 (HGr2)

Grubbs^[50] and Verpoort^{[57][51]} investigated the influence of O,N-chelating Schiff base ligands when attached to the former positions of the PCy₃ group and one of the chlorine atom in Grubbs 1 (7). Schiff base ligands are weakly basic ligands with a general formula of R₁R₂C=NR₃ where R₃ is an aryl or alkyl group which makes the Schiff base ligand a stable imine.^[58] The addition of this Schiff base ligand increased the thermal stability and reactivity of the catalyst.^{[16][48][49][51]} When this Schiff base was attached to Grubbs 2, the stability and activity of the catalyst increased even more, because the combination of the sterically hindered NHC-group with the Schiff base stabilized the reactive catalytic intermediate which prevented decomposition of the carbene.^[49]

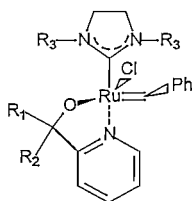


7

R₁, R₂ = H, R = 2,6-*i*-PrC₆H₃
 R₂ = Me, R₁ = NO₂, R = 2,6-*i*-PrC₆H₃
 R₂ = H, R₁ = NO₂, R = 2,6-*i*-PrC₆H₃
 R₂ = H, R₁ = NO₂, R = 2,6-Me-4-MeOC₆H₂
 R₂ = H, R₁ = NO₂, R = 2,6-Me-4-BrC₆H₂
 R₂ = H, R₁ = NO₂, R = 2,6-Cl-4-CF₃C₆H₂
 R₂ = H, R₁ = NO₂, R = 2,6-*i*-Pr-4-NO₂C₆H₃
 R₂ = H, R₁ = NO₂, R = CH₂-Ad



In 2002 Herrmann and coworkers^[48] developed a catalyst system where a hemilabile pyridinyl alcoholate ligand was coordinated to a Grubbs 2 type of catalyst (8). In the alkene metathesis reaction, these catalyst systems showed an increase in activity at higher reaction temperatures.^[48]



8

$R_1 = R_2 = \text{Me}; R_3 = \text{Cy}$
 $R_1 = R_2 = \text{Me}; R_3 = \text{CH}_2\text{CH}_2\text{Ph}$
 $R_{1/2} = (\text{CH}_2)_5; R_3 = \text{CH}_2\text{CH}_2\text{Ph}$
 $R_{1/2} = (\text{CH}_2)_5; R_3 = \text{Cy}$

Jordaan^[3] investigated different kinds of hemilabile ligands and concluded that aromatic N^O hemilabile ligands increased the catalyst lifetime of Grubbs-type metal carbene pre-catalysts in alkene metathesis. She developed the Puk-Grubbs 2 pre-catalyst (1) where an N^O hemilabile ligand with two phenyl groups was coordinated to the Grubbs 2 catalyst which showed a longer lifetime and a better activity in comparison to Grubbs 2.^[59]

2.3 Properties of metathesis catalysts

As a result of the growing interest in alkene metathesis, researchers started to investigate several catalytic systems to obtain better metathesis results. A catalytic system can be effective when it consists of one component, but it is also possible that a catalyst needs a co-catalyst or promoter to activate the catalyst first. Since the development of well-defined 'second generation' catalysts^[2], the use of a co-catalyst or promoter is not necessarily needed.

After Fischer and Schrock developed the metal carbene catalysts as mentioned in §2.2, the metal carbene was found to be a significant part of the catalyst, but only after the acceptance of Chauvin's metal carbene mechanism (§2.4), the metal carbene was proven to be the active species of the catalyst. From here, catalytic systems can be divided into three different categories^[4]:

- where the catalytic system contains an alkyl group that can act as a co-catalyst, leaving the metal carbene;
- where neither a carbene nor an alkyl group is present in the catalytic system and the metal carbene can only be formed by an interaction of the substrate alkene itself with the metal centre; and
- where the catalytic system consists of a metal carbene.

To design a catalyst for alkene metathesis with higher catalytic activity as well as selectivity, not only the carbene group needs to be discussed. It is also important to understand the influences of the transition metals as well as the ligands that are attached to the metal.

2.3.1 Transition metals

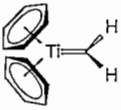
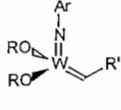
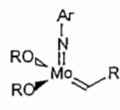
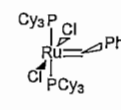
A transition metal, according to IUPAC, is "an element whose atom has an incomplete d sub-shell, or which can give rise to cations with an incomplete d sub-shell."^[60] Although transition metals have similar properties than main group metals, there are some differences which make transition metals of great importance in the design of a catalyst. This can be explained by the molecular orbital theory. Several transition metals have an 18 electron configuration around the central metal atom which means that an 18 electron situation can be found after sharing electrons with ligands.^[61] The bond formation between a transition metal and a ligand takes place via its σ - as well as a π -orbitals (Figures 2.6 and 2.7).^[18]

The σ -bond takes place after the empty σ -orbital of the metal overlapped with the filled π -orbital of the ligand and the π -bond forms through the interaction between the empty π -orbitals of the ligand with the filled d-orbitals of the metal. The last situation is better known as metal-to-ligand backdonation.^[18] Due to the combination of this σ - and π -bonding, the transition metal has the ability to form a very strong bond with the alkene, which makes the complex more stable.^[62] Although complexes where 9 ligands are attached called well-established^[63], most complexes only have 4 to 6 ligands attached. The ability to form more bonds than metals makes transition metals more stable which makes them more suitable for catalytic properties.

Just like the ability to adopt different coordination numbers, transition metals can show a wide range of oxidation states, i.e. Mn^{2+} , $(\text{Mn}^{3+})_2(\text{O}_3)^{6-}$ and $\text{Mn}^{4+}(\text{O}_2)^{4-}$ which they can change during the reaction.^[64] For this reason, transition metals contribute to a wide range of catalytic activity.

Although the number of catalytic systems that are used for alkene metathesis is very large, the most important catalytic systems are based on the following transition metals: titanium (Ti), niobium (Nb), tantalum (Ta), molybdenum (Mo), tungsten (W), rhenium (Re), ruthenium (Ru), osmium (Os) and iridium (Ir).^[2] Due to several investigations on these types of transition metals over the last years, the relationship between structure and reactivity could be more clearly defined.^[3] Grubbs^[22] investigated titanium, tungsten, molybdenum and ruthenium catalysts and found that when early transition metals were used, the reactivity towards alkenes became lower because the metal carbene preferred to react with polar functional groups (Table 2.1).^[65] The catalysts which contain late transition metals like ruthenium preferred to react with alkenes. For this reason a ruthenium catalyst was found to be very suitable for alkene metathesis reactions.

Table 2.1: Functional group tolerance of catalysts with different transition metals^{[3][22]}

			
Titanium	Tungsten	Molybdenum	Ruthenium
Acids	Acids	Acids	Alkenes
Alcohols, Water	Alcohols, Water	Alcohols, Water	Acids
Aldehydes	Aldehydes	Aldehydes	Alcohols, Water
Ketones	Ketones	Alkenes	Aldehydes
Esters, Amides	Alkenes	Ketones	Ketones
Alkenes	Esters, Amides	Esters, Amides	Esters, Amides

2.3.2 Attached ligands

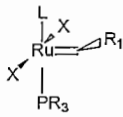
Since a molecule or group can only become a ligand when it has electrons that can be donated to an empty metal orbital^[66] most of the transition metals are electrophilic. They act like Lewis acids from where they can coordinate to nucleophilic ligands (Lewis bases).

The ligands can be divided into three different categories^[2]:

- monodentate ligands, which can either be neutral (e.g. H₂O or alkene) or charged (e.g. Cl⁻ or OH⁻)^[63] and have the ability to coordinate to the metal with one bond;
- bidentate ligands which can coordinate to the metal with two bonds; and
- multidentate ligands which can coordinate to the metal with three or more bonds.

Another important factor of transition metals is that they have the ability to accommodate both participative and non-participative ligands. Participative ligands are ligands that take part in the reaction the catalyst is used for and non-participative ligands are ligands that do not take part in the reaction. By coordinating non-participative ligands with certain electronic and structural properties to the metal, it is possible to influence the behaviour of the catalyst.^[3] How the different ligands coordinated to a Grubbs 2-type of catalyst can influence initiation or activity, is shown in Table 2.2.^[67]

Table 2.2: Influence of ligands on activity and initiation of Grubbs 2-type of complexes

Increasing activity ←		Increasing initiation →
$X = \text{Cl, Br, I}$ $R_1 = \text{CO}_2\text{R, Alkyl, Ph, H}$ $L = \text{H}_2\text{Mes, IMes}$ $\text{PR}_3 = \text{P}(\text{p-CF}_3\text{C}_6\text{H}_4)_3, \text{PPh}_3, \text{PCy}_3$		$X = \text{Cl, Br, I}$ $R_1 = \text{H, Ph, Alkyl, CO}_2\text{R}$ $L = \text{H}_2\text{Mes, IMes}$ $\text{PR}_3 = \text{PCy}_3, \text{PPh}_3, \text{P}(\text{p-CF}_3\text{C}_6\text{H}_4)_3$

Chelating ligands, as discussed in §2.2, can either be bidentate or multidentate and form, when coordinated to a transition metal, more stable complexes than the normally used monodentate ligands. Because the ligands can coordinate to the transition metal with a combination of soft and hard donor atoms, these ligands have the ability to create a vacant coordination site at the metal when a small molecule substrate enters the coordination sphere of the transition metal.^{[68][52]} This “free coordination site on demand” prevents the catalyst from decomposition which results in a more stable and more active catalyst. By changing the coordination sphere of the transition metal, several catalysts are already fine-tuned to obtain great activities, selectivities and stabilities.^{[48][56][57]} For this reason, chelating ligands are an important factor to create a more efficient catalyst in the field of alkene metathesis (§2.2).

2.4 The mechanism of 1-octene metathesis reactions with Grubbs-type catalysts

Before Chauvin proposed the metal carbene mechanism in 1970^[2], people believed that the mechanism responsible for the exchange of atoms during an alkene metathesis reactions was the so-called pairwise mechanism (Figure 2.9). The pairwise mechanism stated that, during an alkene metathesis reaction, the orbitals of the transition metal overlapped with those of the two double bonds so that a weakly held cyclobutane intermediate was obtained.^{[2][69]} Because research groups interpreted this mechanism differently, several proposed mechanisms were found in literature.^{[70][71][72][73]}

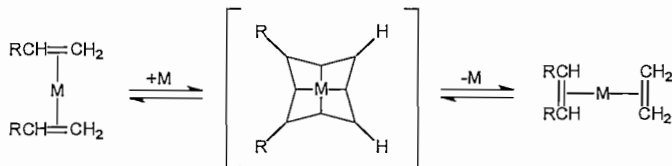
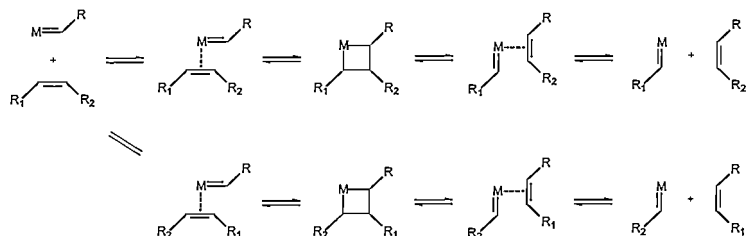


Figure 2.9: An example of the pairwise mechanism^[70]

The opposite was proven when Schrock^{[20][74]} and Kress^{[75][76][77][78]} obtained ^1H and ^{13}C NMR data of the initiating and propagation steps of these types of catalysts. This data showed the presence of the metallocyclobutadiene intermediate and so proved the pairwise mechanism to be wrong for most of the catalysts. A new mechanism was formulated, which proved to be responsible for the alkene metathesis reactions, called the Chauvin metal carbene mechanism (Figure 2.10).

Initiation:



Propagation:

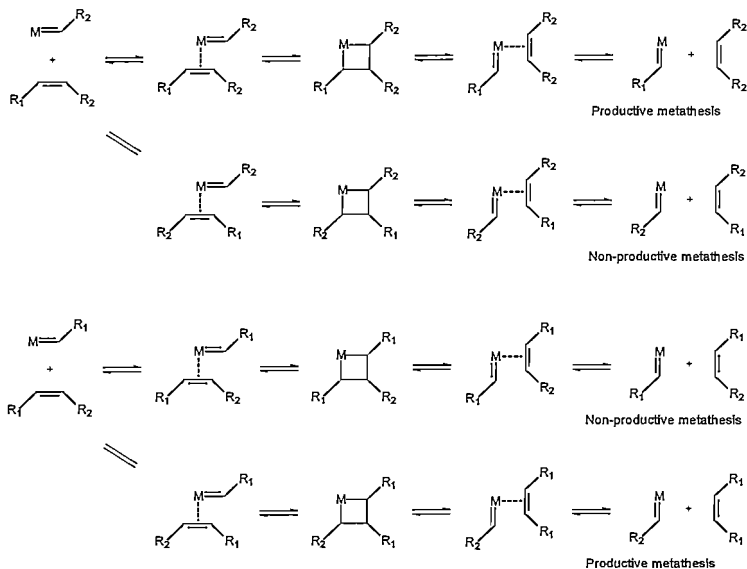


Figure 2.10: Example of the Chauvin metal carbene mechanism^[79]

After Grubbs^{[80][81]} and Chen^{[82][83]} investigated the Chauvin mechanism for Grubbs 1 and 2 via kinetic and mechanistic studies, the mechanism for alkene metathesis reactions was found to be dissociative. This means that a vacant site is created on the metal first by removing a 'soft' bonded ligand, followed by the coordination of a substrate to the metal. In an associative mechanism, which is the opposite of a dissociative mechanism, the substrate will start to coordinate first and the ligand will be removed after which the coordination number will be restored. Examples of a dissociative and an associative mechanism are shown in Figures 2.11 and 2.12.

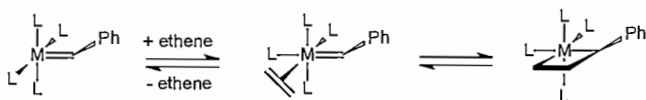


Figure 2.11: An example of an associative mechanism (M = metal, L = ligand)

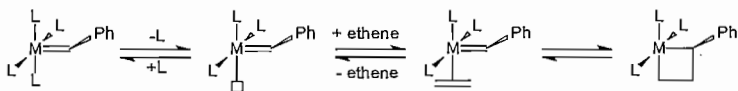


Figure 2.12: An example of a dissociative mechanism (M = metal, L = ligand)

Since this study is based on the improvement of 1 and the dissociative mechanism was used in the previous study of 1^[3], the dissociative mechanism of 1 in an alkene metathesis reaction will be explained. The mechanism consists of two steps; the initiation/activation step (B to F) where the alkene is coordinated to the metal (Figures 2.13 and 2.14), followed by propagation (F to J) where a new metal carbene catalyst and an alkene are formed (Figure 2.15).

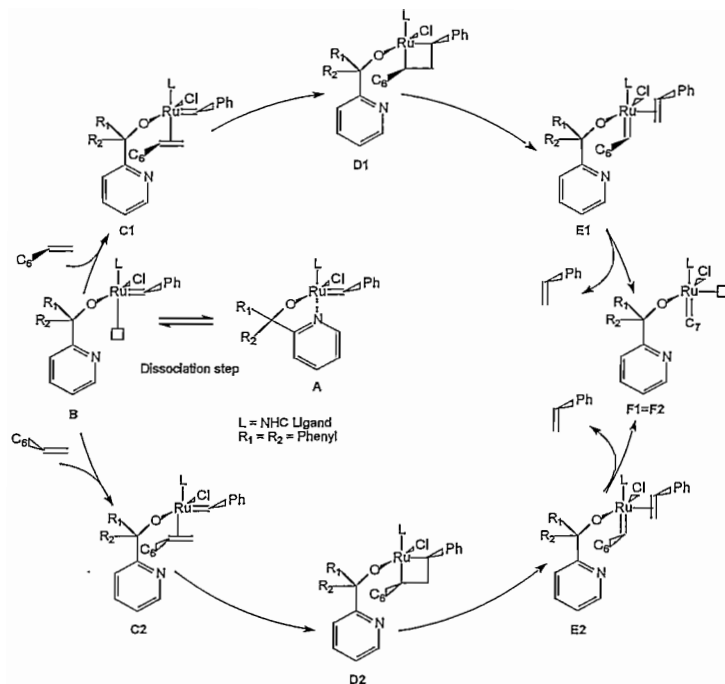


Figure 2.13: Activation cycle of the dissociative metathesis mechanism of **1** with 1-octene

Activation of the dissociative mechanism, as shown in **Figure 2.13**, starts with the opening up or dissociation step (A to B) of the hemilabile ligand to accommodate the coordination of the incoming alkene to the ruthenium atom from where it can form D. The double bonds are then changed and because the orientation of the alkene (1-octene) can be either in a *cis* position (path 2) or in a *trans* position (path 1); an activated catalyst with C₆ in both the *cis* (F2) and *trans* (F1) position will be obtained (**Figure 2.13**).

Since 1-octene can coordinate to the pre-catalyst by orientating its C₆ chain in the direction of the oxygen atom (**Figure 2.13**), as well as orientating it in the same direction as the phenyl of the carbene (**Figure 2.14**), F1 (=F2) (**Figure 2.13**) together with styrene as well as F3 (=F4) (**Figure 2.14**) with 1-phenyl-1-octene will be obtained after activation of the catalyst.

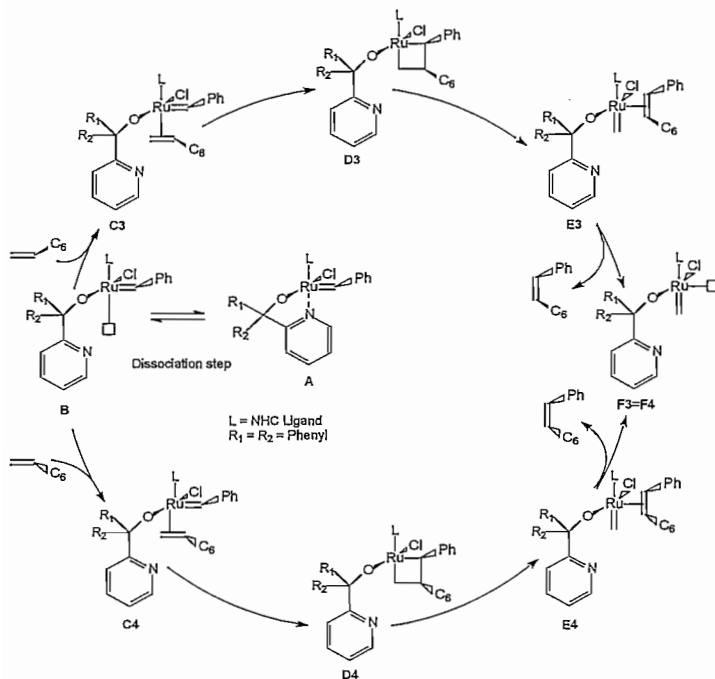


Figure 2.14: Activation cycle of the dissociative mechanism of 1 with 1-octene (with alternative orientation of 1-octene)

After the activation cycle, the two activated catalysts F1 (=F2) and F3 (=F4) enter the propagation cycle where they will react again with 1-octene to form a metallacyclobutane. When F1 (=F2) is reacting, it results in J1 (=J2) which is the same as F3 (=F4) (Figure 2.15). When F1 (=F2) is reacting with a different orientation of 1-octene, it results in J3 (=J4) which is the same as F1 (=F2) (Figure 2.16) and thus, is called an unproductive reaction. When F3 (=F4) enters the propagation cycle, it also results in F1 (=F2) and F3 (=F4) from which the last one is an unproductive reaction. Both catalysts can be reused as they are the same as the activated catalysts. The obtained alkenes are 1-octene, ethylene and 7-tetradecene from which ethylene and 7-tetradecene are called the primary metathesis products (PMP), 1-octene can be reused in the reaction.

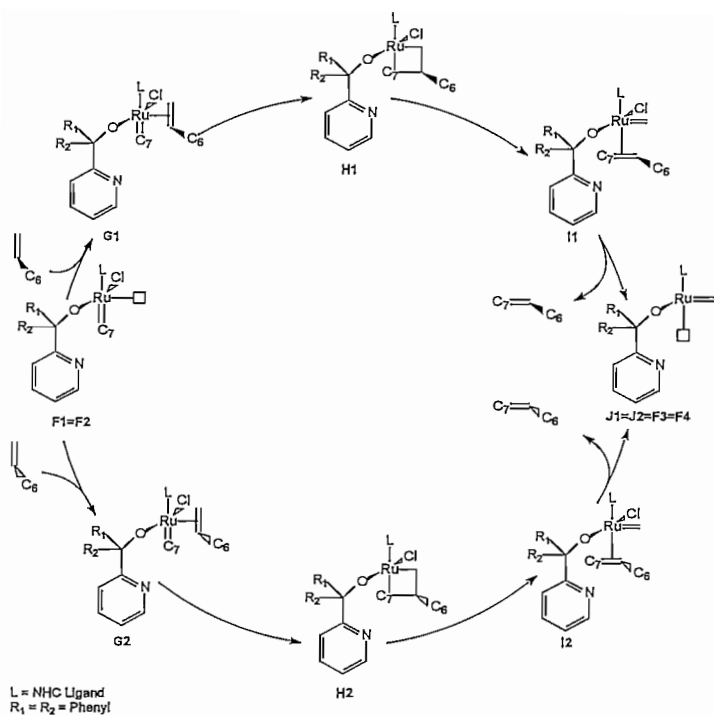


Figure 2.15: Propagation cycle of the dissociative metathesis mechanism of **1** with 1-octene

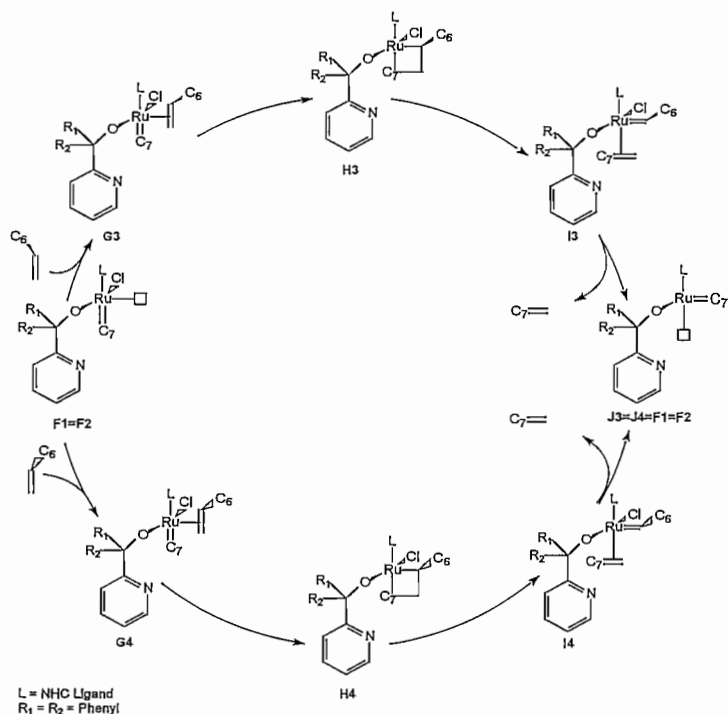


Figure 2.16: Unproductive propagation cycle of the dissociative metathesis mechanism of 1 with 1-octene (with alternative orientation of 1-octene)

Because there is also a small amount of styrene (Figure 2.13) and 1-phenyl-1-octene (Figure 2.14) in the reaction mixture, it is also possible for the activated catalysts and pre-catalyst to react with these alkenes obtaining pre-catalyst B, activated catalysts F1 (=F2), F3 (=F4) and 1-octene which can be reused as they are the starting materials of the two reaction cycles. The primary metathesis products ethene and 7-tetradecene are also obtained as well as the alkenes 1-phenyl-1-octene and styrene which were already obtained in the activation step. In the next figures, only styrene will be outlined since the same products will be obtained for 1-phenyl-1-octene.

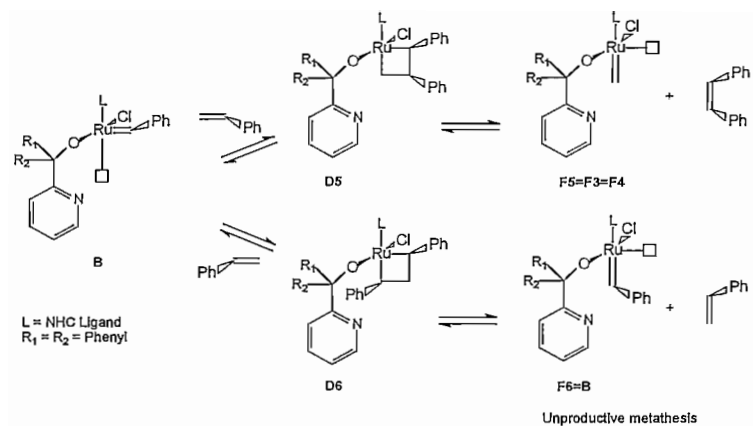


Figure 2.17: Styrene coordinating to pre-catalyst during the activation cycle

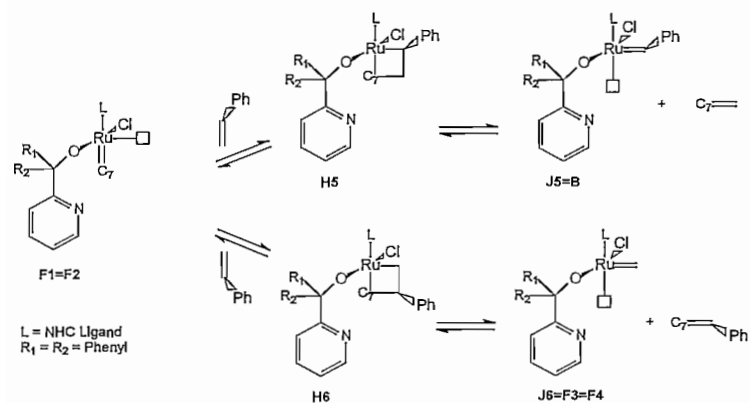


Figure 2.18: Styrene coordinating to initiated catalyst F1 (=F2) during the propagation cycle

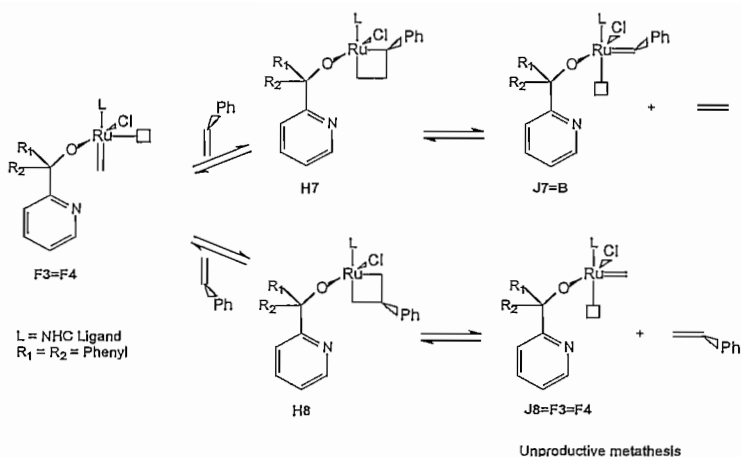


Figure 2.19: Styrene coordinating to initiated catalyst $F3 (=F4)$ during the propagation cycle

However, as a result of isomerisation, several isomerisation products (i.e. 2-octene, 4-octene) can be formed in the reaction mixture which can start to participate in the metathesis reaction. The products that are formed as a result of isomerisation products are so-called secondary metathesis products (SMP). The SMP which are obtained with the Puk-Grubbs 2 type pre-catalysts (1) and 1-octene are nonene (C_9), decene (C_{10}), undecene (C_{11}), dodecene (C_{12}), tridecene (C_{13}), pentadecene (C_{15}) and hexadecene (C_{16}). The isomerisation product 2-octene was used as an example to explain how the SMP products C_{12} and C_4 are obtained.

When 2-octene is taking part in a metathesis reaction with Puk-Grubbs 2 type of catalysts, it can activate pre-catalyst B from which catalysts F7 and F8 can be obtained (Figure 2.20).

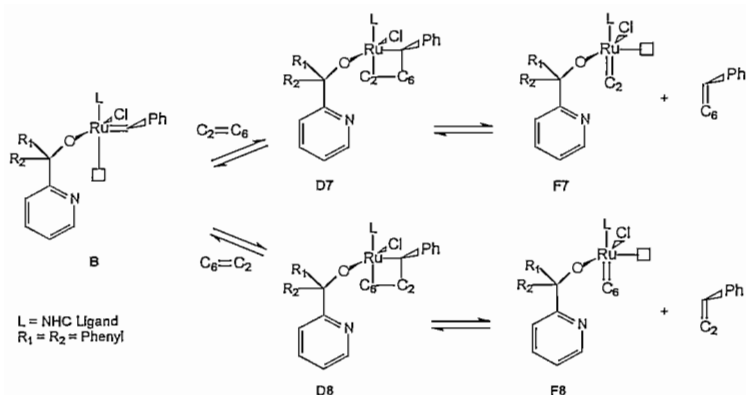


Figure 2.20: Activation cycle of the dissociative metathesis mechanism using two different orientations of 2-octene

In the propagation cycle, 2-octene can undergo a metathesis reaction with the activated catalysts F7 or F8. When F7 is reacting with 2-octene, it results in J10 and C₄ as well as J9 which is the same as F7 (Figure 2.21). The last mentioned reaction is called an unproductive reaction since the catalyst and alkenes remain the same.

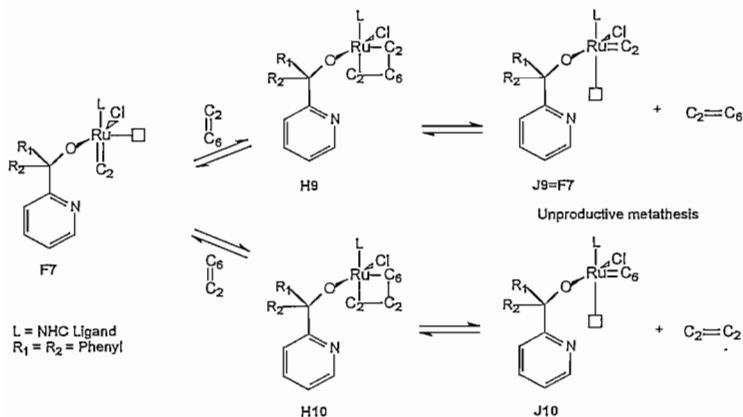


Figure 2.21: Propagation cycle of the dissociative metathesis mechanism with two different orientations of 2-octene and activated catalyst F7

When F8 is reacting with 2-octene, it results in J11 and C₁₂ as well as J9 which is the same as F8 (Figure 2.22). The last mentioned reaction is called an unproductive reaction since the catalyst and alkenes remain the same.

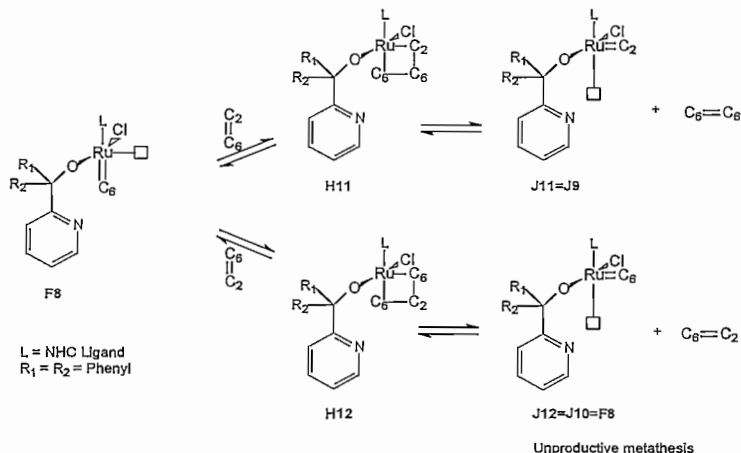


Figure 2.22: Propagation cycle of the dissociative metathesis mechanism with two different orientations of 2-octene and activated catalyst F8

Just like PMP, SMP will increase during the metathesis reaction. The increase of SMP depends on the rate of isomerisation which can be different for each catalyst. Because 1-octene and catalyst B are mostly present in the reaction mixture, since they are the starting materials of this reaction, the activated catalysts F1 (=F2) and F3 (=F4) are together with the PMP the main products of a metathesis reaction.

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Chapter 3: Theoretical background of molecular modelling

3.1 Introduction

Molecular modelling is a way of representing molecular structures mathematically and simulating their behaviour^{[1][2]} by applying existing algorithms and computer programs. Chemists together with physicists develop these algorithms and computer programs to calculate and present molecular data including geometries (bond lengths, bond angles, torsion angles), electronic properties (moments, charges, ionization potential, electron affinity), energies (heat of formation, activation energy), spectroscopic properties (vibrational modes, chemical shifts) and bulk properties (volumes, surface areas, diffusion, viscosity).^{[1][3]} With this data, chemists have the ability to explain observations from experimental work or predict the course of a reaction.^[4] More sophisticated computer hardware and software has been developed during the last several decades. The high computing power in combination with faster and more efficient numerical algorithms resulted in the growth of efficient molecular modelling calculations.^[5]

The three most important mathematical models are^[6]:

- Molecular mechanic models that use mathematical equations deduced of classic mechanics and electrostatic laws to give the best correlation
- Quantum mechanic models that use simplifications of the Schrödinger equation and different mathematical parameters to rectify the errors what occurred due to those simplifications
- Density functional theory models where the wavefunction used in quantum mechanic models is replaced by electron density functions.

3.2 Development of molecular modelling

The basics of molecular modelling started with the conception of the tetrahedral carbon atom of Le Bell and van 't Hoff in 1874.^{[7][12]} But only in the beginning of the 20th century Schrödinger developed an equation that could describe the wavefunction of hydrogen, namely^{[13][14]}.

$$H\Psi = E\Psi$$

where H stands for the Hamiltonian operator, Ψ for the wavefunction and E for the eigenvalue.

The Schrödinger equation which is mathematical impossible to solve for molecules with more than one electron, motivated scientists like Heisenberg, Bohr, Pauli, Born, Oppenheimer, Dirac, de Broglie and Hund to investigate this equation further in order to find a way to describe molecules and their behaviour.^{[15][16][17]}

The three models as mentioned in Chapter 3.1 are discussed further below.

3.2.1 Molecular mechanics

In 1976, Allinger^{[18][19]} described molecular mechanics as a calculation method. Molecular mechanics is based on a simple classical-mechanical model of molecular structures in which atoms are treated as hard spheres and bonds as bendable and extendible springs. The forces what are necessary to distort the angles and bondlengths can be described in mathematical equations, force field functions. The sum of these energies contributions is called the molecular mechanics energy (MME)^[20], which can be described by the following equation:

$$MME = \sum E_{str} + \sum E_{bend} + \sum E_{tor} + \sum E_{vdw} + \sum E_{el}$$

where E_{str} stands for the energy necessary to stretch or compress a bond, E_{bend} for the energy to change bond angles, E_{tor} for energy to twist bonds, E_{vdw} for energy due to van der Waals non-bonded interactions and E_{el} for energy due to electrostatic interactions.

The total force field function, as mentioned above, is the basic form of a molecular mechanics force field. To use a more sophisticated force field, other force field functions (for example hydrogen bonding interactions) have to be added. These force field functions, use relatively simple expressions which could for example be based on Hook's Law.^{[6][20]} They can be solved rapidly with computers and contain adjustable parameters that are optimized to give the best fit of experimental and calculated data.

In the last 40 years several molecular mechanic force fields were developed to estimate the correct geometry of the structure.^{[21][22]} In the 70's the two force fields that were widely used were Allinger's MM1 method^[23] and the EAS force field^[24], developed by Engler, Andose and Schleyer. They gave good predictions of structures and energy differences for a wide variety of hydrocarbon molecules.^{[25][26]} But because this method was not reliable for molecules which contain hetero-atoms^[22], a new method was developed in 1977, the MM2 force field.^[20] It was found that this method was not suitable for molecules containing conjugated systems so the MMP1 and later the MMP2 was developed.^{[6][27]} Both MMP1 and MMP2 contained some quantum mechanic calculations which will be discussed in the next paragraph.

In the 1980's the optimization of the force fields were improved and extended.^{[28][29][30]} The force fields were also made user-friendly.^{[31][32]} This was all summarized in the new MM3 force field, which is still often used in molecular modelling.^{[33][34][35]}

Molecular mechanics calculations give a good approximation of structures, but when an accurate determination of interactions, transition states etc. is necessary, the more sophisticated quantum mechanical methods are required.^[36]

3.2.2 Quantum mechanics

"The underlying physical laws necessary for the mathematical theory of a large part of physics and the whole of chemistry are thus completely known, and the difficulty is only that the exact application of these laws leads to equations much too complicated to be soluble."^[20]

P.A.M. Dirac

In the early part of the 20th century it became clear that molecular mechanics models could not predict the properties of small objects like electrons.^[6] By introducing the Schrödinger equation where it was stated that particles can behave like waves, it was possible to describe a particle by a mathematical equation, namely a wavefunction (Ψ). When the wavefunction of a particle is known, the molecule and his properties can be described.^{[6][20]} But the Schrödinger equation can only be solved for the hydrogen atom. The quantum mechanical models that were developed using simplifications of the Schrödinger equation, were found to be extremely successful for larger molecules.^{[6][37]}

In an attempt to take account of the influence that particles can have on other particles, Born and Oppenheimer introduced an approximation (the BO approximation) where the nuclei were treated as unmoving objects in comparison to the electrons.

This simplification was however not enough and further investigation were done which lead to the Hartree-Fock approximation.^[6] The average effect of all electrons except one will be used to investigate the movement of the one electron left. After this movement is averaged, the movement of another electron will be investigated. This is repeated until electrons do not move anymore and the self-consistent product is obtained. To use this approximation, the electrons in the average field have to be treated as they are moving independently from each other.^[20] To determine the first average effect of electrons, a linear combination of molecular orbitals (LMO) can be used. These orbitals of multi-electron atoms are called basis sets. Different kind of basis sets can be used, depending on the type of molecule you want to calculate. The more basis sets are used in a calculation, the longer the calculation time which can result in a more accurate calculation. The combination of the Hartree-Fock approximation

with LCMO is better known as the Hartree-Fock model. The calculation method used for the Hartree-Fock model can be summarized in the Roothaan-Hall equation^{[38][5]}:

$$\sum (F_{ij} - \epsilon_i S_{ij}) A_{ij} = 0$$

where F stands for the Hamiltonian operator, ϵ for the orbital energy and S for the overlap matrix.

The basis sets which are used for Hartree-Fock models are Slater-type atomic orbitals (STO) which provides reasonable representations of atomic orbitals^[39] and Gaussian-type of orbitals (G) which are easy to manipulate and give a good approximation of atomic orbitals by using two or more Gaussian functions.^[20] The minimum basis sets are combinations of Gaussian functions (i.e. STO-3G) which show a relative good correlation between accuracy and reaction time. To obtain a more accurate calculation, a combination of more Gaussian functions (i.e. 6-31G) split into a set for the core calculations and the valence calculations is needed.

Because the Hartree-Fock model does not consider that the movements of electrons are correlated to each other, a theory was developed for the correction of the Hartree-Fock model. This simplification, as introduced by Moller and Plesset, is commonly used where by using second (MP2), third (MP3) or fourth (MP4) order levels, a greater accuracy is obtained.^{[20][40]}

Calculations that are based on Hartree-Fock as well as Moller-Plesset type of models are found to be very accurate but with a long calculation time which makes these type of models only suitable for small molecules.^[36] The reason for this long calculation time is because these models contain, in contrast with the molecular mechanic models which are fully parameterized, no parameters. Fully parameterized models are called empirical and models where no parameters are used ab initio. In order to find a reasonable accurate model with a shorter calculation time, semi-empirical methods were introduced.^[20] In semi-empirical methods only the orbitals of the valence electrons are calculated, the interactions of the other orbitals are introduced through parameters.

Pople^{[41][42]} and Dewar^[43] developed the first semi-empirical models, CNDO and MINDO/3, where the parameters were developed from ab initio models. Dewar started to introduce parameters derived from experimental data and developed the well-known MNDO^[44] and AM1^[45] models which was followed by the development of Stewart's PM3^[46] model. Both ab initio and semi-empirical models are often used these days. Which model is chosen, depends on the calculation you want to do and how accurate the calculation has to be. In

1998, Pople got a nobel prize which emphasizes the great work that was done on development of these models.

3.2.3 Density functional theory

Another method for the calculation of the electronic structure of molecules is called density functional theory (DFT).^[47] Where quantum mechanics uses several simplifications on wavefunctions, DFT uses electron density functions to calculate the energy of the ground state.^{[20][48]} This can be described in the following equation:

$$E(\rho) = E_{ke}(\rho) + E_c(\rho) + E_h(\rho) + E_{xc}(\rho)$$

where $E(\rho)$ is the total energy, $E_{ke}(\rho)$ the kinetic energy, $E_c(\rho)$ the Coulomb energy between electron and nuclei, $E_h(\rho)$ the Coulomb energy between electrons and $E_{xc}(\rho)$ the correlation- and exchange energy.

The electron density functions can be derived from the sum of the filled orbitals (LCMO) which can be calculated by using Slater and Gaussian type of basis sets on an approximate idea of the structure. This approximate structure may often be obtained by molecular mechanics. The correlation- and exchange energy is difficult to calculate because the exact function is not-known. But when the approximation is made that the electron density distribution is semi-homogeneous, it is possible to calculate this function. This approximation is called the local density approximation (LDA).^{[36][48]}

Because the electron distribution is not semi-homogeneous and LDA can predict too high bond energies as a result of that, another approximation was used to describe a non-homogeneous distribution of the electrons. This approximation is called the generalized gradient application (GGA).^[36]

The first DFT model was reported by Thomas-Fermi^[49] and Weiszacker^[50] in 1935, but because this model showed a 1% error in kinetic energy, the Thomas-Fermi-Weiszacker (TFW) model was not used until Kohn and Sham^[51] introduced a model that could calculate the kinetic energy exactly.^[52] After Stoll^{[53][54]} investigated DFT models for several years, Perdew^[55] and Becke^[56], developed the Becke-Perdew (BP) model which is today an often used DFT model.

Because DFT includes correlation- and exchange energy and results in a shorter calculation time in comparison to the quantum mechanical HF models, DFT models are often used. But

because there is still a lot of investigation that needs to be done on DFT models, DFT models are not necessarily better.

The calculation time in HF models increases with (the number of atoms)⁴ and in DFT models this will be (the number of atoms)³, and for that reason DFT will be more suitable for larger molecules. DFT calculations were also found to be more suitable for transition state metal complexes.^[20]

3.3 Molecular modelling in the field of alkene metathesis

Due to the growing interest on alkene metathesis, the amount of computational studies in this field have increased in the last few years, which means that the database which are used for molecular modelling are well investigated.^{[57][60]} The use of molecular modelling in the field of alkene metathesis helps chemists of today to solve problems, which can be anywhere between the design of a new catalytic system and the calculation of transition states.^[36]

Vyboishchikov^[61] investigated the alkene metathesis mechanism of Grubbs 1 and 2 catalysts by using DFT and it was found that the dissociative mechanism is more favorable than the associative mechanism. Since this study is based on designing a new catalytic system, the use of molecular modelling in transition states or mechanisms will not be discussed further. Only the effect of ligands on catalytic systems will be discussed.

In 2004 Adihart^[62] investigated the role of the PCy₃ and H₂I-Mes ligands of Grubbs-type of complexes by computational studies. He found that the metallacyclobutane intermediate of the catalyst which contained the H₂I-Mes ligand is more stable than that of the catalyst with PCy₃ due to the more strongly σ -donating effect of the H₂I-Mes ligand. They also indicated that the type of alkene substrate as well as the ancillary ligands attached to the catalyst have a big influence on the reaction.

After investigating the influence of phenol on ruthenium based catalysts, Forman^[63] and Grubbs^[64] found that the hemilabile interaction of the OH group with the metal centre results in an improved stability of the catalysts. In the experimental investigation, this increase in stability could be observed by an increase of activity and lifetime of Grubbs 1 and Grubbs 2 complexes.^{[63][64]}

Jordaan^[65] was the first one to report a computational investigation on ruthenium carbene complexes with chelating ligands. Several kinds of hemilabile ligands were investigated and it was found that aromatic R groups coordinated to the N⁺O hemilabile ligand resulted in a higher stability, activity, lifetime and selectivity of the Grubbs 2 catalyst. The influence of

hemilabile N⁺O ligands with aromatic groups on Grubbs 2 were not investigated further and will be the main aim of this study.

3.4 The role of molecular modelling in this project

As mentioned before, molecular modelling is used to support experimental results or to predict the course of a reaction.^[3] By calculating the molecular orbitals, it is possible to predict if a ligand has the ability to coordinate to a catalyst, in this study a Grubbs 2-type of catalyst. A ligand can coordinate to the Grubbs 2 catalyst, if the highest occupied molecular orbital (HOMO) of the ligand overlap with the lowest unoccupied molecular orbital (LUMO) of the Grubbs 2 catalyst to form a bond. In case of a hemilabile ligand, the ligand must at least have two HOMO orbitals that can overlap to form bonds. The electronic charge distribution can also be calculated with molecular modelling which gives an insight whether a ligand will act nucleophilic or electrophilic. A representation of these electronic properties in combination with some experimental results will make it possible to predict if ligands will coordinate to a catalyst or whether a new catalyst will show the desired results in a certain reaction.

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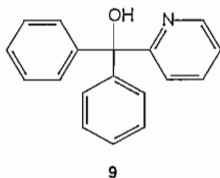
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Chapter 4: Experimental

4.1 Introduction

For this project it was necessary to find alcohols that do not differ too much from W.A. Hermann's, 1,1-Diphenyl-1-(2'-pyridyl) methanol (**9**), because the ligand derived from this alcohol when attached to the Grubbs 2 pre-catalyst (**4**) showed good activity and lifetime.^[1] The bulkiness of the two phenyl groups on ligand **9** improved the properties of the pre-catalyst. The aim of this project was to see if it is possible to improve the activity, selectivity and lifetime of the pre-catalyst by changing the R_1 and R_2 groups of the ligand derived from the alcohol **9**.



A comprehensive literature search for alcohols with the general structure of **9** with various R_1 and R_2 groups was done, using the Beilstein program. The search was conducted by submitting fragments as shown in Figure 4.1 to the Beilstein program to find possible alcohols with different R_1 and R_2 groups that already have been synthesized.

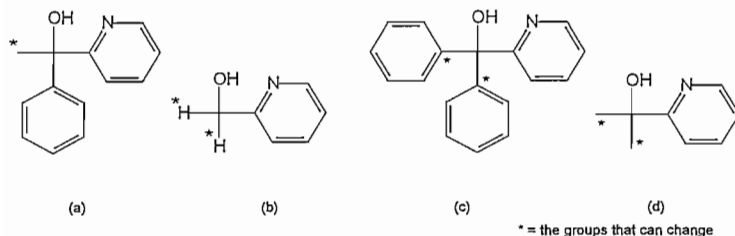


Figure 4.1: Fragments that were submitted to Beilstein

4.2 Computational details

4.2.1 Hardware

For the molecular modelling part of my study two types of hardware were used:

- A personal computer (1CPU), which was used for conformer search calculations, with the following specifications :
Operating system: Microsoft XP with service pack 2
Processor: Intel Pentium 4 2.6
Memory: 1 GB RAM (2.67 GHz)
- A 52 CPU cluster, which was used for the geometric optimizations and energy calculations, with the following specifications :
1 X Masternode (4CPU) : HP DL385 – 2 x 2.8 MHz AMD Opteron 64,
2 GB LSG, 2 x 72 GB HDD
12 X Compute nodes (4CPU each) : HP DL145G2 – 2 x 2.8 MHz AMD Opteron 64,
2 GB LSG, 2 x 36 GB HDD
Operating system on compute nodes : Redhat Enterprise Linux 4
Cluster operating system : HPC CMU v3.0 cluster

4.2.2 Software

All modelling calculations were done using Accelrys Material Studio 4.0 or 4.2. Geometric optimizations and determinations of properties were calculated with the Density Functional Theory (DFT) method DMol³ using the GGA functional PW91 together with the following specifications:

- A medium quality of convergence tolerance using 2×10^{-5} Ha (Energy), 0.004 Ha/Å (Max. force) and 0.005 Å (Max. displacement)
- A medium self consisted field (SCF) of 1×10^{-5} Ha using a maximum of 1000 SCF cycles and octupole multipolar expansion
- A double numeric polarized (DNP) basis set

For all 5 complexes conformer search calculations were done using system grid scan as search method and study table and trajectory as output while the dihedral angle of Ru-O-C-C(pyridine ring) was changed every 5° so that 72 conformers were obtained.

The following parameters were used:

- Scale van der Waals radii to 40%
- Scale vicinal radii to 40%
- Scale H-bond radii to 40%
- Restraint force constant 1000 kcal/mol/rad²
- Using perturb reference structure (PRS)

4.3 Reagents and solvents

Diethyl ether (Labchem, b.p.: 34.6°C), tetrahydrofuran (Saarchem, b.p.: 66°C) and toluene (Merck, b.p.: 110-111°C) were distilled under N₂ from sodium with benzophenone as indicator. Pentane (Labchem, b.p.: 35 - 36 °C) was distilled under N₂ from CaH₂. Tetrahydrofuran and toluene were stored over 4Å mol sieves. Diethyl ether and pentane were used straight from the distillation.

The 1-octene (98%, Sigma-Aldrich) was purified by filtering the solution through an alumina column after the alumina was dried over night at 700°C. The solution was stored over 3Å mol sieves.

n-Butyl lithium, 2-Bromopyridine (99%), Isobutyro-phenone, 2-methyl benzophenone, 2'-methyl acetophenone, 2-adamantanone and Grubbs catalyst 2nd generation were purchased from Aldrich and used as received, *tert*-Butyl hydroperoxide (5.5M in decane) and nonane (99%) were purchased by Fluka from which the first mentioned was stored over 4Å mol sieves. Camphor was purchased by Merck and used as it is.

All gasses which were used during this study were supplied by Afrox.

4.4 General method for the preparation of the ligands

Diethyl ether (100 mL) was placed in a 3-neckflask which was cooled down to -78°C (acetone and dry ice). 2-Bromopyridine (9 mL, 95 mmol) was reacted with a butyl lithium solution (40 mL, 100 mmol, 2.5 M) obtaining a lithium pyridine intermediate under inert (Ar) conditions. The temperature was kept below -40°C during the slow addition of a diluted 2-bromopyridine solution to prevent the decomposition of the intermediate.

After stirring for about 30 minutes at -78°C, a dark red solution was formed and after the temperature was increased to -50°C the ketone (Tables 4.1 - 4.5, 105 mmol) was added. 2-Methyl benzophenone (10), 2'-Methylacetophenone (11) and Isobutyrophenone (12) were solutions so they were added with a syringe through the septum. 2-Adamantanone (13) and Camphor (14) were first dissolved in ether before addition to the reaction mixture. It is very important to add 14 very slowly and to keep the temperature below -40°C because camphor is very reactive, which means that it will react with all possible by-products of the lithium pyridine intermediate.^{[2][3][4]}

The solution was stirred for 3 hours while the temperature was increased from -50°C to room temperature (25°C).

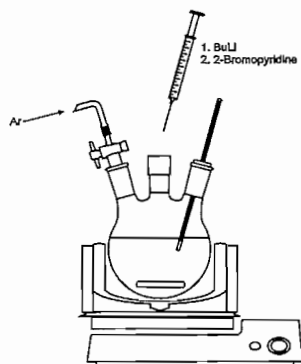
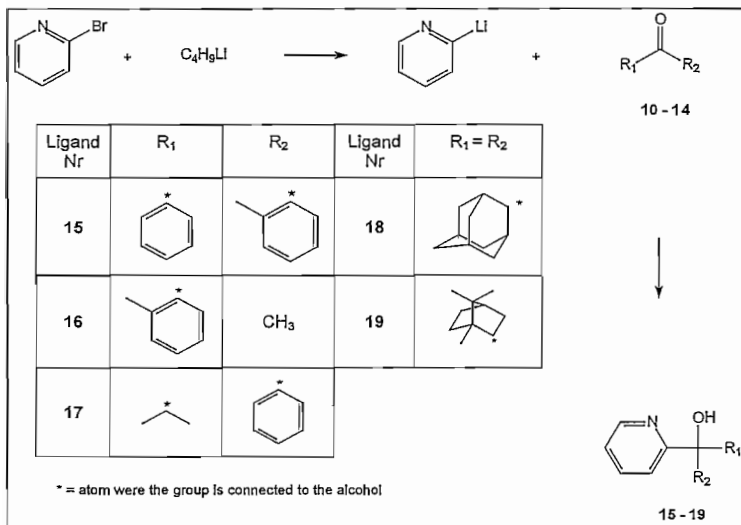


Figure 4.2: Experimental setup for preparation of ligands

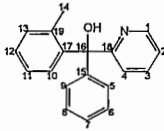
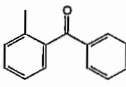


Scheme 4.1: Synthetic route for ligands

After three hours of stirring, the reaction mixture was warmed to room temperature, hydrolysed with water, washed with a 2M HCl (3 X 30 mL) solution and neutralized with a 2M NaOH solution. The reaction mixture was extracted with diethyl ether (4 x 100 mL) until the aqueous layer turned colourless. The ether layer was treated with charcoal and filtered until the light yellow solvent turned colourless which was normally after about 5 times. The solution

was dried with anhydrous Na_2SO_4 , filtered and the solvent was removed to yield colourless to light-yellow crystals which were characterized by melting point determination, NMR, IR and GC-MS (Tables 4.1 - 4.5).

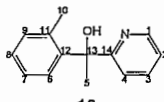
Table 4.1: Synthesized ligand 15

Alcohols	Ketones	Product information
 15 Phenyl-[2]-pyridyl-o-tolyl methanol	 10	Colour : white Yield : 52% Melting point : 103 °C
IR : (KBr) ν_{max} 3432.4 (O-H stretch), 3046.8 (aromatic C-H stretch), 1588.4-1569.9 (C=C and C=N stretch) cm^{-1} GC-MS (EI) : 275 m/z $^1\text{H NMR}$ 1: (CDCl_3, 600 MHz) : δ_{H} 8.599 (1H, d, H_1), 7.640-7.559 (1H, dd, H_3), 7.398-7.107 (9H, m, H_{5-13}), 7.073-7.001 (1H, d, H_4), 6.992-6.920 (1H, dd, H_2), 6.245-6.146 (1H, s, OH), 2.151-2.086 (3H, s, H_{14}) ppm $^{13}\text{C NMR}$ 2: (CDCl_3, 600 MHz) : δ_{C} 163.69 (S, C_{18}), 147.841 (D, C_1), 146.305 (S, C_{15}), 144.016 (S, C_{17}), 139.183 (S, C_{19}), 136.246 (D, C_3), 132.555 (D, C_6), 128.955 (D, C_{13}), 128.020 (D, C_8), 127.676 (D, C_{12}), 127.088 (D, C_7), 123.251 (D, C_4), 122.166 (D, C_2), 81.813 (S, C_{16}), 21.700 (Q, C_{14}) ppm		

*1: small letters indicate H-H coupling

*2: capital letters indicate direct coupling of C-H

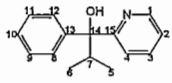
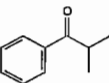
Table 4.2: Synthesized ligand 16

Alcohols	Ketones	Product information
 16 1-[2]-pyridyl-1-o-tolyl ethanol	 11	Colour : yellow Yield : 47% Melting point : 89-91 °C
GC-MS (EI) : 213 m/z $^1\text{H NMR}$ 1: (CDCl_3, 600 MHz) : δ_{H} 8.544 (1H, d, H_1), 7.620-7.608 (1H, dd, H_3), 7.548-7.520 (1H, d, H_4), 7.220-7.059 (4H, m, H_{5-9}), 6.924-6.911 (1H, dd, H_2), 5.454 (1H, s, OH), 1.921 (3H, s, H_5), 1.861 (3H, s, H_{10}) ppm $^{13}\text{C NMR}$ 2: (CDCl_3, 600 MHz) : δ_{C} 165.88 (S, C_{14}), 147.26 (D, C_1), 142.92 (S, C_{12}), 138.21 (S, C_{11}), 136.83 (D, C_3), 132.39 (D, C_9), 127.78 (D, C_8), 126.86 (D, C_7), 125.34 (D, C_6), 121.74 (D, C_4), 120.27 (D, C_2), 76.21 (S, C_{13}), 31.63 (Q, C_5), 21.08 (Q, C_{10}) ppm		

*1: small letters indicate H-H coupling

*2: capital letters indicate direct coupling of C-H

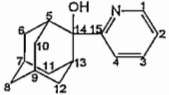
Table 4.3: Synthesized ligand 17

Alcohols	Ketones	Product information
 17 2-methyl-1-phenyl-1-pyridin-2-ylpropan-1-ol	 12	Colour : beige Yield : 67% Melting point : 67-70 °C
IR : (KBr) ν_{max} 3291.3 (O-H stretch), 3049.9 (aromatic C-H stretch), 2967.8-2865.1 (aliphatic C-H stretch), 1596.6 (C=C and C=N stretch) cm^{-1} GC-MS (EI) : 227 m/z $^1\text{H NMR}$ 1: (CDCl_3, 600 MHz) : δ_{H} 8.446 (1H, d, H_1), 7.637-7.588 (3H, m, H_{9-11}), 7.446-7.433 (1H, dd, H_3), 7.296-7.270 (2H, m, H_{8+12}), 7.170-7.146 (1H, d, H_4), 7.103-7.082 (1H, dd, H_2), 5.887 (1H, s, OH), 2.840-2.796 (1H, m, H_7), 0.954-0.943 (3H, m, H_5), 0.746-0.734 (3H, m, H_6) ppm $^{13}\text{C NMR}$ 2: (CDCl_3, 600 MHz) : δ_{C} 163.921 (S, C_{15}), 146.928 (D, C_1), 146.440 (S, C_{13}), 136.849 (D, C_3), 128.130 (D, C_{10}), 126.481 (D, C_{12}), 126.064 (D, C_{11}), 121.675 (D, C_4), 120.466 (D, C_2), 79.610 (S, C_{14}), 36.119 (D, C_7), 17.188 (Q, C_6), 16.735 (Q, C_5) ppm		

*1: small letters indicate H-H coupling

*2: capital letters indicate direct coupling of C-H

Table 4.4: Synthesized ligand 18

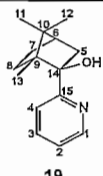
Alcohols	Ketones	Product information
 18 2-pyridin-2-yl-adamantan-2-ol	 13	Colour : light yellow Yield : 72% Melting point : 109 °C
IR : (KBr) ν_{max} 3395.0 (O-H stretch), 2932.7-2855.6 (aliphatic C-H stretch), 1592.7 (C=C and C=N stretch) cm^{-1} GC-MS (EI) : 229 m/z $^1\text{H NMR}$ 1: (CDCl_3, 600 MHz) : δ_{H} 8.567 (1H, d, H_1), 7.660-7.634 (1H, dd, H_3), 7.475-7.462 (1H, d, H_4), 7.138-7.119 (1H, dd, H_2), 2.649-2.425 (4H, m, H_{11-12}), 2.054 (1H, s, OH), 1.889 (1H, s, H_{13}), 1.775-1.665 (9H, m, H_{5-10}) ppm $^{13}\text{C NMR}$ 2: (CDCl_3, 600 MHz) : δ_{C} 164.547 (S, C_{15}), 149.235 (D, C_1), 136.448 (D, C_3), 121.987 (D, C_4), 120.158 (D, C_2), 77.210 (S, C_{14}), 37.923 (D, C_8), 35.310 (T, C_6), 34.993 (T, C_8), 33.071 (D, C_7), 27.569 (T, C_{12}), 27.229 (D, C_{13}) ppm		

*1: small letters indicate H-H coupling

*2: capital letters indicate direct coupling of C-H

For the preparation of **19**, the literature^[2] followed method B which is different from method C which is used in this project. The reason for using method C was because of a lack of the chemicals for method B. Purification of ligand **19** by filtration over celite followed by recrystallisation from methanol or flash chromatography with an ethyl acetate : hexane ratio of 1 :1 instead of using charcoal was done, but the purity of the ligand was not improved. Attempts to hydrolyze alcohol **19** with NH_4Cl instead of water did not improve the yield.

Table 4.5: Synthesized ligand **19**

Alcohols	Ketones	Product information
 19 1,7,7-trimethyl-2-(2'-pyridyl)- bicyclo[2.2.1]heptan-2-ol	 14	Colour : white Yield : 16% Melting point : 56-61 °C
IR : (KBr) ν_{max} 3446.2 (O-H stretch), 2958.5-2928.3 (aliphatic C-H stretch), 1571.4-1590.4 (C=C and C=N stretch) cm^{-1} GC-MS (EI) : 231 m/z $^1\text{H NMR}^1$: (CDCl_3, 600 MHz) : δ_{H} 8.507 (1H, d, H_1), 7.636-7.624 (1H, dd, H_3), 7.410-7.397 (1H, d, H_4), 7.144-7.141 (1H, dd, H_2), 5.240 (1H, s, OH), 0.983-0.803 (9H, m, H_{11-13}), 1.394-1.250 (7H, m, H_{5-8}) ppm $^{13}\text{C NMR}^2$: (CDCl_3, 600 MHz) : δ_{C} 163.54 (S, C_{15}), 147.36 (D, C_1), 135.52 (D, C_3), 121.56 (D, C_4), 120.58 (D, C_2), 82.64 (S, C_{14}), 57.67 (S, C_9), 46.76 (S, C_{10}), 43.27 (T, C_5), 43.03 (D, C_6), 29.89 (T, C_8), 27.02 (T, C_7), 19.75 (Q, C_{12}), 19.12 (Q, C_{11}), 9.22 (Q, C_{13}) ppm		

*1: small letters indicate H-H coupling

*2: capital letters indicate direct coupling of C-H

4.5 Preparation of complexes

Using the lithium salts of the ligands (§ 4.4) the new Grubbs 2-type pre-catalysts were synthesized.

4.5.1 General method for the preparation of lithium salt

For the preparation of lithium salts, the alcohol (4 mmol) was dissolved in THF (40 mL) and *n*-butyl lithium (1.8 mL, 4 mmol, 2.5M) was added dropwise to the reaction mixture. Also this reaction was performed under inert (Ar) conditions because the *n*-butyl lithium is very reactive to water and because of the instability of the desired lithium salt. This reaction was carried out at room temperature, so it was very important to add the *n*-butyl lithium very slowly due to the exothermic character of the reaction.

After 2 hours of stirring the solution became slightly yellow and no precipitation was formed. However when the THF was removed under reduced pressure a yellow solid was obtained.

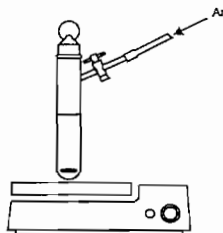
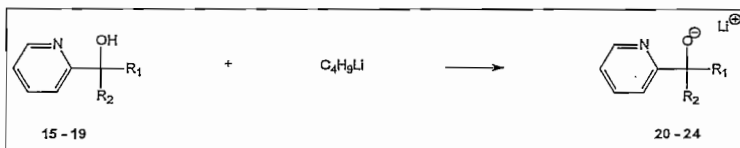


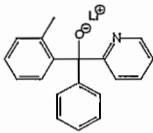
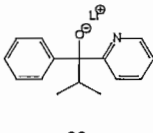
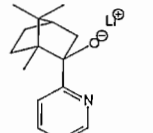
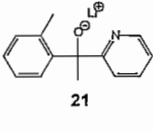
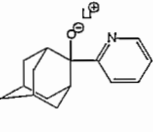
Figure 4.3: Experimental setup for preparation of Li-salt



Scheme 4.2: Preparation of lithium salt

The powder was washed with dry pentane (5 x 20 mL) forming a white powder. In this washing step it is important that the solid particles did not get patched to the glass otherwise these particles were not washed carefully and the yellow impurities were not washed out. The white powder was dried under vacuum and used without further characterization or purification, due to its sensitivity to air.

Table 4.6: Synthesized lithium salts 20-24

Salts	Yields	Salts	Yields	Salts	Yields
 20	60%	 22	90%	 24	18%
 21	84%	 23	87%		

4.5.2 General method for the reaction of the lithium salt with Grubbs 2 (4)

For the preparation of the ruthenium complex it was very important to carry out this reaction under inert (Ar) conditions because of a possible instability of the ruthenium complex when in solution. The complex with **9** attached was found to be unstable when in solution^[5] so all five produced complexes were treated like they were unstable because they look similar to the complex with **9**.

The lithium salt (1.1 mmol) and Grubbs 2 pre-catalyst (**4**) (934 mg, 1.1 mmol) were placed in a Schlenk tube and evacuated. THF (20 mL) was added and after 1 hour of stirring at room temperature (25 °C) the Schlenk tube was placed in a water bath that was kept between 35 and 40 °C.

The solution was stirred while the reaction was monitored by TLC which showed a large green spot on formation of the complexes.

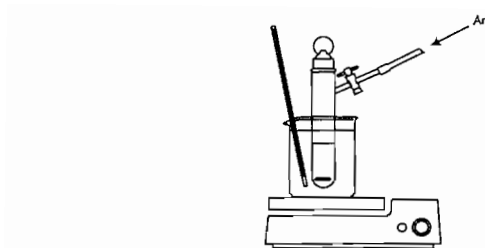
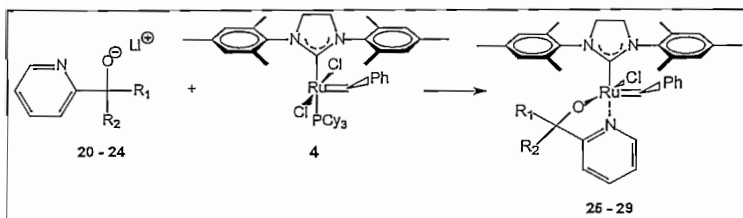


Figure 4.4: Experimental setup for preparation of complex

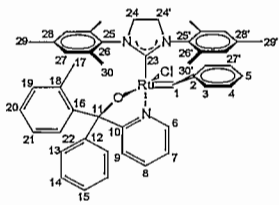
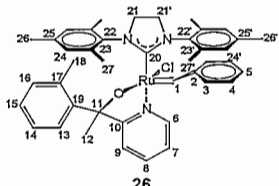
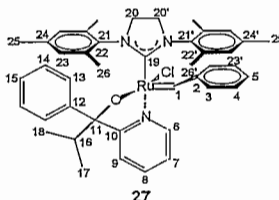
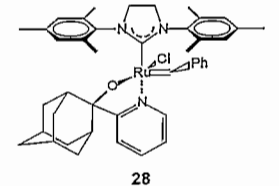
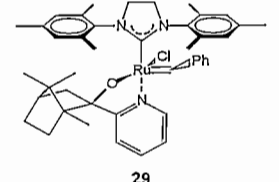


Scheme 4.3: Preparation of PUK Grubbs 2-type pre-catalysts

After the reaction was completed the THF was evaporated, the black residue was dissolved in 15 mL of toluene and filtrated by a syringe filter to remove the formed lithium chloride. Then the toluene was evaporated and the black solid was dissolved in 1 mL THF and 40 mL cold pentane. The Schlenk tube was sealed and placed in the ultrasonic bath for about 10 minutes to remove impurities. For all complexes a green or red precipitation occurred which was washed with pentane (5 x 20 mL). Then the solid was dried under vacuum leaving complexes 25, 26, 27 and 29 as green solids and complex 28 as a red solid.

Characterization was done by NMR and MALDI-TOF (Table 4.7). It is very important that the complexes are pure and show just one carbene peak on ^1H NMR because they will be tested for metathesis and only the product formed by the carbenes of the synthesized complexes have to be monitored. When the complex showed more than 2 carbene peaks on ^1H NMR and a phosphorus peak on ^{31}P NMR, 1 mL THF and 50 mL pentane was added again and the whole washing procedure was repeated. This was done until only one carbene peak and no phosphorus peak was obtained.

Table 4.7: Synthesized Complex 25-29

Complexes	Product Information
 25	Yield : 16% Maldi-TOF : 807 m/z ¹H NMR [†]: (CDCl₃, 600 MHz) : δ_{H} 17.327 (1H, s, H₁), 9.758-9.527 (1H, d, H₈), 7.096-7.084 (2H, dd, H₅₊₈), 7.084-6.987 (13H, m, H₁₃-H₁₅+H₁₉-H₂₂+H₂₇+27'), 6.676-6.551 (2H, t, H₄₊₇), 6.444-6.355 (1H, d, H₉), 6.355-6.164 (1H, d, H₃), 3.728-3.466 (4H, m, H₂₄+24'), 2.494-1.834 (18H, sss, H₂₉₊₃₀), 1.235 (3H, s, H₁₇) ppm
 26	Yield : 27% Maldi-TOF : 745 m/z ¹H NMR [†]: (CDCl₃, 300 MHz) : δ_{H} 17.318 (1H, s, H₁), 9.871-9.463 (1H, d, H₈), 7.436-7.261 (1H, d, H₃), 7.125-6.990 (2H, m, H₅₊₈), 6.965-6.719 (8H, m, H₁₃-H₁₆+H₂₄+24'), 6.701-6.574 (2H, t, H₄₊₇), 6.333-6.000 (1H, d, H₉), 4.239-3.777 (4H, t, H₂₁+21'), 2.601-2.364 (18H, m, H₂₆+27), 1.571 (3H, s, H₁₂), 1.406-1.086 (3H, m, H₁₈) ppm
 27	Yield : 49% Maldi-TOF : 758 m/z ¹H NMR [†]: (CDCl₃, 600 MHz) : δ_{H} 17.332 (1H, s, H₁), 9.393-9.384 (1H, d, H₈), 7.291-7.266 (1H, d, H₃), 7.034 (3H, m, H₁₃-H₁₅), 6.940 (2H, m, H₅₊₈), 6.868-6.835 (2H, m, H₂₃+23'), 6.592-6.567 (2H, t, H₄₊₇), 4.082-4.002 (4H, t, H₂₀+20'), 2.716-2.122 (18H, m, H₂₅+26), 1.278-1.235 (3H, m, H₁₇), 0.649-0.638 (3H, m, H₁₈), 1.549-1.342 (1H, t, H₁₆) ppm
 28	This complex was not obtained due to decomposition during washing procedure (§5.2.4).
 29	This complex was not obtained due to decomposition during washing procedure (§5.2.4).

[†]1: small letters indicate H-H coupling

[†]2: capital letters indicate direct coupling of C-H

4.6 Characterization of products

For the characterization of the synthesized ligands and complexes, the following apparatus were used:

- A Buchi B-540 melting point device: for the determination of the melting points of the alcohols
- A Nicolet FTIR 550 infrared spectrophotometer (IR) using 10 scans over a wave number range of 400–4000 cm^{-1} : for the determination of alcohol, aliphatic, aromatic and double bond stretches. Because all alcohols were solids, pellets were prepared using 0.005 g alcohol and 0.28 g dry KBr.
- A micromass Autospec Mass spectrometer: for the determination of the molecular mass of the alcohols.
- An Agilent Technologies 6890N Gas Chromatographer-MSD equipped with a Phenomenex 010287 (ZB-1) column (30m x 320 μm x 1 μm) and an Agilent Technologies 7683B Series autoinjector in combination with an Agilent Technologies 5973 Network Mass selective detector: for the determination of the purity as well as the mass of the alcohol. Samples were prepared by dissolving the solid in diethyl ether. The following oven program was used:

60°C for 5 min

60 to 110°C at 25°C/min

110°C for 5 min

110 to 290°C at 25°C/min

300°C for 8 min

- A Bruker 600 Nuclear Magnetic Resonance spectrometer (NMR): for the determination of hydrogen and carbon atoms in all products as well as to see if there is any phosphorus in the complex. For the preparation of the samples 20 mg product was dissolved in 1.5 mL chloroform, the samples of the complexes were made under inert condition using freeze dried chloroform.
- A Bruker Ultraflex III TOF/TOF (TOFMS): for the determination of the molecular mass of the complexes.

4.7 Testing the complexes for metathesis

All metathesis reactions were carried out in two of the same reaction setups (Figure 4.5) which were placed in the same fumehood, each on a nitrogen line from the same manifold. The reaction temperature was controlled by an oil bath which was calibrated to the desired temperature before the metathesis reaction.

The ruthenium pre-catalyst (0.0139 mmol) was weighted in the 3-neckflask, after which it was flushed with N_2 for several minutes. In another flask a mixture of 1-octene (20 mL, 0.125 mol) and nonane (1 mL, 5.6 mmol) were preheated to 60°C under inert conditions (Ar) and then added to the ruthenium pre-catalyst.

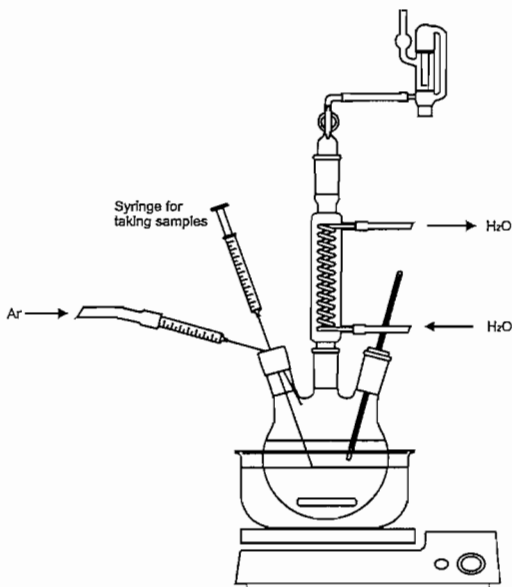


Figure 4.5: Experimental setup for performing a metathesis reaction

In order to follow the progress of the metathesis reaction, samples were taken for GC analysis at 0, 2, 5, 10, 30 and 60 minutes. 0.3 mL of the sample was added to a GC vial which contains:

- 0.3 mL toluene to make up the volume of the sample; and
- 2 drops of *tert*-butyl hydrogen peroxide to quench the reaction

4.8 GC analysis and calculation methods used for the metathesis reactions

4.8.1 The GC and programs used

The metathesis reaction was monitored by Agilent Technologies 6890N GC-FID equipped with a Phenomenon 7JG-G001-17 (ZB-1) column (50m x 250 μ m x 0.5 μ m) and an Agilent Technologies 7683 series autoinjector.

The next settings were used:

Injection volume:	0.2 μ L
Split ratio:	50.4 : 1
Inlet temperature:	200°C
N ₂ carrier gas flow:	1.4 mL/min
H ₂ flow rate:	40 mL/min
Air flow rate:	450 mL/min
Oven programming:	60 to 110°C at 25°C/min 110°C for 16 min 110 to 300°C at 25°C/min 300°C for 5 min
Detector temperature:	300°C

A typical chromatogram of a 1-octene metathesis reaction with a Grubbs 2-type catalyst is given in Figure 4.6.

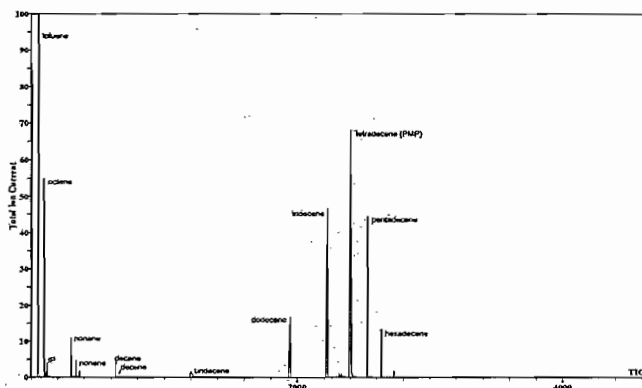


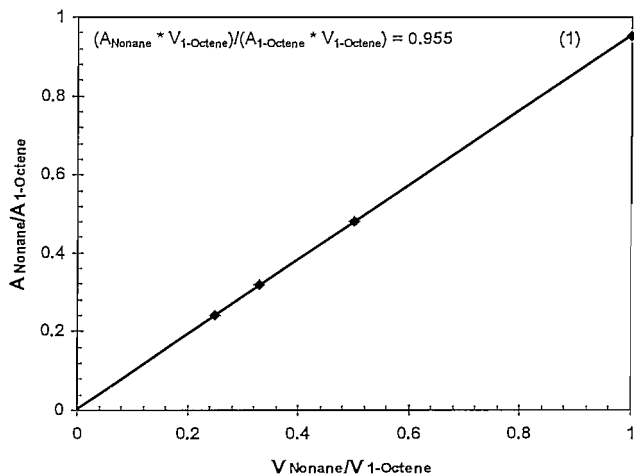
Figure 4.6: GC chromatogram during metathesis reaction with Grubbs 2-type of complex at 60 °C and with a 1-octene : complex molar ratio of 9000

4.8.2 Instrument calibration: Response factor

Before the GC spectrum can be used, the response factor has to be determined. 4 vials were prepared containing:

- 0.25 mL nonane + 1.00 mL 1-octene
- 0.25 mL nonane + 0.75 mL 1-octene
- 0.25 mL nonane + 0.50 mL 1-octene
- 0.25 mL nonane + 0.25 mL 1-octene

These samples were injected to the GC and the response factor was calculated by plotting $A_{\text{nonane}}/A_{\text{1-octene}}$ against $V_{\text{nonane}}/V_{\text{1-octene}}$ obtaining the following graph (Graph 4.1). The gradient of this line gives a response factor of 0.955.



Graph 4.1: Graph for the determination of the response factor

4.8.3 Determination of the mole percentages, selectivities and turnover number

To calculate the decrease of 1-octene, the increase of primary metathesis products (PMP) and secondary metathesis products (SMP) and the formation of Isomerisation products (IP) the following formulas were used:

- For the determination of the volumes of 1-octene, PMP, IP or SMP

$$V_x = V_{is} * (A_x/A_{is}) * (1/Rf) \quad (2)$$

where V_x = Volume of 1-octene, PMP, IP or SMP

V_{is} = Volume of internal standard nonane at $t = 0$

$$V_{is} = V_{nonane}/V_{1-octene} * V_{sample} \quad (3)$$

where V_{nonane} = Volume of nonane at $t = 0$ (1 mL)

$V_{1-octene}$ = Volume of 1-octene at $t = 0$ (20 mL)

V_{sample} = Volume of sample taken from the flask (0.3 mL)
 $= 1 / 20 * 0.3 = 0.015$

A_x = Area of 1-octene, PMP, IP or SMP

A_{is} = Area of internal standard nonane

Rf = Response factor

- For the determination of the moles of 1-octene, PMP, IP or SMP

$$n_x = V_x * \rho_x / Mw_x \quad (4)$$

where n_x = Moles of 1-octene, PMP, IP or SMP

V_x = Volume of 1-octene, PMP, IP or SMP

ρ_x = Density of 1-octene, PMP, IP or SMP

Mw_x = Molecular weight of 1-octene, PMP, IP or SMP

- For the determination of the mole percentage of 1-octene, PMP, IP or SMP

$$\%n_x = (n_x / n_{tot}) * 100\% \quad (5)$$

where $\%n_x$ = Mole percentage of 1-octene, PMP, IP or SMP

n_x = Moles of 1-octene, PMP, IP or SMP

n_{tot} = Sum of moles of 1-octene, PMP, IP and SMP

- For the determination of the selectivity

$$\%selectivity = (\%PMP / \%(PMP+SMP)) * 100\% \quad (6)$$

- For the determination of the turnover number

$$TON = (\%PMP * (Oct/Ru))/100\% \quad (7)$$

where Oct/Ru = Molar ratio complex : 1-octene at $t = 0$

4.8.4 Stability of the synthesized complexes

Because the stability of complex 1, which can be expressed in lifetime, increased in comparison to complex 4^[1], it is interesting to see what the lifetime of the synthesized complexes are. To investigate this, metathesis reactions were done using the optimal conditions for complex 1, as determined in a previous study^[5]. During the metathesis reaction when less than 1% 1-octene remained in the reaction mixture, 20 mL 1-octene was added. This was repeated four times for all three synthesized complexes, however when 1-octene was added for the fifth time (or the fourth time in the case of complex 25) the internal standard nonane could not be monitored anymore. This was because the nonane was diluted so that the GC signal was too weak to measure.

4.9 References

- [1] Herrmann, W.A., *J. Mol. Cat. A*, 1997, 117, 144
- [2] Kuhn, F.E., Santos, A.M., Lopes, A.D., Goncalves, I.S., Rodriguez-Borges, J.E., Pillinger, M. and Romao, C.C., *J. Organomet. Chem.*, 2001, 621, 207
- [3] Herrmann, W.A., Halder, J.J., Fridgen, J., Lobmaier, G.M., Spiegler, M., *J. Organomet. Chem.*, 2000, 603, 69
- [4] Goto, S., Velder, J., El Sheikh, S., Sakamoto, Y., Mitani, M., Elmas, S., Adler, A., Becker, A., Neudörfl, J., Lex, J. and Schmalz, H.-G., *Synlett*, 2008, 9, 1361
- [5] Jordaan, M., *Experimental and Theoretical investigation of New Grubbs-type Catalysts for the Metathesis of Alkenes*, PhD-thesis, (North-West University), 2007

Chapter 5: Results and discussion

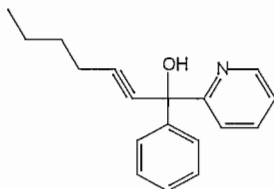
5.1 Modelling

5.1.1 Introduction

More than 3000 alcohols of the type as shown in Figure 4.1 were identified, but not all were suitable for this project. Only 202 alcohols were identified that could be investigated as possible ligands for this project (See Appendix I).

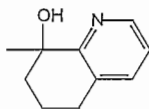
The alcohols that were identified were subdivided into different types of alcohols to be investigated. The best alcohols for each subdivision after comparison to 9 are shown below:

- Alcohols with two different R groups, for example 1-Phenyl-1-pyridyl-2-heptyn-1-ol (30):



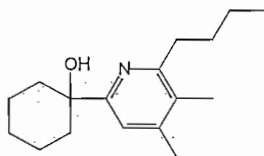
30

- Alcohols where R₂ is connected to the pyridine ring by another type of ring (which can be subdivided into cyclopentylrings, cyclohexylrings or cycloheptylrings), for example 8-Methyl-5,6,7,8-tetrahydroquinolin-8-ol (31):



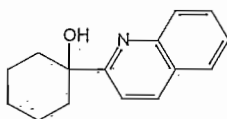
31

- Alcohols with a methyl or short chain attached to the pyridine ring, for example 1-(6-Butyl-4,5-dimethyl-pyridin-2-yl)-cyclohexanol (32):



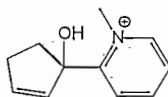
32

- Alcohols with a phenyl group attached to the pyridine (which can be subdivided into alcohols where the phenyl group is attached to the pyridine by a benzyl group or alcohols where the phenyl and pyridine ring share a bond), for example 1-[2]-Quinoly]-cyclohexanol (33):



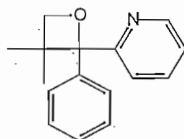
33

- Alcohols where the nitrogen has a fourth bond, for example N-methyl-2-(1-hydroxy-2-cyclopentyl)-pyridinium (34):



34

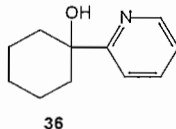
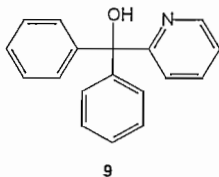
- Alcohols where the OH-group is replaced by an ether, for example 2-(3,3-Dimethyl-2-phenyl-oxetan-2-yl)-pyridine (35):



35

5.1.2 Modelling and screening of the 202 alcohols

Firstly, the geometry of **9** and 1-Pyridin-2-yl-cyclohexanol (**36**) were optimized and various properties calculated using Material Studio software (§4.2.2). The choice of the two alcohols mentioned above was motivated by the fact that the first one made the catalyst lifetime longer and proved to be very active in the metathesis reactions when coordinated to the Grubbs 2 pre-catalyst (**4**), while the second one was shown to be less active with a shorter lifetime.^[1] Since the R groups of the alcohols were the only differences between these complexes, it can be concluded that the type of R groups attached to the complex has a great influence in the metathesis reaction.



The 202 identified alcohols were geometrically optimized and the following properties were calculated for each: HOMO, LUMO, total electron density and Fukui functions (see Appendix I). These properties were compared with those of the two alcohols mentioned above. The comparisons were done visually, which means that there were no values connected to the observations.

All the calculations were done using the method as described in Chapter 4 (§4.2.2).

As mentioned in the literature reviews (Chapter 2 and 3) the HOMO of the alcohol overlaps with the LUMO of the ruthenium complex during the coordination of the alcohol to the ruthenium metal in **4**.

This means the form and orientation of the HOMO around the oxygen and nitrogen atoms of the alcohol are very important because they are, together with the LUMO of the ruthenium metal, necessary to form bonds when the ligand coordinates to **4**. It is also important to calculate the total electron density map in combination with the electrophilic Fukui function because it indicates where the electron rich and electron poor centers in the alcohol are. If the oxygen or nitrogen atoms are shown to be electron rich, it will be possible for the alcohol to form bonds with the ruthenium complex.

During the comparison of the calculated properties of **9** and **36**, the HOMO's, their directions around the O and N atoms, the LUMO's in the pyridine ring and the direction of the LUMO's around the O atom (see **Figures 5.1** and **5.2**) were compared.

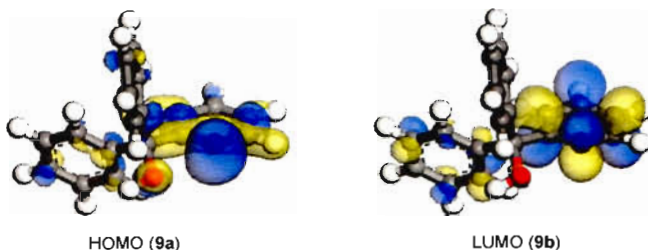


Figure 5.1: HOMO and LUMO of **9**

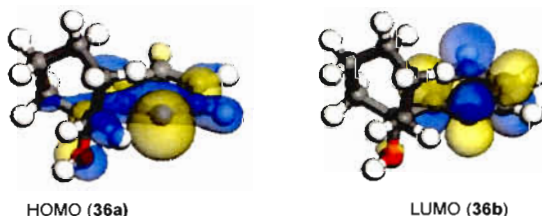


Figure 5.2: HOMO and LUMO of **36**

The HOMO and LUMO around the nitrogen atom looked almost identical in both alcohols, but the HOMO and LUMO around the oxygen looked different. In the case of **9**, the most electron rich part as shown by the electron density map combined with the electrophilic Fukui function (**Figure 5.3**) was found around the nitrogen atom (a red spot), a less electron rich part was found around the oxygen atom (a yellow spot) whilst the rest of the molecule remained neutral (blue, green or slightly yellow). In the case of **36**, the electron rich part around the oxygen appeared to be more yellow and the rest of the ligand generally appeared more electron rich than **9** (more yellow instead of green/blue). This could be because the cyclohexyl group of **36** is more electron withdrawing due to the inductive effect of an alkyl group which leads to a more electron rich oxygen atom and, because of the resonance effect of the two phenyl groups of **9**, electrons are more delocalized. This corresponds with the location of the HOMO's of the alcohols.

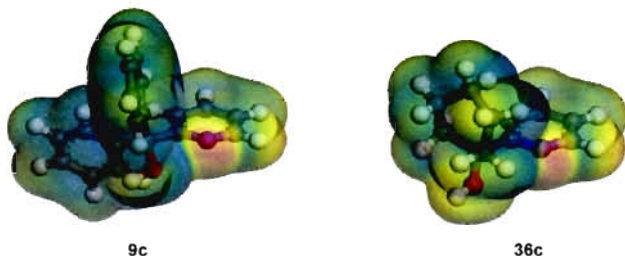


Figure 5.3: Electron density with electrophilic Fukui function of **9** and **36**

Coordination of an alcohol to **4** consists of two steps; removal of the hydrogen atom from the alcohol group so that a negatively charged oxygen atom is obtained and reacting this to **4**. In the first step, butyl lithium is added to the alcohol to remove the hydrogen atom which changes the slightly electron rich oxygen atom into a strongly electron rich O^- atom (Figure 5.4). Then **4** is added and a strong bond is formed between the ruthenium and the oxygen while a weaker bond forms between the ruthenium and the nitrogen so that this alcohol can behave like a hemilabile ligand.

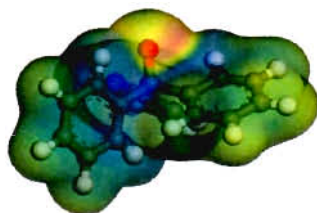


Figure 5.4: Electron density with the electrophilic Fukui function of **9** with an O^- atom

Since the only difference between **9** and **36** is the kind of R group that is attached, it can be concluded that this difference in R groups has to be the reason why **36** was less active for metathesis than **9**.

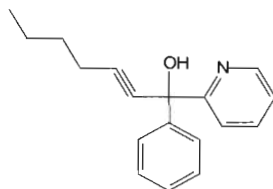
It was important to compare the position and size of the two different R groups, because the R groups are responsible for the sterical hindrance around the nitrogen and oxygen atoms. The orientation as well as the size of the R groups of the hemilabile ligand determine whether this ligand is favourably orientated for complexation to the metal. When these R groups are very bulky, the nitrogen and oxygen atoms are so sterically hindered that they cannot form bonds with the ruthenium complex, the HOMO of the alcohol will not overlap with the LUMO of the ruthenium complex. The cyclohexyl group of **36** is much smaller than the two bulky

phenyl groups of **9** and the O-C-N dihedral angle between the oxygen and nitrogen atoms of **9** is -35.38° where **36** is -81.54° . This means that the cyclohexyl group in **36** changed the position of the oxygen atom and this changed the orientation of the orbitals (see **Figure 5.2**).

In the following section 8 of the 202 alcohols, the best and the worst alcohol of each of 4 subdivisions, will be discussed and compared with **9** and **36**. The last two subdivisions can not act as hemilabile ligands and will thus not be discussed further.

- **Two examples from the subdivision of alcohols with two different R groups**

1-Phenyl-1-pyridyl-2-heptyn-1-ol (**30**)



30

The HOMO and LUMO as shown in **Figure 5.5** were compared with the HOMO and LUMO of **9** (**Figure 5.1**) and **36** (**Figure 5.2**). It was found that the HOMO around the nitrogen atom looked identical to **9a** and **36a**, and the HOMO around the oxygen was in almost the same direction as the HOMO of **9**. The same trend was observed for the LUMO.

According to these observations, this alcohol has similar or even better electronic properties than **9**.

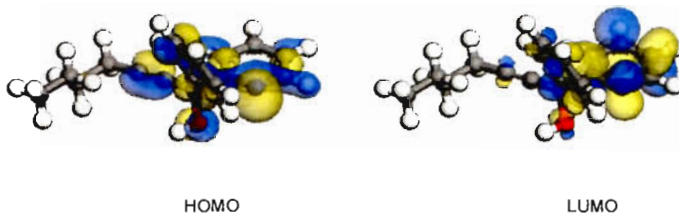


Figure 5.5: HOMO and LUMO of **30**

The electron rich parts of the electrophilic Fukui function (Figure 5.6) around the nitrogen looks the same as that of **9c** (Figure 5.3), but the rest of the molecule is too electron rich, even more electron rich than **36c**.

In comparison to **36**, this alcohol (with the two bulky R groups) is more bulky than the cyclohexyl group of **36**. The bulkiness of this alcohol is similar to that of **9c**, however the phenyl ring is situated closer to the oxygen atom which may lead to more sterical hindrance and the O-C-C-N dihedral angle between the oxygen and nitrogen atoms is -55.80° , where **9** is -35.38° and **36** is -81.54° .

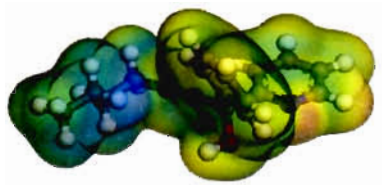
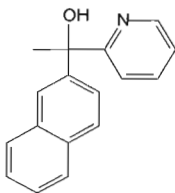


Figure 5.6: Electron density with electrophilic Fukui function of **30**

1-Naphthalen-1-yl-1-pyridin-2-yl ethanol (**37**)



37

The HOMO and LUMO as shown in Figure 5.7 were compared with the HOMO and LUMO of **9** (Figure 5.1) and **36** (Figure 5.2). It was found that the HOMO is more concentrated in the naphthalene part of the alcohol than on the nitrogen and oxygen atoms. The same trend was observed for the LUMO's.

According to these observations, this alcohol will not have similar electronic properties as **9** or **36**.

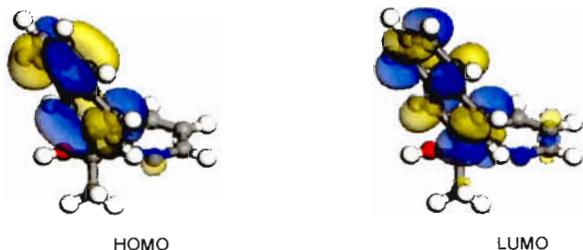


Figure 5.7: HOMO and LUMO of **37**

As expected from the observations above, the electrophilic Fukui function (**Figure 5.8**) also differs from both **9c** and **36c** (**Figure 5.3**). The electron rich part is more concentrated on the naphthalene group and not around the nitrogen and oxygen atoms as in **9c** or **36c**. The electrons are delocalized.

The bulkiness of this alcohol is different from the bulkiness of **9c** or **36c**. The naphthalene group is very bulky, whereas the methyl group is very small and the O-C-C-N dihedral angle between the oxygen and nitrogen atoms of this alcohol is -164.01° where **9** showed an angle of -35.38° and **36** of -81.54° . Because this bulky group is in the opposite direction from the oxygen and nitrogen atoms, this difference is not necessarily a disadvantage.

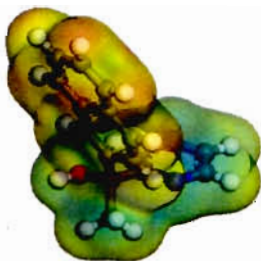


Figure 5.8: Electron density with electrophilic Fukui function of **37**

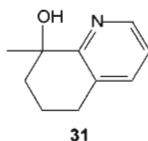
Overall discussion of alcohols in this subdivision with two different R groups

In this subdivision the results of the HOMO, LUMO and electrophilic Fukui function vary for almost each ligand. What they look like depends on the kind of R groups that are attached. When electron withdrawing R groups are used, the nitrogen and oxygen

atoms will be more electron poor, which makes it probably impossible for them to form bonds with the ruthenium complex. However, when electron donating groups are used, the nitrogen and oxygen atoms will be electron rich, which makes this alcohol suitable as a possible ligand for the ruthenium complex. When the R groups are less bulky there will be less sterical hindrance, which makes it easier for the HOMO's of the alcohol to overlap with the LUMO's of the ruthenium complex to form a bond. When, however, the R groups change the direction of the oxygen atom and so the orientation of the orbitals in respect to the orbitals of the nitrogen atom, it will be difficult for both HOMO's to overlap with the LUMO's of the ruthenium complex.

- **Two examples from the subdivision of alcohols where R_2 is connected to the pyridine ring by another type of ring**

8-Methyl-5,6,7,8-tetrahydroquinolin-8-ol (31)



The HOMO and LUMO as shown in **Figure 5.9** were compared with the HOMO and LUMO of **9** (**Figure 5.1**) and **36** (**Figure 5.2**). It was found that the HOMO around the nitrogen atom looked identical to **9a** and **36a** and the HOMO around the oxygen was in almost the same direction as the HOMO of **9**. Both LUMO's looked identical to **9b**.

According to these observations, this alcohol has similar or even better electronic properties than **9**.

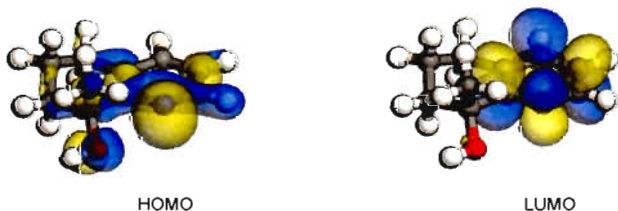


Figure 5.9: HOMO and LUMO of 31

The electron rich parts of the electrophilic Fukui function (**Figure 5.10**) around the nitrogen looks the same as that of **9c** (**Figure 5.3**), but the oxygen atom looked similar to the more electron rich **36c**.

The bulkiness of this alcohol is slightly different than the bulkiness of **9c**, because of the smaller R groups of this alcohol and the O-C-C-N dihedral angle between the oxygen and nitrogen atoms is -51.70° , where **9** showed an angle of -35.38° and **36** of -81.54° . This means that the oxygen and nitrogen atoms are less sterically hindered. In combination with the right orientation of the orbitals around the oxygen and nitrogen atoms as explained above, this can make it easier for **4** to coordinate to this alcohol.

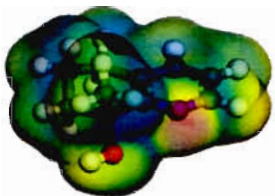
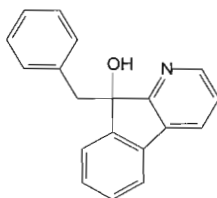


Figure 5.10: Electron density with electrophilic Fukui function **31**

9-Benzyl-1-azafluoren-9-ol (**38**)



38

The HOMO and LUMO as shown in **Figure 5.11** were compared with the HOMO and LUMO of **9** (**Figure 5.1**) and **36** (**Figure 5.2**). It was found that the HOMO around the pyridine ring differed from both **9** and **36**. The HOMO around the oxygen atom was also different because the benzyl group has changed the position of the oxygen atom and this changed the orientation of the orbitals more in the direction of **36**. The O-C-C-N dihedral angle between the oxygen and nitrogen atoms of this alcohol is -64.68° where **9** showed an angle of -35.38° and **36** showed an angle of -81.54° . The LUMO were spread over the three rings instead of being concentrated

on the nitrogen as seen in **9b** and **36b**. The orientations around the oxygen also changed due to the benzyl group.

According to these observations this alcohol will not have similar electronic properties than **9** or **36**.

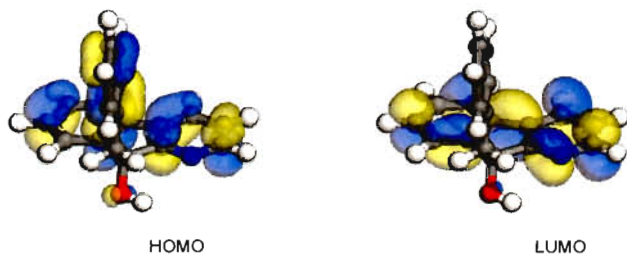


Figure 5.11: HOMO and LUMO of **38**

The bulkiness of this alcohol seen in the electrophilic Fukui function (**Figure 5.12**) looked the same as that of **9c** (**Figure 5.3**).

The electron rich part is not concentrated on the nitrogen and oxygen atoms as in **9c** or **36c**, but spread over the whole molecule. The electrons are delocalized.

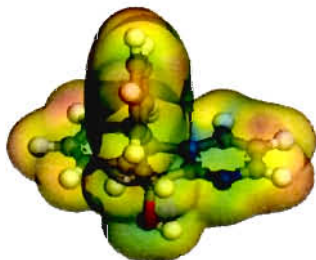


Figure 5.12: Electron density with electrophilic Fukui function **38**

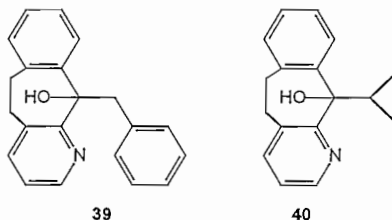
Overall discussion of alcohols in this subdivision where R_2 is connected to the pyridine ring by another type of ring

In this subdivision, the results of the HOMO, LUMO and Fukui function vary, depending mostly on the kind of rings that attach R_2 to the pyridine ring. This is probably because the strain/aromaticity in the different kind of rings is not the same.

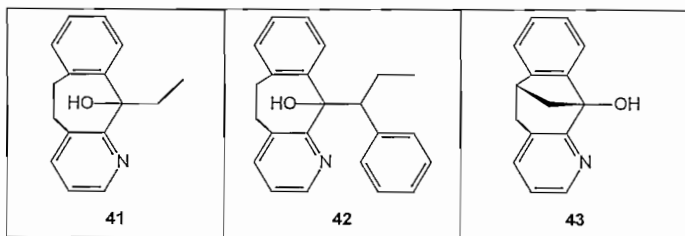
The alcohols where R_2 is connected to the pyridine ring by a cyclopentyl ring show almost identical HOMO's and LUMO's as 38. The Fukui function looks the same, but the bulkiness depends on the kind of R_1 group that is attached to the alcohol.

For alcohols where R_2 is connected to the pyridine ring, by a cyclohexyl ring the HOMO, LUMO and Fukui function looked generally the same as 9, but here the bulkiness also depends on the kind of R_1 group that is attached to the alcohol.

The third type of alcohol in this subdivision that was examined were alcohols where a cycloheptyl ring attached the R_2 with the pyridine ring. The following two alcohols appeared to be almost identical to 9: 11-Benzyl-6,11-dihydro-5H-benzo[5,6]-cyclohepta[1,2-b] pyridine-11-ol (39) and 11-Isopropyl-6,11-dihydro-5H-benzo[5,6]-cyclohepta[1,2-b] pyridine-11-ol (40) (see Appendix I).



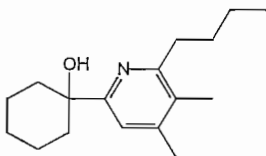
The three other alcohols left in this subdivision are: 11-Ethyl-6,11-dihydro-5H-benzo[5,6]cyclohepta[1,2-b] pyridine-11-ol (41), 11-(1-Phenyl-propyl)-6,11-dihydro-5H-benzo-[5,6] cyclohepta[1,2-b] pyridin-11-ol (42) and 11-Hydroxy-6,11-dihydro-6,11-methano-5H-benzo[5,6]cyclohepta[1,2-b]pyridine (43) (see Appendix I). The HOMO's of these alcohols looked the same as the HOMO of 37 (Figure 5.7). However, the LUMO's and the Fukui function appeared to be almost the same as 9c. Generally the bulkiness around these alcohols looked like 9.



As mentioned before, the alcohols where the pyridine is attached to R_2 by a cyclohexyl ring were shown to be almost identical to 9. According to this it is likely that the ligands from this subdivision will behave similar or even better than 9.

- *Two examples from the subdivision of alcohols with a methyl or short chain attached to the pyridine ring*

1-(6-Butyl-4,5-dimethyl-pyridin-2-yl)cyclohexanol (32)



32

The HOMO and LUMO as shown in Figure 5.13 were compared with the HOMO and LUMO of 9 (Figure 5.1) and 36 (Figure 5.2). It was found that the HOMO around the nitrogen atom looked identical to 9a and 36a, but the HOMO around the oxygen did not look the same as 9a or 36a. The reason for this is that the cyclohexyl group has changed the position of the oxygen atom and this changed the orientation of the orbitals. The O-C-C-N dihedral angle between the oxygen and nitrogen atoms of this alcohol is -57.42° where 36 showed an angle of -81.54° and 9 of -35.38° . The LUMO around the nitrogen looked the same as 9, but around the oxygen the orientation changed due to the cyclohexyl group that changed the position of the oxygen. This alcohol will not have similar electronic properties as 9 or 36.

Since this type of ligands have to act as hemilabile ligands which coordinate to 4 with a strong bond between the oxygen and ruthenium and a weaker bond between the nitrogen and ruthenium. It is not possible for the HOMO around the oxygen and the HOMO around the nitrogen to overlap with the LUMO of 4 to form bonds. Because if this alcohol coordinate to 4 with a ruthenium-nitrogen bond (or ruthenium-oxygen bond), it will act like a monodentate ligand instead of a hemilabile ligand.

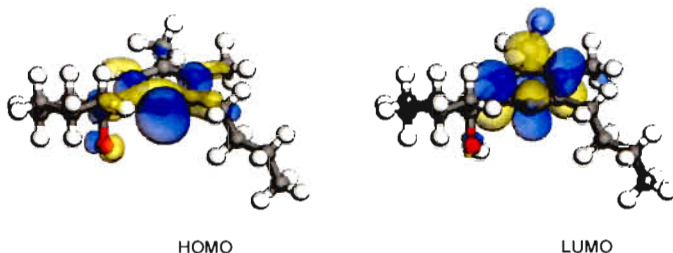


Figure 5.13: HOMO and LUMO of **32**

The electron rich parts of the electrophilic Fukui function (**Figure 5.14**) were concentrated around the nitrogen and oxygen as seen for **9c** (**Figure 5.3**).

The bulkiness of this alcohol was different from the bulkiness of **9c**. The cyclohexyl group was not as bulky as the two phenyl groups of **9** and after comparing this ligand with **36**, it was found that the cyclohexyl group of this ligand was pointed in a different direction than that of **36**. The groups attached to the pyridine ring made this ligand more bulky than **9** and **36**. The small chain attached to the pyridine was situated close to the nitrogen atom which can lead to sterical hindrance. The small methyl groups attached to the pyridine ring were not in a position where they could lead to sterical hindrance.

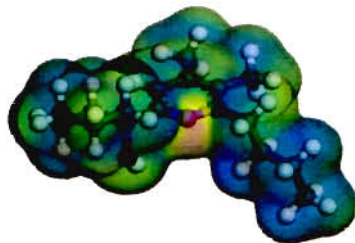
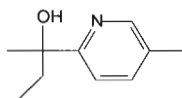


Figure 5.14: Electron density with electrophilic Fukui function of **32**

2-(5-Methyl-pyridin-2-yl)-butan-2-ol (44)



44

The HOMO and LUMO as shown in **Figure 5.15** were compared with the HOMO and LUMO of **9** (**Figure 5.1**) and **36** (**Figure 5.2**). It was found that the HOMO around the pyridine ring looked different because they were more concentrated on the two R groups and the oxygen atom. The orbitals around the oxygen also looked different because the small R groups changed the orientation of the oxygen atom. The O-C-C-N dihedral angle between the oxygen and nitrogen atoms of this alcohol is -1.67° where **9** showed an angle of -35.38° and **36** of -81.54° . The LUMO around the nitrogen looked the same as **9** and **36**, but around the oxygen no orbital could be observed.

According to these observations, this alcohol will not have similar electronic properties as **9** or **36**.

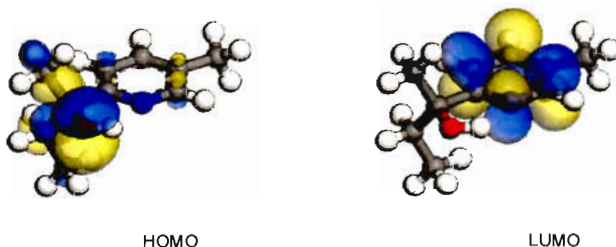


Figure 5.15: HOMO and LUMO of **44**

The bulkiness of this alcohol (**Figure 5.16**) was different from the bulkiness of both **9c** and **36c** (**Figure 5.3**) because of the smaller R groups of this alcohol.

The electron rich part is not concentrated on the nitrogen atom as in **9c** and **36c**, and the electron rich part around the oxygen is very strong. So when coordinating this alcohol to **4**, it is most likely that the HOMO around the oxygen atom will overlap with the LUMO of the ruthenium complex to form a strong bond, but around the nitrogen

atom no HOMO is available to form a bond. For this reason the ligand will not be able to act as a hemilabile ligand.

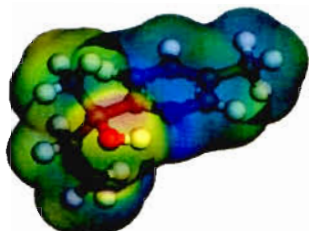


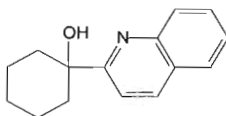
Figure 5.16: Electron density with electrophilic Fukui function of **44**

Overall discussion of alcohols in this subdivision with a methyl or short chain attached to the pyridine ring

When a small group like methyl is attached to the pyridine ring, it would not influence the properties of an alcohol because the steric hindrance around the nitrogen atom is low. But with a pentyl group attached close to the nitrogen, the steric hindrance will be larger which will make it harder for the alcohol to coordinate to **4**. Steric hindrance around the oxygen atom depends on the kind of R groups that are attached to the ligand. When the oxygen or nitrogen atom of an alcohol is sterically hindered and the other atom has the possibility to coordinate to **4**, it is possible that such a ligand will not act as a hemilabile ligand but as a monodentate ligand.

- **Two examples from the subdivision of alcohols with a phenyl group attached to the pyridine**

1-[2]-quinolyl- cyclohexanol (**33**)



33

The HOMO and LUMO as shown in **Figure 5.17** were compared with the HOMO and LUMO of **9** (**Figure 5.1**) and **36** (**Figure 5.2**). It was found that the HOMO around the

nitrogen atom looked the same, but the HOMO around the oxygen was orientated differently due to the cyclohexyl group that changed the position of the oxygen. The O-C-C-N dihedral angle between the oxygen and nitrogen atoms of this alcohol is 123.57° where **9** showed an angle of -35.38° and **36** of -81.54° . The LUMO around the pyridine was different from that of **9b** (Figure 5.1) and **36b** (Figure 5.2), because the orbitals were spread over the two rings. Around the oxygen the LUMO was orientated differently due to the cyclohexyl group that changed the position of the oxygen.

According to these observations, this alcohol does not have similar electronic properties than **9** or **36**.

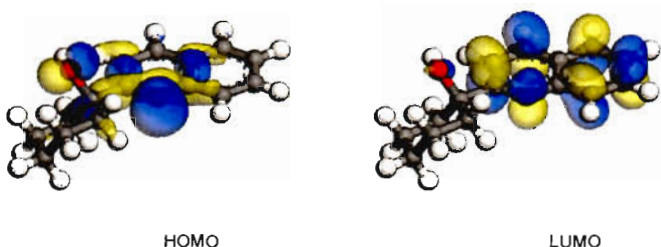


Figure 5.17: HOMO and LUMO of **33**

The electron rich parts of the electrophilic Fukui function (Figure 5.18) were concentrated around the nitrogen and oxygen as seen for **9c** (Figure 5.3).

The bulkiness of this alcohol was different from the bulkiness of **9c** because of the cyclohexyl group of this alcohol. However, from the left side of the pyridine ring it looked identical to **36c**. The phenyl group attached to the pyridine ring is situated close to the nitrogen atom which will make the steric hindrance around the nitrogen atom higher than that of **9c** and **36c** (Figure 5.3).

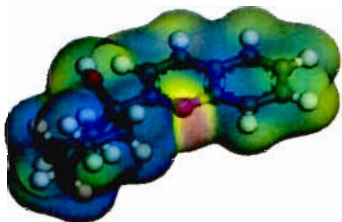
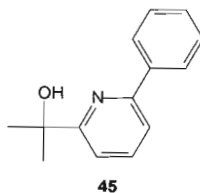


Figure 5.18: Electron density with electrophilic Fukui function of **33**

2-(6-phenyl-pyridin-2-yl) propan-2-ol (**45**)



The HOMO and LUMO as shown in **Figure 5.19** were compared with the HOMO and LUMO of **9** (**Figure 5.1**) and **36** (**Figure 5.2**). It was found that the HOMO around the pyridine ring as well as around the oxygen looked different because the two small R groups have changed the position of the oxygen atom which changed the orientation of the HOMO. The O-C-C-N dihedral angle between the oxygen and nitrogen atoms of this alcohol is 173.17° where **9** showed an angle of -35.38° and **36** of -81.54°. The LUMO were spread over the two rings instead of being concentrated on the nitrogen as seen in **9** and **36**. No LUMO was observed around the oxygen atom.

According to these observations this alcohol will not have similar electronic properties as **9** or **36**.

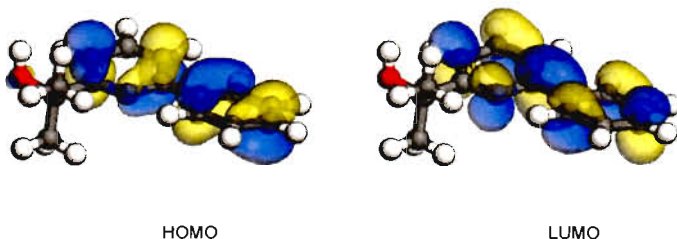


Figure 5.19: HOMO and LUMO of **45**

As expected from the observation above, the Fukui function (**Figure 5.20**) also differs from **9c** and **36c**. The electron rich parts are not concentrated on the nitrogen and oxygen atoms as in **9** or **36**, but concentrated on the benzyl group as well as the pyridine ring which is the result of delocalisation which can occur in those groups.

The bulkiness of this alcohol as seen in the electrophilic Fukui function (**Figure 5.20**) was completely different from the bulkiness of **9c** (**Figure 5.3**) or **36c** because of the smaller R groups on the left side of this alcohol, but also because of the large benzyl group attached to the right side of the alcohol. Due to the steric hindrance of the benzyl group and the position of the oxygen and nitrogen atoms, it is impossible for this alcohol to coordinate to **4** as a hemilabile ligand.



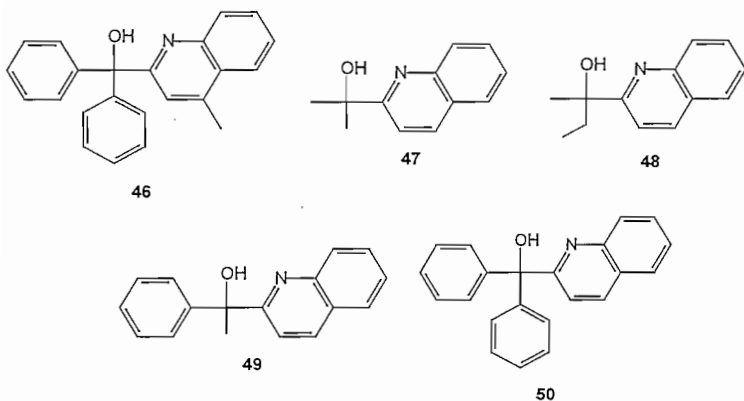
Figure 5.20: Electron density with electrophilic Fukui function of **45**

Overall discussion of alcohols in this subdivision with a phenyl group attached to the pyridine

This subdivision can be divided in two different groups: alcohols where the phenyl group is attached to the pyridine as a benzyl group or alcohols where the phenyl and pyridine ring share a bond.

The alcohols where the phenyl group is attached to the pyridine as a benzyl group shows about identical HOMO's and LUMO's as **45** (Figure 5.19). The electrophilic Fukui function also looks the same although the bulkiness depends on the kind of R groups that are attached to the ligand and the position of the benzyl group on the pyridine ring.

The HOMO and LUMO orbitals of the alcohols where the phenyl and pyridine ring share a bond were spread over the two rings and the electron rich part of the electrophilic Fukui function was not concentrated on the nitrogen and oxygen atoms as seen for **9c** or **36c** (Figure 5.3), but spread over the whole molecule because of delocalization. However, in this small group of alcohols there were some exceptions because especially the HOMO and electrophilic Fukui function of (4-methyl-quinolin-2-yl)-diphenyl methanol (**46**), 2-quinolin-2-yl-propan-2-ol (**47**), 2-[2]-quinolyl-butan-2-ol (**48**), 1-[2]-quinolyl-1-phenyl ethanol (**49**) and [2]-quinolyl-diphenyl methanol(**50**) looked different. For these alcohols it was possible to see the electron rich parts of the electrophilic Fukui function around the oxygen and nitrogen atoms and the HOMO also looked the same as the HOMO of **9** (Figure 5.1).



Summary after screening of the 202 alcohols

After the screening it was found that, when electron withdrawing groups were attached to the alcohol, the electron rich parts were concentrated on these groups instead of being concentrated around the nitrogen and oxygen atoms. This leads to small HOMO's around these atoms which makes it very hard for these alcohols to form bonds with the ruthenium complex. When the R groups are electron donating like in **9**, the electron rich parts can be

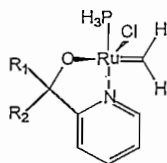
found around the nitrogen and oxygen atoms which results in larger HOMO's and a possibility to form bonds with the ruthenium complex. The O-C-C-N dihedral angle was also found to be important because when this differs too much from 9, the orientation of the orbitals changed so that it became difficult to form bonds. The bulkiness of the R groups was also an important factor to find alcohols which have similar or better properties than **9**, because when the R groups are too bulky the oxygen and nitrogen atoms will be sterically hindered so that it is impossible for the HOMO to overlap with the LUMO of the ruthenium complex.

After all these factors were taken into consideration, 41 alcohols from the 4 subdivisions were identified to be comparable to **9** (Table 5.1).

Table 5.1: The 41 alcohols after the first screening with their subdivisions

Number of ligands left after first screening	Name of subdivision
24	Ligands with two different R groups
4	Ligands where R ₂ is connected to the pyridine ring by another type of ring
11	Ligands with a methyl or small chain attached to the pyridine ring
2	Ligands with a phenyl group attached to the pyridine

These alcohols were coordinated to a simplified Grubbs pre-catalyst (**51**) as ligands and modeled again for the second screening.



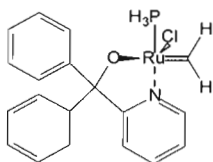
51

5.1.3 Modelling and screening of 41 simplified Grubbs pre-catalysts

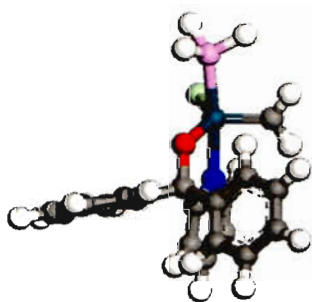
The 41 simplified Grubbs pre-catalysts (**51**) were geometrically optimized. The same optimization method was used as in the first screening (Chapter 4, §4.2.2). The HOMO, LUMO, electron density and nucleophilic Fukui functions were calculated. The results were visually compared with the HOMO, LUMO and Fukui functions of **9** and **36**, when coordinated as shown in **51**.

If a dissociative mechanism is assumed in an alkene metathesis reaction, the hemilabile ligand of the complex will open up after which the incoming alkene coordinates to the active site on the ruthenium atom. The HOMO of the alkene overlaps with the LUMO of the carbene to form the metallacyclobutane intermediate (Chapter 2). This means the form and orientation of the LUMO around the carbene group of **51** is very important because they are, together with the HOMO of the alkene, necessary to undergo a metathesis reaction. It is also important to calculate the total electron density map in combination with the nucleophilic Fukui function because it indicates where the electron rich (blue) and poor (red) centers in the complex are. If the metal in the metal carbene group is electron poor, it will be possible for the LUMO of the metal carbene to overlap with the HOMO of the alkene. The electron density is also important to see whether the R groups of the ligand will have an influence on the steric hindrance as well as the position of the orbitals of the metal carbene group.

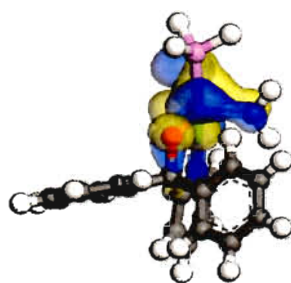
During the comparison of the calculated properties of **9** and **36** when coordinated as shown in **51** (**52** and **53**), the HOMO, LUMO and their orientation and shape around the ruthenium atom as well as the metal carbene were compared. However, because the oxygen, chlorine and phosphorus atoms, as well as the pyridine ring were close to the metal carbene, those HOMO's and LUMO's were compared as well (Figures 5.21 and 5.22).



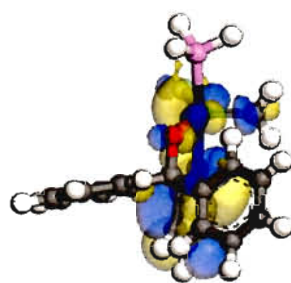
52



52 (3d-structure)

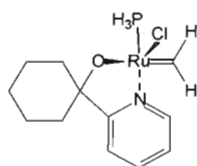


HOMO

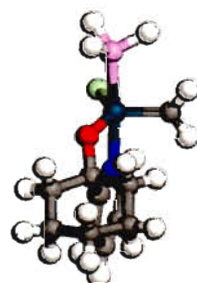


LUMO

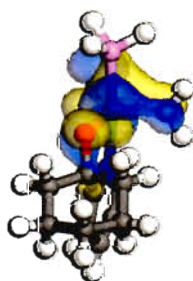
Figure 5.21: HOMO and LUMO of 52



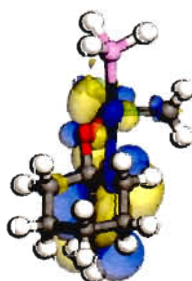
53



53 (3d-structure)



HOMO



LUMO

Figure 5.22: HOMO and LUMO of 53

The HOMO of **52** appeared to be slightly smaller around the metal carbene group as well as the oxygen atom and around the phosphorus atom the HOMO looked larger in this complex. The LUMO around the carbene did not look the same in both complexes. In **52**, the LUMO around the ruthenium was larger than in **53** and also the orientation of this orbital did not look the same. The same phenomenon was observed for the LUMO around the carbon atom of the metal carbene. Since the metathesis reaction occurs at the ruthenium carbene group and different carbene LUMO's were obtained for both complexes, this might be the reason why **53** was not as active for metathesis as **52**.

For **52**, the most electron poor parts, as shown by the electron density map combined with the nucleophilic Fukui function (Figure 5.23), were found around the pyridine ring (slightly red/yellow), the phosphorus atom (yellow) and the metal carbene group (yellow), while the rest of the complex remained neutral (green). For **53**, the electron poor parts around the pyridine ring, the phosphorus atom as well as the metal carbene group were less electron poor (Figure 5.23). This corresponds with the location of the LUMO of the complexes.

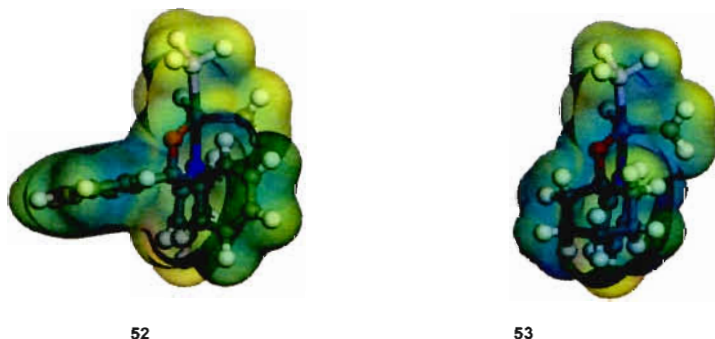


Figure 5.23: Electron density with nucleophilic Fukui function of **52** and **53**

The bulkiness of the ligands was also important to compare, because when the ligand is too bulky the metathesis reaction will slow down due to steric hindrance. It is also important that the coordinated ligand is not too small, because then it is possible that the incoming alkene will not be guided well enough to the active site which can have an influence on the selectivity of the catalyst.

Some differences in the bond lengths and angles are summarized in Table 5.2. It was found that the bond lengths and angles were the same for both simplified complexes, but the dihedral angles were different because of the different R groups attached to the complexes.

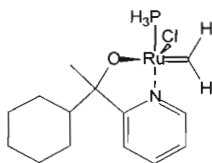
Table 5.2: Angles (°) and bond distances (Å) of **52** and **53**

	52	53
Ru-N	2.1	2.1
Ru-P	2.3	2.3
Ru-C	1.9	1.9
O-Ru-N	80.2	79.4
C-O-Ru	117.6	117.0
Ru-N-C	114.0	113.9
C-Ru-P	91.4	90.7
O-C-C-N	13.3	20.7

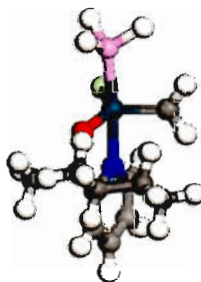
In the following section the best and worst simplified Grubbs pre-catalysts (**51**) with ligands from each sub division will be discussed and compared with **52** and **53**.

- **Two examples from the subdivision of ligands with two different R groups**

Simplified complex with 1-cyclohexyl-1-[2]-pyridyl ethanol ligand (**54**)

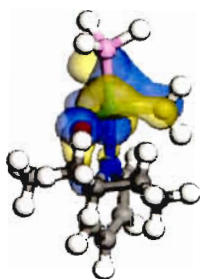


54

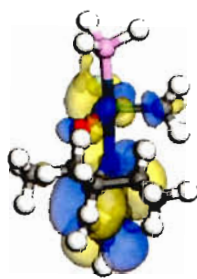


54 (3d-structure)

The HOMO and LUMO as shown in **Figure 5.24** were compared with the HOMO and LUMO of **52** (**Figure 5.21**) and **53** (**Figure 5.22**). It was found that the HOMO looked almost identical to that of **52** and the LUMO around the phosphorus atom was larger than in **52** and **53**. The LUMO around the ruthenium atom was orientated in a slightly different direction than that of **52** and the LUMO around the carbon atom of the carbene looked identical to **52**.



HOMO



LUMO

Figure 5.24: HOMO and LUMO of **54**

The nucleophilic Fukui function (Figure 5.25) was the same as that of **52** (Figure 5.23). The bulkiness of the one bulky group and one small group of the coordinated ligand looked a little different than the two bulky groups of **52**, but it looked totally different than the cyclohexyl group of **53**.

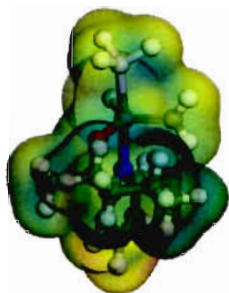
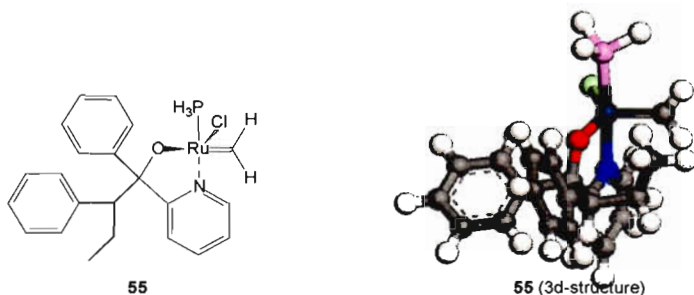


Figure 5.25: Electron density with nucleophilic Fukui function of **54**

According to these observations, **54** has similar or even better electronic properties than **52**.

Simplified complex with 1,2-diphenyl-1-pyridin-2-yl-butan-1-ol ligand (55)



The HOMO and LUMO as shown in **Figure 5.26** were compared with the HOMO and LUMO of **52** (**Figure 5.21**) and **53** (**Figure 5.22**). Although the HOMO around the carbene looked identical to that of **52**, it was found that the orientation of the HOMO around the oxygen atom looked different from that of **52** or **53**. The same was observed for the LUMO; the orientation of the LUMO around the oxygen atom as well as the LUMO around the phosphorus-ruthenium bond looked different.

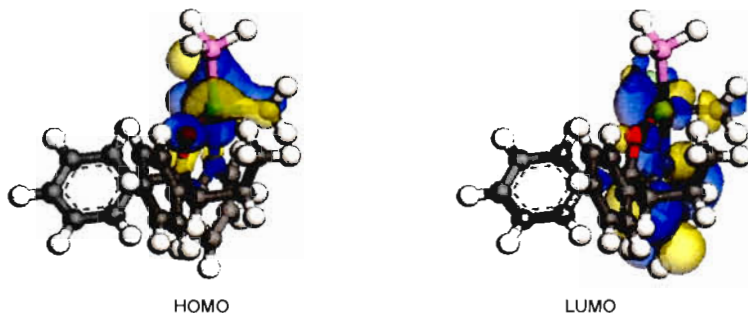


Figure 5.26: HOMO and LUMO of 55

Although the nucleophilic Fukui function (**Figure 5.27**) around the carbene and oxygen atom was similar to that of **52** (**Figure 5.23**), the phosphorus atom was too electron poor (more yellow and green colours instead of blue). The bulkiness looked different too because the bulky groups were orientated in a different direction than the two phenyl groups of **52**.

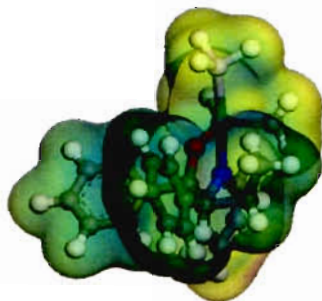


Figure 5.27: Electron density with nucleophilic Fukui function of **55**

According to these observations it is impossible that this complex will have similar electronic properties than **52** or **53**.

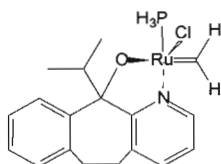
Overall discussion of ligands in this subdivision where two different R groups are attached

In this subdivision the results of the HOMO, LUMO and nucleophilic Fukui function vary for almost each ligand coordinated to **51**, mostly depending on the kind of R groups that are attached to the ligand. When electron withdrawing R groups are used, the carbene group will be more electron rich which makes it impossible to overlap (back bond) with the incoming alkene, but when electron donating groups are used the carbene group will be electron poor which makes it possible for the HOMO of the alkene to overlap with the LUMO of the carbene.

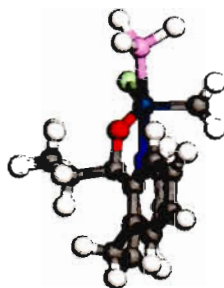
When the R groups are less bulky there will be less steric hindrance around the carbene, which makes it easier for the carbene LUMO of the complex to overlap with the HOMO of the incoming alkene to start a metathesis reaction. For the same reason, bulky R groups can cause steric hindrance so that it is not possible for the incoming alkene to overlap with the complex. However, when the R groups are not bulky at all it is also possible that the incoming alkene will not be guided well enough to the active site which can have an influence on the selectivity of the catalyst. Furthermore, when the LUMO is in a more sterically hindered position than it was in **52**, it can be difficult for the HOMO to overlap

- Two examples from the subdivision of ligands where R_2 is connected to the pyridine ring by another type of ring

Simplified complex with 11-isopropyl-6,11-dihydro-5H-benzo[5,6]cyclohepta[1,2-b]pyridine-11-ol ligand (**56**)

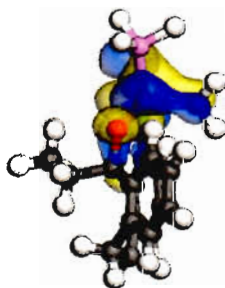


56

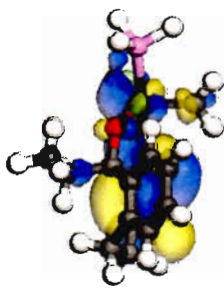


56 (3d-structure)

The HOMO and LUMO as shown in **Figure 5.28** were compared with the HOMO and LUMO of **52** (**Figure 5.21**) and **53** (**Figure 5.22**). It was found that the HOMO was almost identical to that of **52**. The LUMO, which was slightly smaller than that of **52**, looked larger around the phosphorus atom and the orientation of the LUMO around the oxygen atom was different too. The same was observed after comparison with **53**, except for the LUMO around the carbon carbene which looked larger than that of **53** and the LUMO around the ruthenium atom which looked identical to that of **53**.



HOMO



LUMO

Figure 5.28: HOMO and LUMO of **56**

The nucleophilic Fukui function (Figure 5.29) was shown to be the same as that of **52** (Figure 5.23), but the bulkiness looked slightly different because **56** has one bulky and one small group instead of the two smaller bulky groups of **52**.

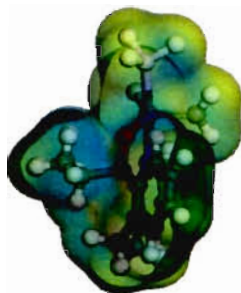
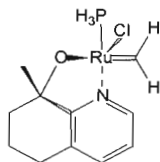


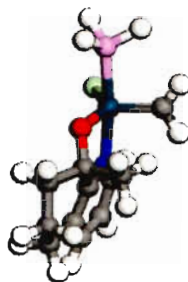
Figure 5.29: Electron density with nucleophilic Fukui function of **56**

According to these observations, it is impossible for this complex to have similar electronic properties than **52**. However, since the LUMO around the ruthenium looks similar than that of **53**, it is possible that **56** has similar electronic properties than **53**.

Simplified complex with 8-methyl-5,6,7,8-tetrahydroquinolin-8-yl ligand (**57**)



57



57 (3d-structure)

The HOMO and LUMO as shown in Figure 5.30 were compared with the HOMO and LUMO of **52** (Figure 5.21) and **53** (Figure 5.22). It was found that the HOMO around the nitrogen-ruthenium bond looked slightly different than that of **52**. The orientation of the LUMO around the ruthenium was different than **52** or **53**, and the LUMO

around the carbene carbon atom was identical to that of **53**. The LUMO around the phosphorus atom showed a small orbital which looked different from **52** or **53**.

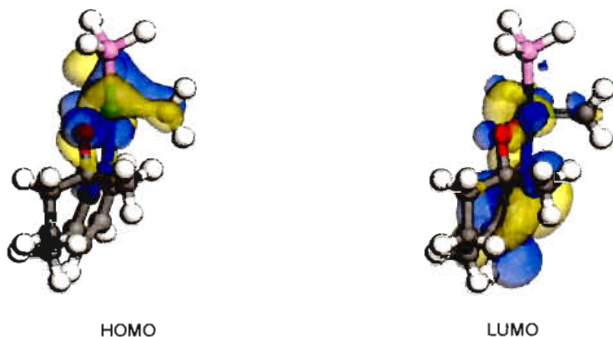


Figure 5.30: HOMO and LUMO of **57**

The nucleophilic Fukui function (**Figure 5.31**) was different than that of **52** (**Figure 5.23**), but it was very similar to **53**. The phosphorus atom and metal carbene were more electron rich compared to **52**. The bulkiness was also different because of the small R groups of this ligand.

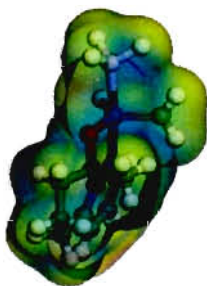


Figure 5.31: Electron density with nucleophilic Fukui function of **57**

According to these observations, it is impossible for this complex to have similar electronic properties than **52**, but it is possible that it has similar electronic properties than **53**.

Overall discussion of ligands in this subdivision where R_2 is connected to the pyridine ring by another type of ring

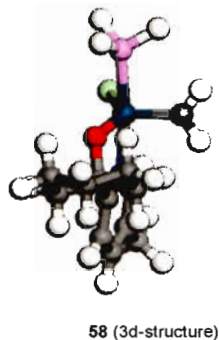
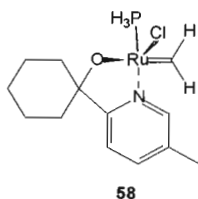
In this subdivision the results of the HOMO, LUMO and nucleophilic Fukui function vary depending on the kind of ring that attaches the pyridine and R_2 group. After the first screening only two subdivisions within this group were left; ligands where R_2 is connected to the pyridine ring by a cyclohexyl ring or where it is connected by a cycloheptyl ring.

For alcohols where R_2 is connected to the pyridine ring by a cyclohexyl ring the HOMO, LUMO and nucleophilic Fukui function looked generally the same as in **57** (Figure 5.30 and 5.31), but the bulkiness of the electron density function depends on the kind of R_1 group that is attached to the coordinated ligand.

For alcohols where R_2 is connected to the pyridine ring by a cycloheptyl ring the HOMO, LUMO and nucleophilic Fukui function looked generally the same as **56** (Figure 5.28 and 5.29). Here the bulkiness of the electron density function also depends on the kind of R_1 group that is attached to the coordinated ligand.

- **Two examples from the subdivision of ligands with a methyl or small chain attached to the pyridine ring**

Simplified complex with 1-(5-methyl-pyridin-2-yl) cyclohexanol ligand (**58**)



The HOMO and LUMO as shown in Figure 5.32 were compared with the HOMO and LUMO of **52** (Figure 5.21) and **53** (Figure 5.22). It was found that the HOMO and LUMO of this complex looked very similar to that of **53**. The only difference with this

complex was that the extra methyl group on the pyridine ring resulted in a larger LUMO around the phosphorus atom as well as around the carbene carbon, but not as large as that of **52**.

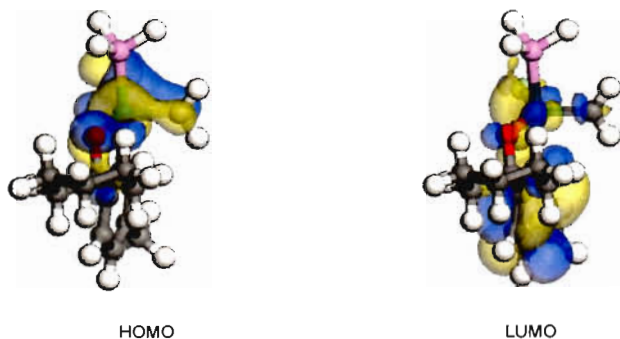


Figure 5.32: HOMO and LUMO of **58**

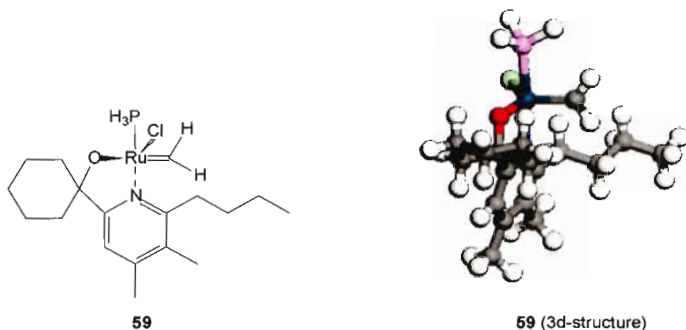
The nucleophilic Fukui function (Figure 5.33) also looked identical to that of **53** (Figure 5.23). Even the bulkiness looked very similar to **53**, but the cyclohexyl R group was pointed more upwards due to the extra methyl group on the pyridine ring.



Figure 5.33: Electron density with nucleophilic Fukui function of **58**

Since the extra methyl group of this complex resulted in a slightly larger LUMO around the carbon carbene group, this complex will behave better than **53** during a metathesis reaction. According to these observations it is found that the extra methyl group on the pyridine ring will increase the activity of **53**.

Simplified complex with 1-(6-butyl-4,5-dimethyl-pyridin-2-yl)cyclohexanol ligand (59)



The HOMO and LUMO orbitals as shown in **Figure 5.34** were compared with the HOMO and LUMO of **52** (**Figure 5.21**) and **53** (**Figure 5.22**). It was found that the HOMO around the nitrogen-ruthenium bond as well as the carbene carbon atom looked smaller than the HOMO's of both **52** and **53**. Although the LUMO's looked larger than that of **52** and **53**, the shape and orientations of the LUMO's around the ruthenium atom and carbon carbene looked totally different than that of both complexes.

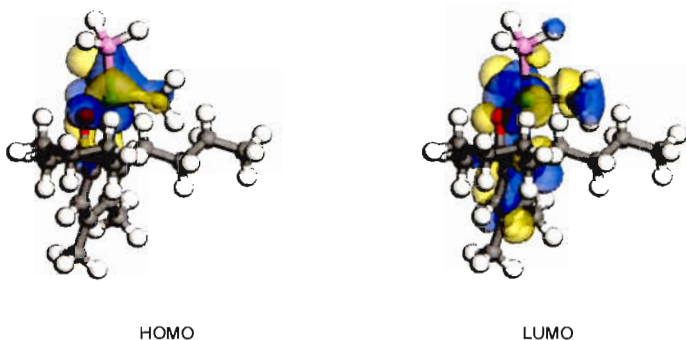


Figure 5.34: HOMO and LUMO of **59**

The nucleophilic Fukui function (**Figure 5.35**) was also different from that of **52** or **53** (**Figure 5.23**). The phosphorus atom as well as the carbon carbene was more electron poor (more yellow/red). Except for the bulky butyl chain which is attached to

the pyridine ring, the bulkiness looked very similar to that of **53**, but the carbene group was more sterically hindered due to this butyl chain.

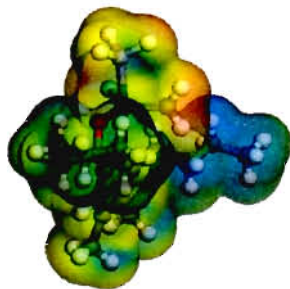


Figure 5.35: Electron density with nucleophilic Fukui function of **59**

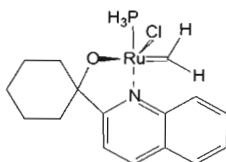
According to these observations, it is impossible that the butyl chain and the two methyl groups which are attached to the pyridine ring will improve the electronic properties of **53**.

Overall discussion of ligands in this subdivision where a methyl or small chain is attached to the pyridine ring

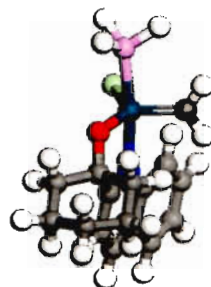
In this subdivision, the results of the HOMO for all the ligands were very similar. The differences in bulkiness depend on the size and position of the groups that are attached to the pyridine ring. When the R groups are not bulky, it is possible that the incoming alkene would not be guided well enough to the active site. However, when the R groups consist of a large chain (butyl group or larger), it will be difficult for the alkene to come in and overlap with the LUMO of the carbene due to steric hindrance. Steric hindrance around the carbene carbon can also result in a different orientation and shape of the LUMO. When the orientation of the orbitals has changed in comparison to **52**, it probably will be difficult to form these bonds and the activity of the complex during a metathesis reaction will be lower than that of **52**.

- Two examples from the subdivision of ligands with a phenyl group attached to the pyridine

Simplified complex with 1-[2]-quinolyl- cyclohexanol ligand (60)

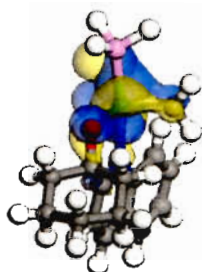


60

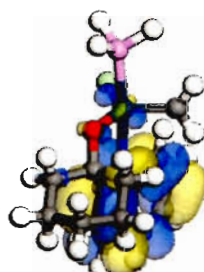


60 (3d-structure)

The HOMO and LUMO as shown in Figure 5.36 were compared with the HOMO and LUMO of 52 (Figure 5.21) and 53 (Figure 5.22). Although the HOMO around the carbene was smaller than that of 52 and 53 due to the electron withdrawing capacity of the quinoline group, the HOMO of the rest of the complex looked very similar to that of 52. The LUMO around the carbene carbon, phosphorus and chlorine atoms were not present at all and the LUMO around the ruthenium and oxygen atoms were very small and orientated in a different direction than that of both 52 and 53.



HOMO



LUMO

Figure 5.36: HOMO and LUMO of 60

The electron density function (Figure 5.37) was identical to that of **53** (Figure 5.23), but more electron rich in comparison to **52**. The bulkiness of this complex looked very similar to that of **53**. The only difference was the bulky quinoline group that is attached to the pyridine ring.

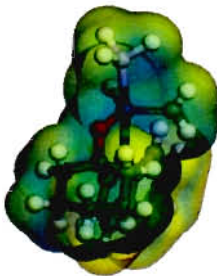
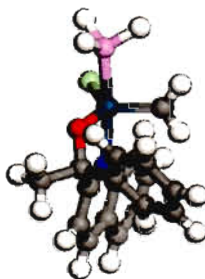
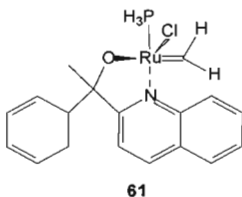


Figure 5.37: Electron density with nucleophilic Fukui function of **60**

According to these observations, it is impossible for this complex to have similar electronic properties than **52**. Since there is no LUMO around the carbene carbon, the quinoline group of this complex will not improve the electronic properties of **53**.

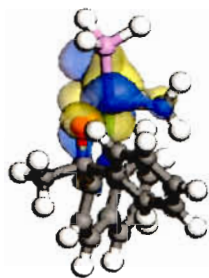
Simplified complex with 1-[2]-quinolyl-1-phenyl ethanol ligand (**61**)



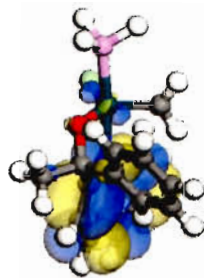
61 (3d-structure)

The HOMO and LUMO as shown in Figure 5.38 were compared with the HOMO and LUMO of **52** (Figure 5.21) and **53** (Figure 5.22). The HOMO around the carbene was smaller than that of both complexes due to the electron withdrawing capacity of the quinoline group and it was even smaller than **60** (Figure 5.36). The LUMO was

different than that of **52** and **53**. The LUMO around the carbene carbon, phosphorus and chlorine atoms were not present at all and the LUMO around the ruthenium and oxygen atoms were very small and orientated in a different direction. However, the LUMO of this complex was identical to that of **60**.



HOMO



LUMO

Figure 5.38: HOMO and LUMO of **61**

The electron density function (**Figure 5.39**) was more electron rich than that of **52** (**Figure 5.25**). The carbene and phosphorus atoms were more green instead of yellow, but more electron poor than **60** (**Figure 5.37**). Although the methyl R group is smaller than the phenyl R group of **52**, this complex is more bulky on the side of the complex where the bulky quinoline group is attached to the pyridine ring.

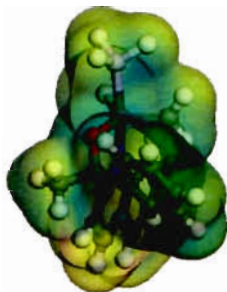


Figure 5.39: Electron density with nucleophilic Fukui function of **61**

Since there is no LUMO around the carbene carbon, the quinoline group of this complex will not improve the electronic properties of **52** and this complex will not behave better than **52** or **53** during a metathesis reaction.

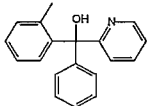
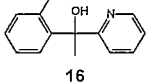
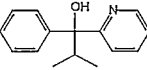
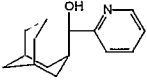
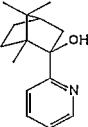
Overall discussion of ligands in this subdivision

After the first screening, only the subdivision of ligands where the phenyl group and pyridine ring share a bond was left within this group. The two ligands left in this subdivision were slightly different from each other due to the different R groups and are explained in the examples above.

Summary after screening of the simplified complexes

After comparison of all 4 subdivisions, it was found that most of the ligands that showed similar electronic properties than **52** came from the subdivision where the ligands with two different R groups were coordinated to **51**. After this screening, 5 ligands from this subdivision were chosen to be theoretically and experimentally investigated further (Table 5.3).

Table 5.3: The 5 chosen ligands that will be investigated further

IUPAC names:	Structure:
Phenyl-[2]-pyridyl-o-tolyl-methanol (15)	 15
1-[2]-pyridyl-1-o-tolyl-ethanol (16)	 16
2-methyl-1-phenyl-1-pyridin-2-yl-propan-1-ol (17)	 17
2-pyridin-2-yl-adamantan-2-ol (18)	 18
(1R,2R,4R)-2-exo-hydroxy-2-endo-(pyridine-2-yl)-1,7,7-trimethylbicyclo[2.2.1] heptane (19)	 19

Alcohols 15, 16 and 17 were chosen as ligands because their electronic properties were very similar to 9 in the first screening as well as in the second screening. The size and directions of the R groups is the only difference between these alcohols. The more sterically hindered the nitrogen and oxygen atoms are, the more difficult it becomes for the alcohol to coordinate to 4. When a bulky catalyst is tested in a metathesis reaction, the bulky R groups can either cause steric hindrance around the carbene, which can make it more difficult for the alkene to react with the carbene, or the bulky R groups can guide the incoming alkene to the active site. Of these 3 alcohols, 15 with the o-tolyl and phenyl R groups is the most bulky alcohol, even slightly more bulky than 9. 17 with the isopropyl and phenyl R groups is less bulky than 15 and 9. 16 with the o-tolyl and methyl R groups has the smallest R groups. In comparison to 36, all alcohols are larger than the cyclohexyl group of 36. It will be interesting to see how active catalysts where these type of ligands are coordinated to 4 will be in a metathesis reaction.

The other two alcohols 18 and 19 that were chosen to be investigated as ligands were not chosen because of their similar HOMO, LUMO and nucleophilic Fukui function to 9, but because of their differences in bulkiness or enantioselectivity. Because these alcohols have one R group, which is similar to the cyclohexyl group of 36, it is also interesting to compare these alcohols with 36.

Ligand 18 has a very bulky adamantane group which will cause a lot more steric hindrance around the nitrogen and oxygen atom of the ligand as well as the carbene group of the complex. It is most unlikely that this ligand will behave the same as 9, but it may be similar to 36. It will be interesting to see what influence this bulky ligand has in a metathesis reaction when coordinated to 4.

Ligand 19 also has a very bulky R group which will make it most unlikely that this ligand will behave the same as 9. The steric hindrance of this ligand is even more than that of the adamantane group of 18. Due to this steric hindrance it is unlikely that this ligand will behave the same as 36. Here it will also be interesting to see how the even larger R group of this ligand as well as the enantioselectivity will influence the activity in a metathesis reaction when coordinated to 4.

5.1.4 Modelling of 5 chosen ligands

5.1.4.1 Modelling of alcohols

- Alcohols 15, 16 and 17

After modelling 15, 16 and 17, the HOMO's and LUMO's as shown in **Figures 5.40**, **5.41** and **5.42** were compared with the HOMO and LUMO of **9** (**Figure 5.1**) and **36** (**Figure 5.2**). It was found that the HOMO's and LUMO's around the nitrogen and oxygen atoms looked almost identical to the HOMO and LUMO of **9**. Only **17** showed a small difference in the HOMO and LUMO, because the R groups changed the position of the oxygen atom which slightly changed the orientation of the orbitals. The O-C-C-N dihedral angle of this alcohol is -28.80° , where **36** has an angle of -81.54° and **9** of -35.38° . **15** showed an angle of -53.60° and **16** of -61.82° . The size of the R group has an influence on the O-C-C-N dihedral angle but there is no specific correlation between them. A larger R group does not necessarily change the dihedral angle.

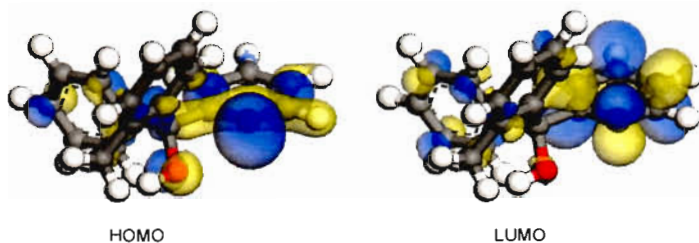


Figure 5.40: HOMO and LUMO of 15

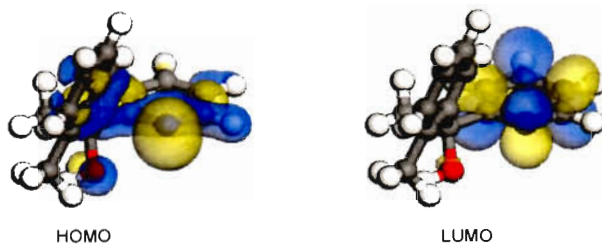


Figure 5.41: HOMO and LUMO of 16

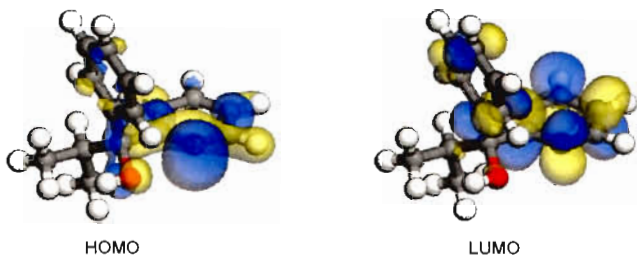


Figure 5.42: HOMO and LUMO of **17**

The electron rich parts of the electrophilic Fukui functions (**Figures 5.43, 5.44 and 5.45**) around the nitrogen and oxygen looked the same as that of **9** (**Figure 5.3**) and even the bulkiness of these alcohols looked very similar to that of **9**, even though **16** and **17** have smaller R groups.

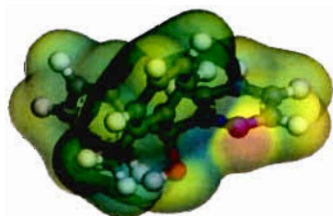


Figure 5.43: Electron density with electrophilic Fukui function of **15**

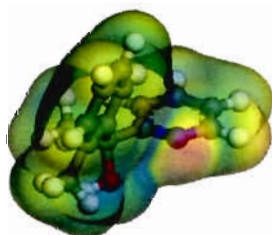


Figure 5.44: Electron density with electrophilic Fukui function of **16**

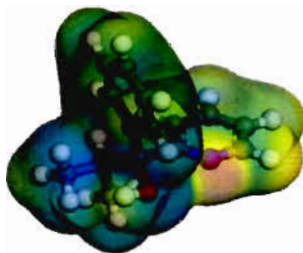


Figure 5.45: Electron density with electrophilic Fukui function of **17**

Since the HOMO, LUMO and electron density with electrophilic Fukui function looks similar to that of **9**, it is found that these 3 alcohols have similar or even better electronic properties than **9**. The slightly different orientation of the HOMO around the oxygen atom can result in an easier overlap with the LUMO of **4**, which results in a shorter reaction time. But when this different orientation is more sterically hindered, it can also make it more difficult for the HOMO to overlap, resulting in a longer reaction time. Because the difference in orientation of the HOMO is only very small, the difference in reaction time is expected to be not even notable.

- **Alcohol 18**

After modelling **18**, the HOMO and LUMO as shown in **Figure 5.46** were compared with the HOMO and LUMO of **9** (**Figure 5.1**) and **36** (**Figure 5.2**). It was found that the HOMO around the nitrogen atom looked identical to the HOMO of **9** and **36**, but the orbitals around the oxygen looked different because the bulky adamantane group has changed the position of the oxygen atom, which changed the orientation of the orbital. The O-C-C-N dihedral angle of this alcohol is 117.95° where **36** has an angle of -81.54° and **9** of -35.38°. Similar observations were made for the LUMO.

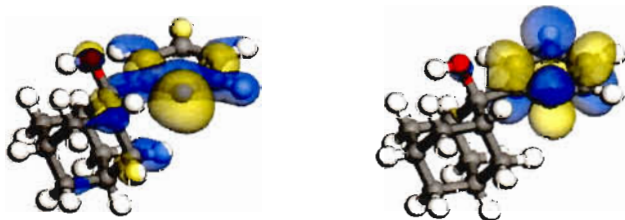


Figure 5.46: HOMO and LUMO of **18**

The bulkiness of this ligand as seen in the electrophilic Fukui function (Figure 5.47) was different than the bulkiness of **9** (Figure 5.3), because **18** has one bulky adamantane group which is slightly smaller than the two bulky phenyl groups of **9**. After comparing the bulkiness of this ligand with the bulkiness of **36**, it was found that they looked similar because they both have one R group instead of the two as in **9**, but the adamantane group of **18** is more bulky than the cyclohexyl group of **36**.

The electron rich parts are concentrated on the nitrogen and oxygen atoms as seen for **36**, the R group and pyridine ring are not blue/green like in **9**, but more green/yellow and the oxygen atom is more yellow instead of green/yellow.

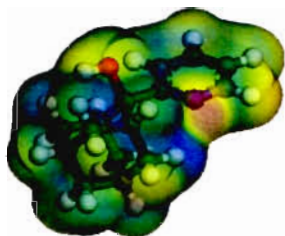


Figure 5.47: Electron density with electrophilic Fukui function of **18**

Since the very bulky adamantane group changed the orientation of the HOMO around the oxygen atom in a different direction than that of **9** or **36**, it is found that it is impossible for this alcohol to have similar electronic properties than **9** or **36**. Due to the orientation of the HOMO around the oxygen atom, it will be hard for this alcohol to coordinate to **4** because the adamantane group moved the oxygen atom almost 160° in comparison to **9**.

- **Alcohol 19**

After modelling **19**, the HOMO and LUMO as shown in Figure 5.48 were compared with the HOMO and LUMO of **9** (Figure 5.1) and **36** (Figure 5.2). It was found that the HOMO around the nitrogen atom looked identical to the HOMO of **9** and **36**, but the orbitals around the oxygen looked different because the bulky R group has changed the position of the oxygen atom, which changed the orientations of the orbitals. The O-C-C-N dihedral angle of this alcohol is -143.26° where **36** has an angle of -81.54° and **9** of -35.38°. Similar observations were made for the LUMO.

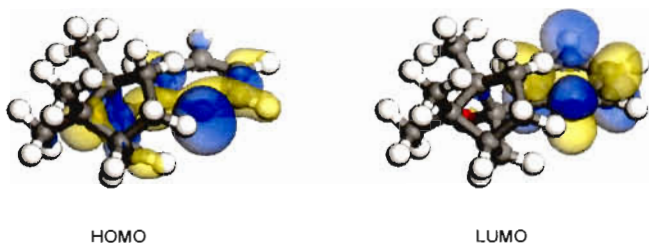


Figure 5.48: HOMO and LUMO of **19**

The bulkiness of this alcohol as seen in the electrophilic Fukui function (**Figure 5.49**) was different compared to the bulkiness of **9**, because **19** has one bulky group that is even larger than the two bulky phenyl groups of **9**. After comparing the bulkiness of this ligand with that of **36**, it was found that they looked similar because they both have one R group instead of the two as in **9**, but the R group of **19** is more bulky than the cyclohexyl group of **36**.

The electron rich parts are concentrated on the nitrogen and oxygen atoms as seen for **36**. The R group and pyridine ring are not blue/green like **9** but green/yellow.

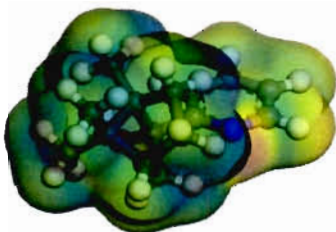


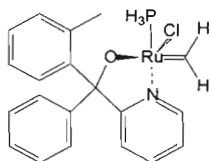
Figure 5.49: Electron density with electrophilic Fukui function of **19**

Since the very bulky R group changed the orientation of the HOMO around the oxygen atom in a different direction than that of **9** or **36**, it is found that it is impossible for this alcohol to have similar electronic properties than **9** or **36**. Due to the bulkiness of this R group as well as the orientation of the HOMO, this alcohol will not coordinate to **4** because the nitrogen and oxygen atoms are highly sterically hindered.

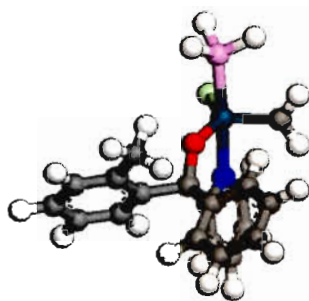
5.1.4.2 Modelling of alcohols when coordinated to 51 (second screening)

The 5 chosen alcohols that were discussed were modelled again when coordinated as ligands to **51**.

- Simplified complex with ligand **15** (**62**)



62



62 (3d-structure)

After modelling **62**, the HOMO and LUMO as shown in **Figure 5.50** were compared with the HOMO and LUMO of **52** (**Figure 5.21**) and **53** (**Figure 5.22**). It was found that the HOMO looked almost identical to the HOMO of **52**. Although the LUMO around the oxygen atom was smaller and around the phosphorus atom larger, the LUMO around the ruthenium atom looked identical to that of **52**. The LUMO around the carbene was in the same direction as that of **52**, but was slightly larger which may result in a higher activity during a metathesis reaction.

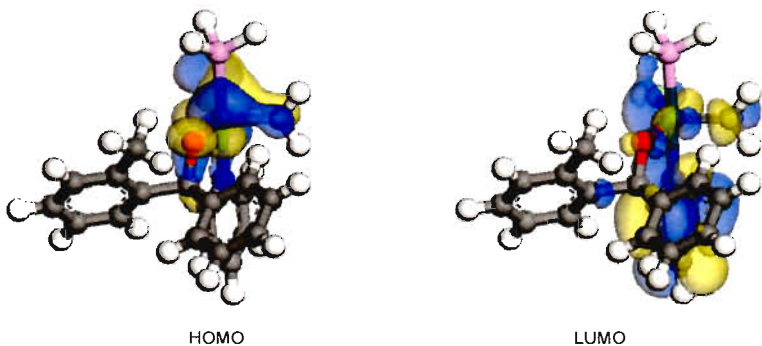


Figure 5.50: HOMO and LUMO of **62**

The nucleophilic Fukui function (**Figure 5.51**) was similar to that of **52** (**Figure 5.23**). The only difference was that the phosphorus atom as well as the carbene carbon were slightly more electron poor (more yellow). Although the *o*-tolyl and phenyl R groups of this complex were in a slightly different direction than the two phenyl groups of **52**, the bulkiness of these complexes looked very similar.

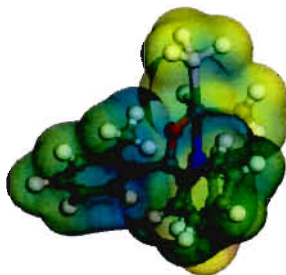
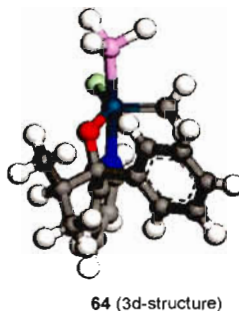
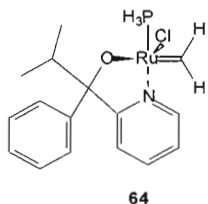
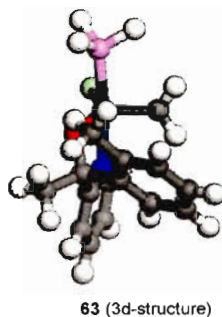
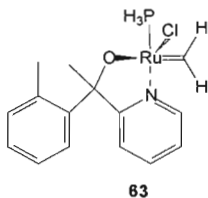


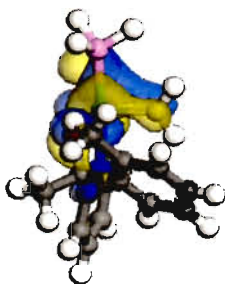
Figure 5.51: Electron density with nucleophilic Fukui function of **62**

Since the LUMO around the carbene group was larger than that of both **52** and **53**, and the LUMO's around the other atoms looked similar to **52**, it is found that this ligand has better electronic properties than **52** and **53**. It is easier for the HOMO of the incoming alkene to overlap with the LUMO of the complex which can result in a higher activity during a metathesis reaction. However, because this ligand was more bulky than **52**, there will be more steric hindrance around the carbene which may result in a lower activity.

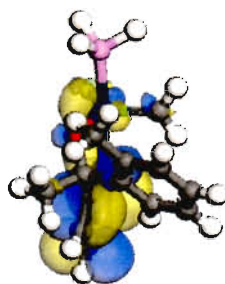
- Simplified complexes with ligands 16 and 17 (63 en 64)



After modelling **63** and **64**, the HOMO's and LUMO's as shown in **Figure 5.52** and **5.53** were compared with the HOMO and LUMO of **52** (**Figure 5.21**) and **53** (**Figure 5.22**). It was found that the HOMO's looked identical to that of **52**. The LUMO around the carbene looked similar to that of **53**. The only difference was that they were slightly larger and the carbene LUMO of **63** was smaller than that of **64**. Although the orientation of the LUMO's around the ruthenium atom looked similar to that of **52**, the size of the orbitals looked similar to that of **53**. The LUMO around the oxygen atom looked identical to that of **52**, but around the phosphorus atom the LUMO was not present at all, which is different from both **52** and **53**. From these observations it can be concluded that the activity of both ligands during a metathesis reaction will be lower than that of **52**, but higher than that of **53**. And **64** will be more active than **63**.

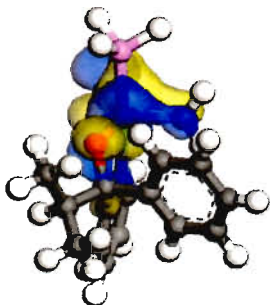


HOMO

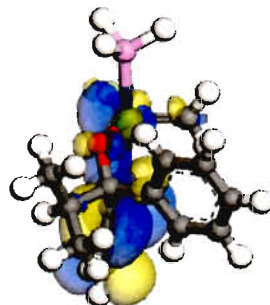


LUMO

Figure 5.52: HOMO and LUMO of **63**



HOMO



LUMO

Figure 5.53: HOMO and LUMO of **64**

The nucleophilic Fukui functions (**Figure 5.54**) were similar to that of **53** (**Figure 5.23**), the only difference was that the ruthenium atom as well as the carbene were more electron poor than that of **53**, more yellow instead of yellow/green. The bulkiness looked very similar to **52**, although the methyl and isopropyl groups of **63** and **64** were a little smaller than the phenyl group of **52** and the *o*-tolyl group of **63** and **62** slightly larger.

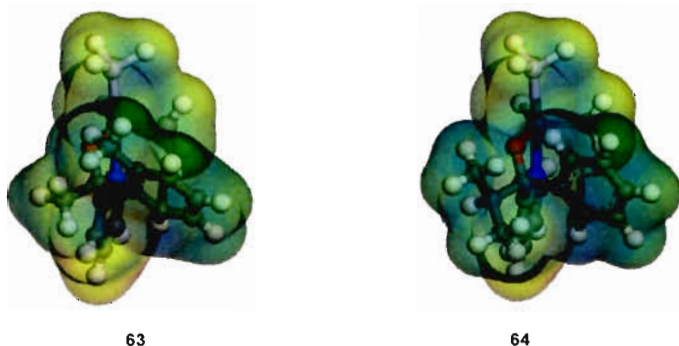
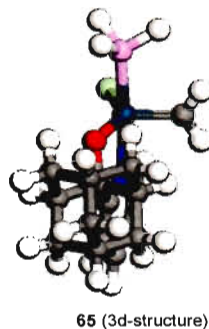
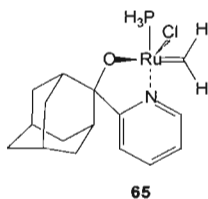


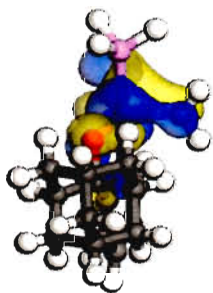
Figure 5.54: Electron density with nucleophilic Fukui function of **63** and **64**

Since the LUMO around the carbene is larger for these complexes than it is for **53**, it can be concluded that it is easier for these complexes to overlap with the HOMO of the incoming alkene, which can result in a higher activity during a metathesis reaction. In comparison to **52**, these complexes will be less active because the carbene LUMO of these complexes is still smaller than that of **52**. However, because the R groups of these ligands are smaller than those of **52**, there will be less steric hindrance around the carbene, which will increase the activity. For this reason it can be concluded that **63** will be more active in a metathesis reaction than **64**. Because **62** has more steric hindrance around the even larger carbene LUMO, this complex will be less active than both **64** and **63**. Since all three complexes have, just like **52**, two R groups instead of the smaller cyclohexyl group of **53**, these complexes will be more active than **53**. The incoming alkene will be guided better to the carbene.

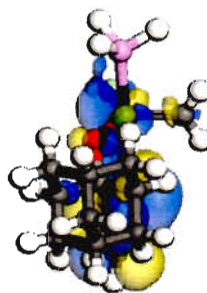
- Simplified complex with ligand 18 (**65**)



After modelling **65**, the HOMO and LUMO as shown in **Figure 5.55** were compared with the HOMO and LUMO of **52** (**Figure 5.21**) and **53** (**Figure 5.22**). It was found that the HOMO around the carbene as well as the orientation of the orbitals around the oxygen atom looked very similar to that of **53**. For the LUMO the same was observed. The LUMO around the carbene carbon, oxygen and ruthenium atoms looked very similar to that of **53**. Only the LUMO around the phosphorus atom was found to be larger as in both **52** and **53**. Because the LUMO around the carbene looked identical to that of **53**, it can be concluded that this complex will have similar electronic properties than **53**.



HOMO



LUMO

Figure 5.55: HOMO and LUMO of **65**

The electron rich parts of the nucleophilic Fukui function (**Figure 5.56**) looked identical to that of **53** (**Figure 5.23**). The bulkiness of this complex was different

because **18** has one bulky adamantane group which is slightly smaller than the two bulky phenyl groups of **52** and larger than the cyclohexyl group of **53**.

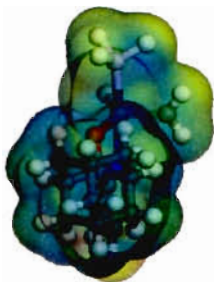
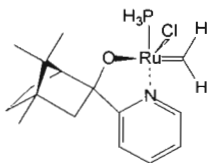


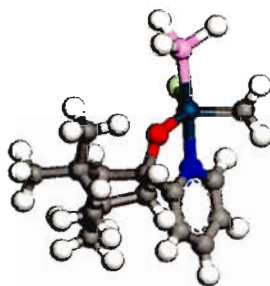
Figure 5.56: Electron density with nucleophilic Fukui function of **65**

Since the direction and size of the LUMO around the carbene looked very similar to that of **53**, it can be concluded that this complex will show a similar activity during a metathesis reaction. However, because the adamantane group is very bulky around the carbene group, it will be hard for the incoming alkene to overlap with the small LUMO of the carbene. For this reason this complex will be less active than both **52** and **53**.

- **Simplified complex with ligand 19 (66)**



66



66 (3d-structure)

After modelling **66**, the HOMO and LUMO as shown in **Figure 5.57** were compared with the HOMO and LUMO of **52** (**Figure 5.21**) and **53** (**Figure 5.22**). It was found

that the HOMO around the carbene was totally different than that of both **52** and **53** and the HOMO of the oxygen atom was also orientated in a different direction. Although the direction of the LUMO around the carbene carbon looked similar to that of **52**, it was found to be smaller. The LUMO around the ruthenium and oxygen atoms was orientated in a different direction and the LUMO around the phosphorus atom was larger. The HOMO of the incoming alkene will overlap with the LUMO of the metal carbene in a metathesis reaction and because the LUMO around the ruthenium atom was orientated in a different direction to that of both **52** and **53**, it can be concluded that this complex will not have better electronic properties than both **52** and **53**, which may result in a lower activity.

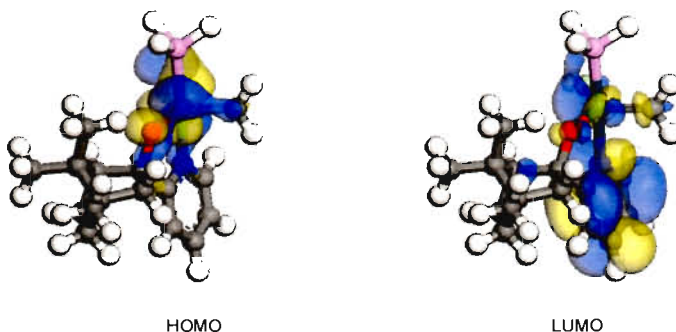


Figure 5.57: HOMO and LUMO of **66**

The electron rich parts of the nucleophilic Fukui function (**Figure 5.58**) looked very similar to that of **53** (**Figure 5.23**), the only difference was that the carbene group and phosphorus atom was more electron poor (more yellow instead of green/yellow). The bulkiness of this complex was also different because this ligand has one bulky R group which is slightly larger than the two bulky phenyl groups of **52** and also larger than the cyclohexyl group of **53**.

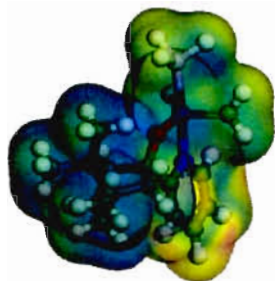
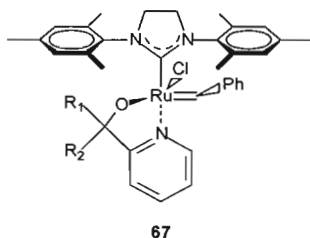


Figure 5.58: Electron density with nucleophilic Fukui function of **66**

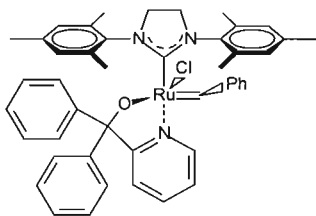
Since the LUMO around the ruthenium was different from that of both **52** and **53** and the R group is very bulky around the carbene group, it will be hard for the incoming alkene to overlap with the LUMO of the carbene. For this reason this complex will be less active in a metathesis reaction than both **52** and **53**.

5.1.5 Modelling of modified Grubbs 2 pre-catalyst with 5 chosen ligands

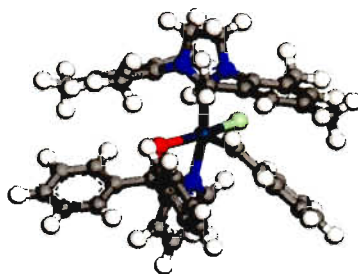
The 5 modified Grubbs 2 pre-catalysts (**67**) were geometrically optimized. The same optimization method was used as described in Chapter 4 (§4.2.2). The HOMO, LUMO, electron density and nucleophilic Fukui functions were calculated and visually compared with that of the complex with ligand **9** (**1**) as well as the complex with ligand **36** (**68**).



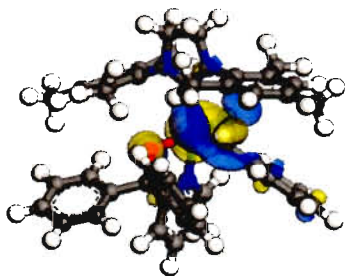
During the comparison it is very important to compare the HOMO's and LUMO's and their orientation and shape around the oxygen, ruthenium atom and carbene group of each complex with the HOMO and LUMO of **1** (Figure 5.59) and **68** (Figure 5.60) because **1** showed to be very active in a metathesis reaction where **68** did not show such a good activity.^[1]



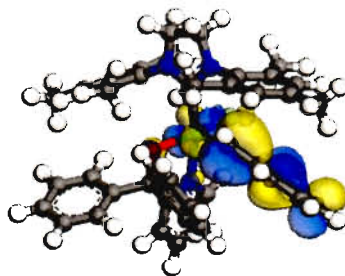
1



1 (3d-structure)



HOMO



LUMO

Figure 5.59: HOMO and LUMO of 1

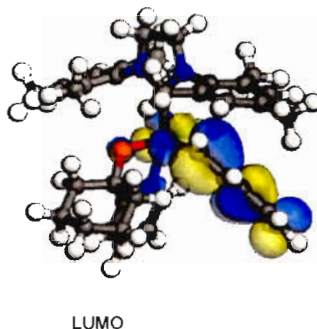
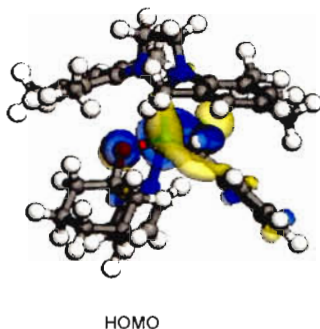
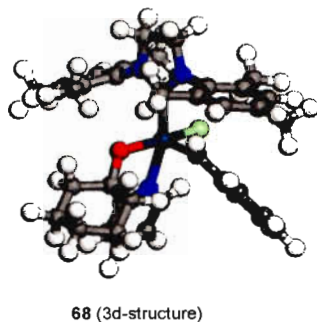
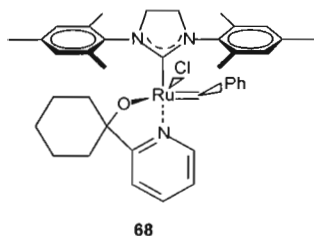


Figure 5.60: HOMO and LUMO of **68**

The HOMO and LUMO of complex **1** was almost identical to **68**, only the orientation of the orbitals around the oxygen atom was slightly different.

For complex **1**, the most electron poor parts as shown by the electron density map combined with the nucleophilic Fukui function (**Figure 5.61**) were found around the carbene (slightly red/yellow), while the rest of the complex remained slightly electron rich (green/blue). **68** was more electron rich (more yellow instead of red/yellow) around the carbene group and more electron poor (more yellow instead of green) around the oxygen atom. When the bulkiness of these complexes was compared, the cyclohexyl R group of **68** appeared to be less bulky than the two phenyl groups of **1**.

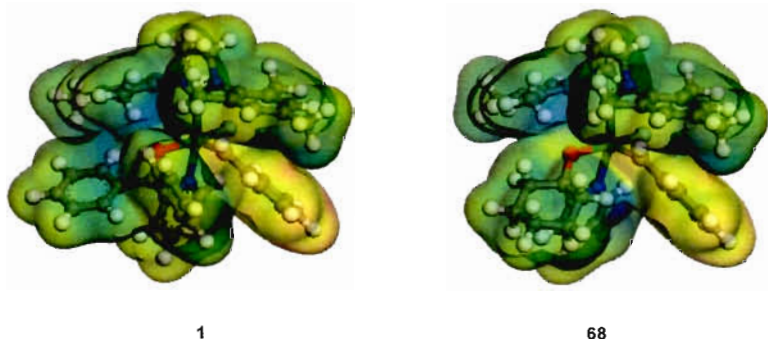


Figure 5.61: Electron density with nucleophilic Fukui function of **1** and **68**

As mentioned in Chapter 2 (§2.2), these types of coordinated ligands are so-called hemilabile ligands, which means that the ligands are bonded with one strong bond and one labile bond. The labile bond between the ruthenium and nitrogen atom is not really a bond; the labile group is coordinated to the ruthenium. In the hemilabile ligands that are used for this study the pyridine ring (N atom) will be the labile group which will open up during a metathesis reaction, leaving a vacant coordination site for the alkene. The incoming alkene will then coordinate to the ruthenium.

For this reason the complexes were modelled again, this time without a ruthenium-nitrogen bond. The HOMO, LUMO, electron density and nucleophilic Fukui functions for the complexes with the ruthenium-nitrogen bond were compared with the HOMO, LUMO, electron density and nucleophilic Fukui functions for the complexes without the ruthenium-nitrogen bond and it was found that those functions looked identical. The electronic properties of the complex did not change when the ruthenium-nitrogen bond was removed. For this reason the modelling results without a ruthenium-nitrogen bond were not discussed again for the other complexes.

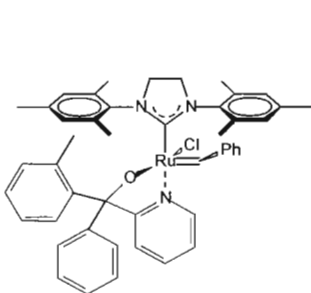
The angles and bond lengths that were obtained for complexes **1** and **68** are shown in **Table 5.4**. It was found that the energy, bond lengths and angles in both complexes did not change when the ruthenium-nitrogen bond was removed.

Table 5.4: Angles (°) and bond distances (Å) of complexes **1** and **68** with and without a ruthenium-nitrogen bond

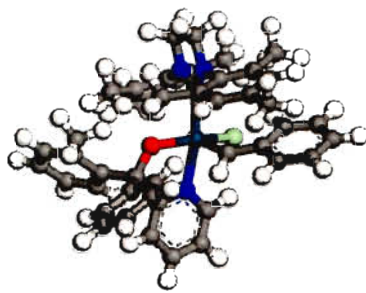
	1		68	
	With a Ru-N bond	Without a Ru-N bond	With a Ru-N bond	Without a Ru-N bond
Ru-O	2.0	2.0	2.0	2.0
N-Ru	2.2	2.2	2.2	2.2
Ru-O-C	115.8	115.8	116.8	117.1
O-C-C	109.4	109.4	108.6	108.9
Ru-O-C-C	-34.1	-34.1	-35.1	-33.4
O-C-C-N	21.2	21.2	26.1	21.8

In the following section all 5 ligands coordinated to **4** will be discussed and compared with **1** as well as with **68**.

- Complex with ligand **15** (**25**)



25



25 (3d-structure)

After modelling **25**, the HOMO and LUMO as shown in Figure 5.62 were compared with the HOMO and LUMO of **1** (Figure 5.59) and **68** (Figure 5.60). It was found that the HOMO around the carbene looked different from that of **1** as well as from that of **68**. The orbitals that were in front of and behind the carbene group, changed. This is probably because the phenyl group that is attached to the carbene is pointed more towards the NHC ligand of the complex, whereas the phenyl group of **1** and **68** were pointed more downwards. The Cl-Ru-C-C dihedral angle of this complex is 39.32° where **1** has an angle of -50.64° and **68** of -53.78°. Since the phenyl group of the NHC ligand is parallel with the phenyl group of the carbene group, π -stacking can

occur between the two rings which will lead to a more stable complex (Chapter 2). The distance between these two rings is 3.9585 Å. A reason why this phenyl group is more pointed towards the NHC ligand is because of the position of the R groups. The phenyl and o-tolyl R groups are orientated in a different direction than the two phenyl groups of **1**, which will lead to more steric hindrance around the carbene group. Due to this steric hindrance, the phenyl group is pushed more towards the NHC ligand. For this reason, the LUMO around the carbene was also orientated in a different direction than that of **1** and **68**. Due to this change in direction, this LUMO is pointing more towards the outside of the complex which will mean that it will be more available to overlap with an incoming alkene. However, because the LUMO is not pointed towards the phenyl R group, it will be difficult for this R group to guide the incoming alkene to the LUMO, which will result in a lower activity than that of complex **1** during a metathesis reaction.

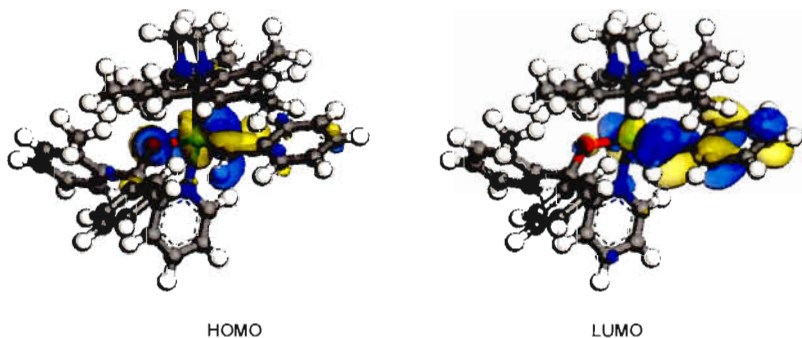


Figure 5.62: HOMO and LUMO of **25**

The nucleophilic Fukui function (**Figure 5.63**) was slightly different from that of **1** as well as **68** (**Figure 5.61**). Because of the changed orientation of the phenyl ring, the electron rich part of the carbene is more concentrated below the carbene. Another difference between this complex and **1** and **68** is that the NHC ligand as well as the hemilabile ligand are more electron rich (more blue instead of green/yellow/blue) in **25**.

Complex **25** has two R groups which are more bulky than the cyclohexyl R group of **68**. Although the bulkiness of this complex does not differ so much from **1**, this carbene is less sterically hindered due to different positions of the two bulky groups as well as the phenyl group attached to the carbene. These changes in position cause an open space below the carbene group.

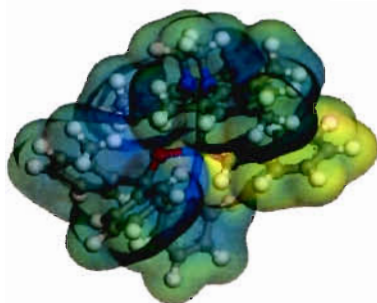
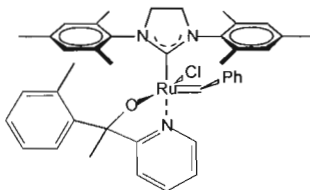


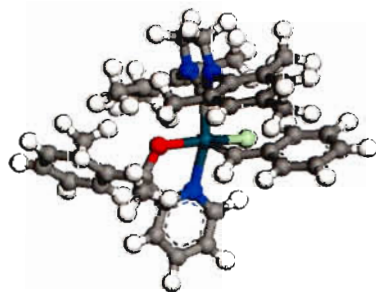
Figure 5.63: Electron density with nucleophilic Fukui function of **25**

Due to the changed orientation of the phenyl group leaving an open space below the carbene group, the activity of this complex should be higher than that of **1** and **68** because there will be more space for an incoming alkene to overlap. However, because the position of one phenyl R group in **1** is orientated more in a vertical direction and the other phenyl R group in horizontal direction, it will guide the incoming alkene molecules to the carbene. In **25** the phenyl R group is orientated more horizontally and is in a straight line with the phenyl group of the NHC ligand, so it would not guide the alkene to the carbene group. Because **68** has only one R group, which is much smaller than the two R groups of **25**, complex **25** would guide the alkene more to the carbene than **68** would do. For this reason it is likely that this complex has a lower activity than that of **1** but a higher activity than **68**.

- **Complex with ligand 16 (26)**



26



26 (3d-structure)

After modelling **26**, the HOMO and LUMO as shown in **Figure 5.64** were compared with the HOMO and LUMO of **1** (**Figure 5.59**) and **68** (**Figure 5.60**). It was found that these orbitals looked identical to the orbitals of **25** (**Figure 5.62**). The orbitals that were in front of and behind the carbene group changed, probably because the phenyl group that is attached to the carbene is pointed more towards the NHC ligand of the complex. The Cl-Ru-C-C dihedral angle of this complex is 33.85° where **1** has an angle of -50.64° and **68** of -53.78°. Since the phenyl group of the NHC ligand is parallel with the phenyl group of the carbene group, π -stacking can occur between the two rings which will lead to a more stable complex (Chapter 2). The distance between these two rings is 3.8675 Å. A reason why this phenyl group is pointed more towards the NHC ligand is because of the position of the R groups. The methyl R group, surrounded by its three hydrogen atoms, is probably more bulky towards the carbene than the vertically orientated phenyl R group of **1**, where the hydrogen atoms are also in the same vertical direction as the rest of the R group, which will push the phenyl group more towards the NHC ligand. Due to this change in direction, this LUMO is pointing more towards the outside of the complex which will mean that it will be more available to overlap with an incoming alkene. However, because the LUMO is not pointed towards the methyl R group, it will be difficult for this small R group to guide the incoming alkene to the LUMO, which will result in a lower activity than that of **1** during a metathesis reaction.

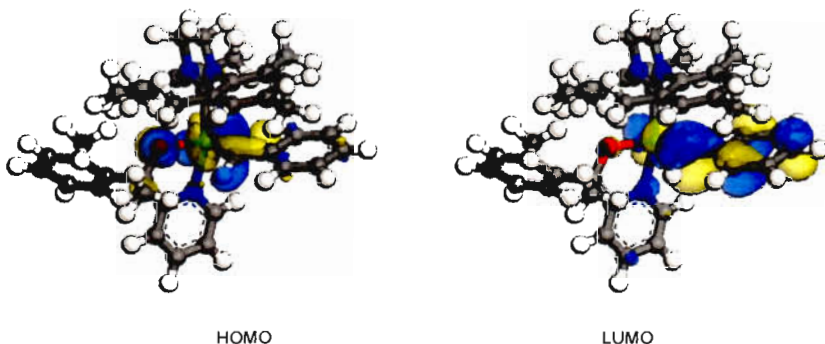


Figure 5.64: HOMO and LUMO of **26**

Also the nucleophilic Fukui function (**Figure 5.65**) was almost identical to **25** (**Figure 5.63**). The electron rich part of the carbene is more concentrated below the carbene.

This complex is more sterically hindered than **68**, but less sterically hindered than **25** as well as **1** due to the less bulky methyl R group that is attached to the ligand as well

as the orientation of phenyl group attached to the carbene. This orientation of the phenyl group will cause an open space below the carbene group.

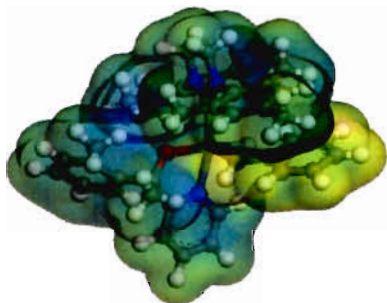
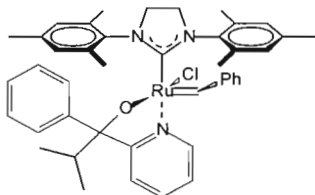


Figure 5.65: Electron density with nucleophilic Fukui function of **26**

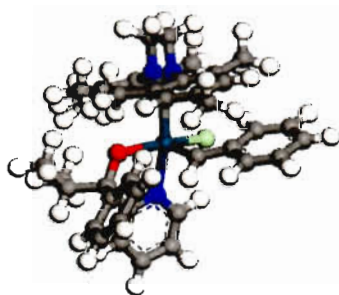
Due to the changed orientation of the phenyl group and the less sterically hindered methyl R group, an open space below the carbene group was created. However, because the position of one phenyl R group in **1** is orientated more in a vertical direction and the other phenyl R group in horizontal direction, it will lead the incoming alkene molecules to the carbene. Although the cyclohexyl R group of **68** is also in a vertical direction, this R group is much smaller than the two R groups of **26**, so **26** has a better ability than **68** to guide the alkene to the carbene. In **26** the methyl R group is in a straight line with the phenyl group of the NHC ligand, so it would not guide the alkene to the carbene group like the phenyl R groups of **1** and **25**.

When the methyl R group of **26** is compared to the phenyl R group of **25**, they both change the position of the phenyl of the carbene group. A reason for that can be that the methyl group, surrounded by its three hydrogen atoms, as well as the phenyl R group of **25**, with the hydrogen atoms in the same horizontal direction, is more bulky in the horizontal direction than the vertically orientated phenyl R group of **1**. The phenyl R group of **25** will be more bulky towards the carbene than the methyl group of **26** and for this reason **26** will be less active than **1** but more active than **25**.

- **Complex with ligand 17 (27)**



27



27 (3d-structure)

After modelling **27**, the HOMO and LUMO as shown in **Figure 5.66** were compared with the HOMO and LUMO of **1** (**Figure 5.59**) and **68** (**Figure 5.60**). It was found that these orbitals looked identical to the orbitals of **25** as well as those of **26** (**Figures 5.62** and **5.64**). The orbitals that were in front of and behind the carbene group changed in comparison to **1** and **68**, which is probably because the phenyl group that is attached to the carbene is pointed more towards the NHC ligand of the complex. The Cl-Ru-C-C dihedral angle of this complex is 40.43° where **1** has an angle of -50.64° and **68** of -53.78° . Since the phenyl group of the NHC ligand is parallel with the phenyl group of the carbene group, π -stacking can occur between the two rings which will lead to a more stable complex (Chapter 2). The distance between these two rings is 4.482 Å. A reason why this phenyl group is pointed more towards the NHC ligand is because of the position of the R groups. The phenyl R group of **27** is just like the phenyl R group of **25** and the methyl R group of **26** more bulky towards the carbene than the vertically orientated phenyl R group of **1**, which will push the phenyl group more towards the NHC ligand. Due to this change in direction, this LUMO is pointing more towards the outside of the complex which will mean that it will be more available to overlap with an incoming alkene. Because the LUMO is not pointed towards the phenyl R group, it will be difficult for this R group to guide the incoming alkene to the LUMO, which will result in a lower activity than that of **1** during a metathesis reaction.

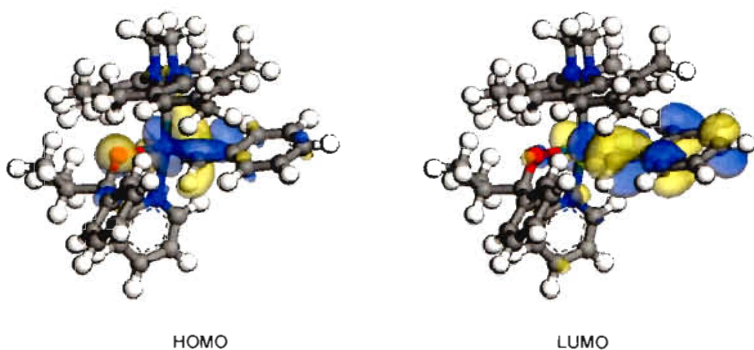


Figure 5.66: HOMO and LUMO of **27**

Also the nucleophilic Fukui function (**Figure 5.67**) was almost identical to **25** as well as to **26** (**Figures 5.63** and **5.65**). The electron rich part of the carbene is more concentrated below the carbene.

This complex is less sterically hindered than **25** as well as **1** and more so than **26** and **68**, but because the phenyl group is pointed towards the carbene, in a horizontal direction like the phenyl in **25**, the steric hindrance around the carbene is very similar to that of **25**. In comparison to **1**, the carbene of **27** is less sterically hindered due to different positions of the two bulky groups as well as the phenyl group attached to the carbene. These changes in position cause an open space below the carbene group which will create more space for an incoming alkene to overlap.

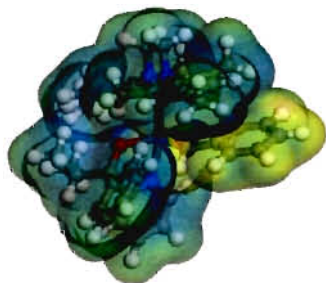


Figure 5.67: Electron density with nucleophilic Fukui function of **27**

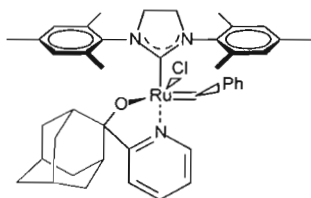
The bulkiness of this ligand looked similar to **25** where the phenyl R group is orientated more horizontally, so that it would not guide the alkene to the carbene group like **1** does. The only difference between this complex and **25** is that the phenyl R group is orientated in a slightly more vertical direction than the phenyl of **25**, which will guide the alkene more to the carbene group.

When this phenyl R group is compared to the methyl group of **26**, the methyl group surrounded by its three hydrogen atoms is more bulky in a vertical direction than the horizontally orientated phenyl R group of this complex, with the hydrogen atoms in the same horizontal direction as the rest of the R group. Therefore, **26** will guide the incoming alkene more to the carbene group

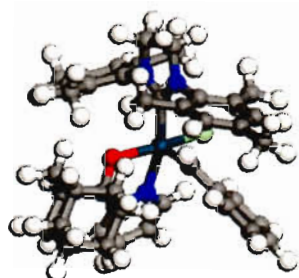
Because **68** has only one R group which is much smaller than the two R groups of **25**, **26** and **27**, it does not have a greater ability to guide the alkene to the carbene than **25**, **26** and **27**.

For these reasons, this complex will obtain a lower activity than **1** as well as **26** in a metathesis reaction, but it will be more active than **25** and **68**.

- **Complex with ligand 18 (28)**



28



28 (3d-structure)

After modelling **28**, the HOMO and LUMO as shown in **Figure 5.68** were compared with the HOMO and LUMO of **1** (**Figure 5.59**) and **68** (**Figure 5.60**). It was found that the orbitals looked identical to the orbitals of **1** and **68**. Because this adamantane R group is, just like the cyclohexyl group of **68**, less bulky towards the carbene than the two phenyl groups of **1**, the phenyl of the carbene group would not move towards the NHC ligand like it did in **25**, **26** and **27**. The Cl-Ru-C-C dihedral angle of this complex

is -54.43° , which is similar to the -53.78° of **68**. For these reasons this complex will have similar electronic properties than **68**.

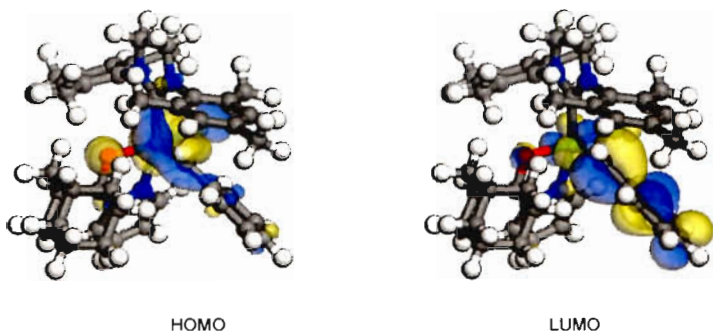


Figure 5.68: HOMO and LUMO of **28**

The nucleophilic Fukui function (Figure 5.69) was identical to **1** (Figure 5.61). The only difference is the bulkiness of the adamantane R group that is attached to the ligand, which was similar to the cyclohexyl group of **68**.

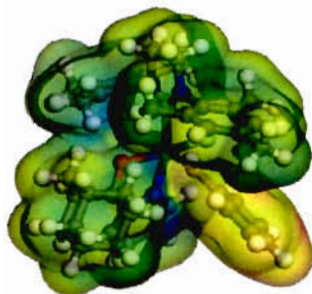
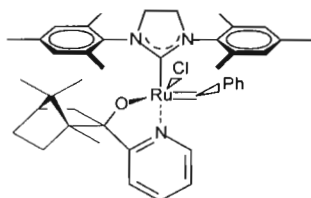


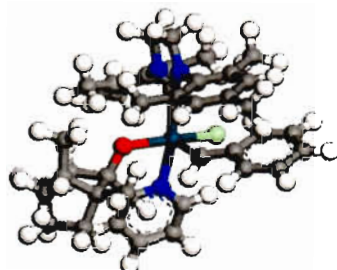
Figure 5.69: Electron density with nucleophilic Fukui function of **28**

Due to this bulky adamantane group and the orientation of the phenyl ring, the carbene group is more sterically hindered than in **25**, **26** and **27**, but less so than **1**. Because the adamantane R group is not as bulky as the phenyl groups of **1**, it would not guide the alkene towards the carbene as well as **1** would do. Because the bulkiness of this adamantane group looks slightly larger than the cyclohexyl R group of **68**, this complex will probably be more active than **68** and less active than **1**.

- **Complex with ligand 19 (29)**



29



29 (3d-structure)

After modelling **29**, the HOMO and LUMO as shown in **Figure 5.70** were compared with the HOMO and LUMO of **1** (**Figure 5.59**) and **68** (**Figure 5.60**). It was found that these orbitals looked identical to the orbitals of **25**, **26** and **27** (**Figure 5.62**, **5.64** and **5.66**). The orbitals that were in front of and behind the carbene group changed, probably because the phenyl group that is attached to the carbene is pointed more towards the NHC ligand of the complex. The Cl-Ru-C-C dihedral angle of this complex is 36.50° where **1** has an angle of -50.64° and **68** of -53.78°. Since the phenyl group of the NHC ligand is parallel with the phenyl group of the carbene group, π -stacking can occur between the two rings which will lead to a more stable complex (Chapter 2). A reason why this phenyl group is more pointed towards the NHC ligand is because of the position of the bulky R group, which is probably more bulky towards the carbene than the vertically orientated phenyl R group of **1** and **68**, which will push the phenyl group more towards the NHC ligand. Due to this change in direction, this LUMO is pointing more towards the outside of the complex which will mean that it will be more available to overlap with an incoming alkene. However, because the LUMO is not pointed towards the R group, it will be difficult for this R group to guide the incoming alkene to the LUMO, which will result in a lower activity than **1** during a metathesis reaction.

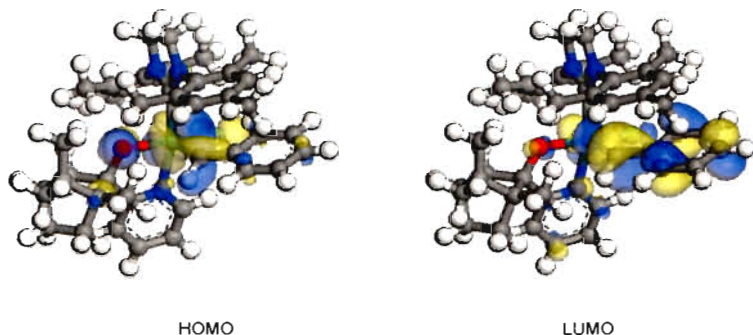


Figure 5.70: HOMO and LUMO of **29**

Also the nucleophilic Fukui function (Figure 5.71) was almost identical to **25**, **26** and **27** (Figures 5.63, 5.65 and 5.67). The electron rich part of the carbene is more concentrated below the carbene.

Because the 1,7,7-trimethylbicyclo[2.2.1] heptane R group of ligand **19** is more bulky than the two phenyl R groups of **1**, the carbene group is sterically hindered so that it can not undergo a metathesis reaction. The phenyl group attached to the carbene moved towards the NHC ligand, which will create a small open space below the carbene group, but this space is not large enough for an alkene to come in because the methyl group on the 1,7,7-trimethylbicyclo[2.2.1] heptane R group blocks the way. For this reason this catalyst will not be active during a metathesis reaction.

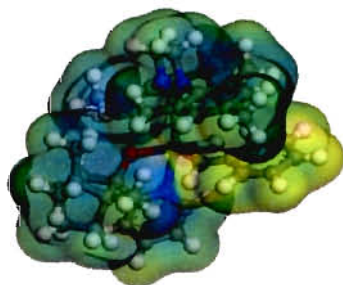


Figure 5.71: Electron density with nucleophilic Fukui function of **29**

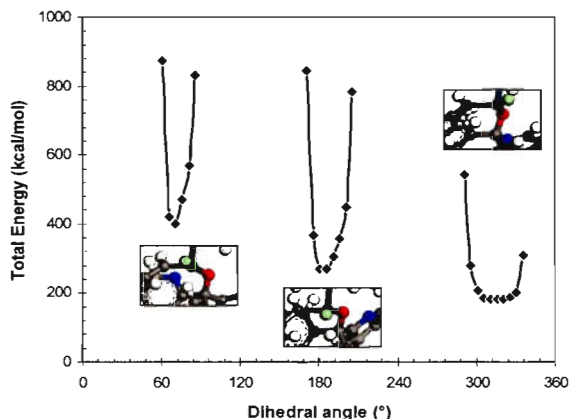
5.1.6 Conformer searches of the Grubbs 2 pre-catalyst with all 5 ligands

During a metathesis reaction, the labile group (pyridine ring) of the complex will open up to allow the incoming alkene to coordinate to the ruthenium atom. In §5.1.5 the same geometric optimized structure was obtained for complexes with a ruthenium-nitrogen bond as well as without a ruthenium-nitrogen bond. From this observation it is clear that the optimized structure was at a minimum, but it can be that the geometric optimization calculation found a local minimum instead of a global minimum. In order to determine if this minimum is a local or global minimum, as well as to determine the "stability" of the various minima, conformer searches were done on each complex. In the conformer search a dihedral angle of the complex can be changed while the energy is calculated for every new structure. The structure where the lowest energy for a complex is calculated will be close to the global minimum of the complex. When that complex is geometrically optimized again, the global minimum of the complex will be calculated.

After 1 was submitted for a conformer search, the energies of 72 conformers were obtained. To see the minima of the complex more clearly, the data points with energies higher than 1000 kcal/mol were omitted (Graph 5.1).

It was found that this complex has three minima: 400 kcal/mol at Ru-O-C-C dihedral angle 71°, 270 kcal/mol at Ru-O-C-C dihedral angle 181° and 181 kcal/mol at Ru-O-C-C dihedral angle 316°, which was shown to be the global minimum. The global minimum was geometrically optimized again and an energy of 175 kcal/mol was obtained with a Ru-O-C-C dihedral angle of -36° (or 324°).

It is also important to discuss the broadness of the curves, because the broader the curve the more stable that minimum will be. For the curves of 1, the global minimum was found to be the most stable minimum.



Graph 5.1: Energy profile of conformer search of **1**

When the global minimum is compared to the minimum obtained after geometric optimization without a ruthenium-nitrogen bond (§5.1.5), it was found that these values look very similar (Table 5.5). This means that the calculation method for optimization of the structure without a ruthenium-nitrogen bond found a structure close to, but slightly from the global minimum.

Table 5.5: Comparison of total energies, dihedral angles and distances of the found structures

	Optimized structure after the Ru-N bond was removed (§5.1.5)	Optimized structure after conformer search
Total energy (kcal/mol)	188	175
Dihedral angle (°)	326	324
Distance of Ru-N (Å)	2.182	2.179

To see whether it is possible for the HOMO of the alkene to reach the LUMO around the carbene and start a metathesis reaction, it is important to overlay the electron density on the LUMO of the complex (Figure 5.72). The point of interaction will be where the LUMO perforates the electron density. For **1** it was found that the LUMO around the carbene did not perforate the surface of the electrons. But because the LUMO around the carbene carbon was found to be very close to perforating the surface of these electrons (indicated by the red circle), this will be the place where the alkene comes in to coordinate to the carbene and initiate a metathesis reaction.

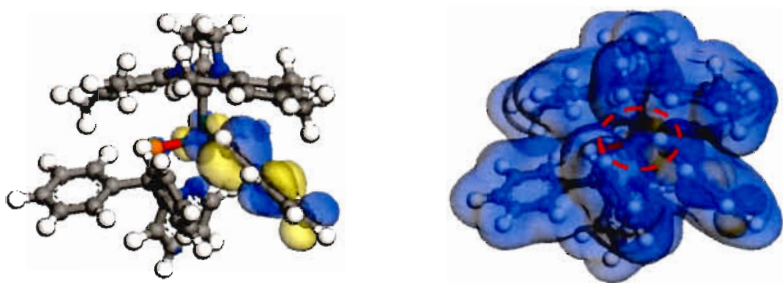
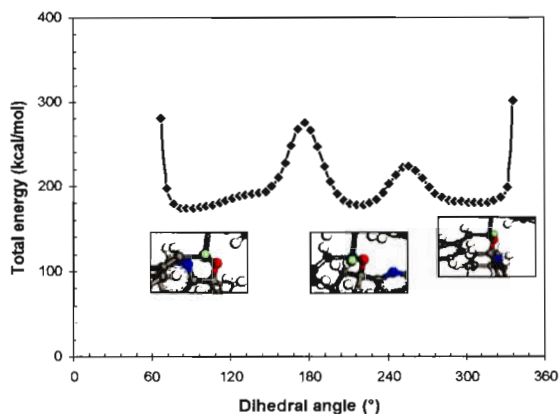


Figure 5.72: LUMO and electron density function of **1**

When **68** was submitted for a conformer search, several energies were obtained. To see the minima of the complex more clearly the data points with energies higher than 1000 kcal/mol were omitted (**Graph 5.2**).

For this complex it was found that it has three minima: 174 kcal/mol at Ru-O-C-C dihedral angle 87°, 178 kcal/mol at Ru-O-C-C dihedral angle 217° and 180 kcal/mol at Ru-O-C-C dihedral angle 312°, from which the first one was shown to be the global minimum. The global minimum was geometrically optimized again and an energy of 162 kcal/mol was obtained with a Ru-O-C-C dihedral angle of 96°.

Since the curve around 90° is the broadest curve of this complex, it can be concluded that for **68** the global minimum was also found to be the most stable minimum.



Graph 5.2: Energy profile of conformer search of **68**.

When the global minimum is compared to the minimum that was found after geometric optimization without a ruthenium-nitrogen bond (§5.1.5), it was found that these values do not look very similar (**Table 5.6**). This means that the calculation method for optimization of the structure without a ruthenium-nitrogen bond found a structure at another minimum, not close to the global minimum.

Table 5.6: Comparison of total energies, dihedral angles and distances of the found structures

	Optimized structure after the Ru-N bond was removed (§5.1.5)	Optimized structure after conformer search
Total energy (kcal/mol)	194	162
Dihedral angle (°)	147	96
Distance of Ru-N (Å)	2.180	4.545

When the electron density of this complex was overlaid on the LUMO (**Figure 5.73**), it was found that the LUMO around the carbene did not perforate the surface of the electrons. However, because the LUMO around the carbene carbon was found to be very close to perforating the surface of these electrons (indicated by the red circle), this will be the place where the alkene comes in to coordinate to the carbene and start a metathesis reaction.

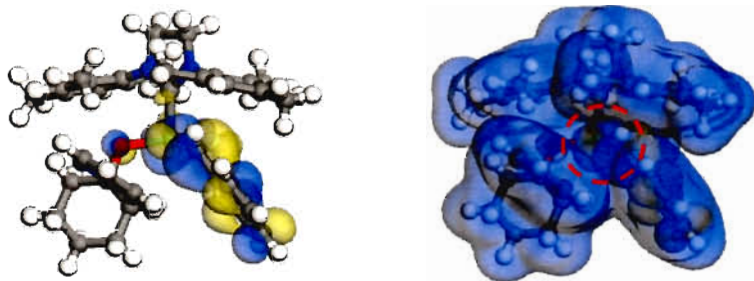


Figure 5.73: LUMO and electron density function of **68**.

After comparing the results of **68** with that of **1**, it was found that the electron density looks very similar for both complexes because the pyridine ring moved to the position where in **1** a phenyl group is situated. The position of the phenyl groups in these complexes is very important because they guide the incoming alkene to the carbene. The only difference between these two complexes is that **1** would guide an incoming alkene more to the space where the LUMO is found to be close to performing. This is due to the positions of the phenyl ring of the hemilabile ligand as well as the phenyl ring of the NHC-ligand.

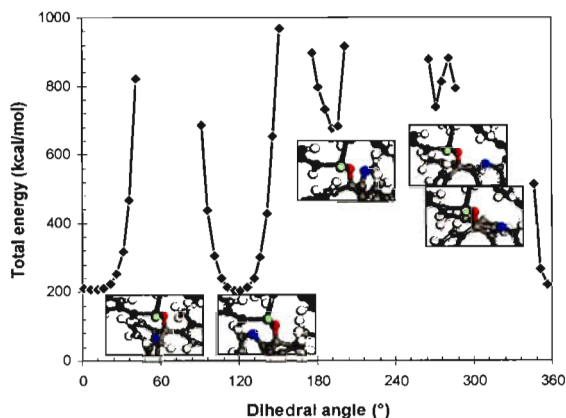
In the following section all 5 complexes will be discussed and compared with **1** as well as **68**.

- **Complex 25**

When **25** was submitted for a conformer search, several energies were obtained. To see the minima of the complex more clearly the data points with higher energies than 1000 kcal/mol were omitted (**Graph 5.3**).

For this complex it was found that it has five minima: 206 kcal/mol at Ru-O-C-C dihedral angle 6°, 203 kcal/mol at Ru-O-C-C dihedral angle 121°, 676 kcal/mol at Ru-O-C-C dihedral angle 191°, 736 kcal/mol at Ru-O-C-C dihedral angle 271° and 793 kcal/mol at Ru-O-C-C dihedral angle 286°, from which the second one was found to be the global minimum.

Since the curve around 121° is the broadest curve of this complex, it can be concluded that for this complex the global minimum was also found to be the most stable minimum.



Graph 5.3: Energy profile of conformer search of 25.

The global minimum was geometrically optimized again and an energy of 111 kcal/mol was obtained with a Ru-O-C-C dihedral angle of 106°.

After comparing the global minimum with the minimum obtained after geometric optimization without a ruthenium-nitrogen bond (§5.1.5), it was found that these values were not very similar (Table 5.7). After optimization without a ruthenium-nitrogen bond, the minimum was found at 6°, which was not the global minimum. After optimization of the minimum found by the conformer search, the global minimum was found at 106°. Therefore, for this complex, the optimization without a ruthenium-nitrogen bond did not give the global minimum.

Table 5.7: Comparison of total energies, dihedral angles and distances of the found structures

	Optimized structure after the Ru-N bond was removed (§5.1.5)	Optimized structure after conformer search
Total energy (kcal/mol)	206	111
Dihedral angle (°)	6	106
Distance of Ru-N (Å)	2.157	3.764

When the electron density of this complex was overlaid on the LUMO (Figure 5.74), it was found that the LUMO around the carbene did not perforate the surface of the

electrons. However, because the LUMO around the carbene carbon was found to be very close to perforating the surface of these electrons (indicated by the red circle), this will be the place where the alkene comes in to coordinate to the carbene and start a metathesis reaction.

A difference between this complex, **1** and **68** is that the LUMO of the carbene in this complex is below the carbene group whereas the LUMO of **1** as well as **68** is in front of the carbene group. As mentioned before (§5.1.5), this is probably because the R groups of this ligand were more bulky towards the carbene which pushed the phenyl group more towards the NHC ligand. This change in position changed the orientation of the LUMO, which made these orbitals more available for metathesis below the carbene group. According to these results, an incoming alkene will start a metathesis reaction with this complex using an associative mechanism where **1** as well as **68** used a dissociative mechanism. However, because of the steric hindrance of the pyridine group around the carbene, this complex will be less active during a metathesis reaction than **1**.

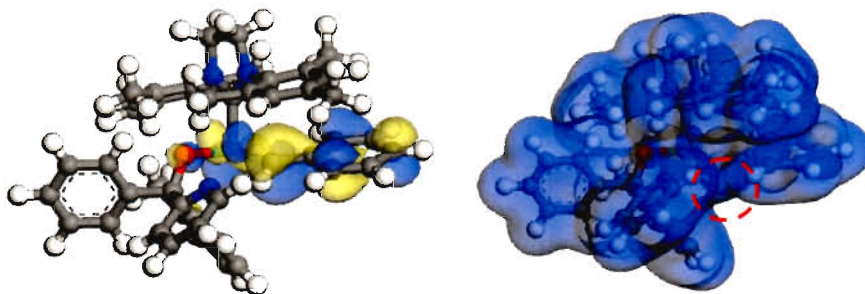


Figure 5.74: LUMO and electron density function of **25**.

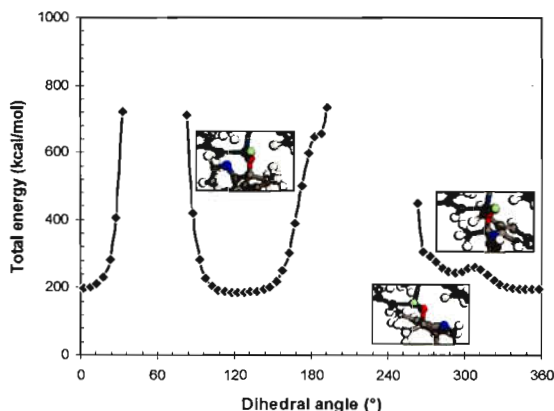
- **Complex 26**

When **26** was submitted for a conformer search, several energies were obtained. To see the minima of the complex more clearly, the data points with higher energies than 1000 kcal/mol were omitted (**Graph 5.4**).

For this complex it was found that it has three minima: 186 kcal/mol at Ru-O-C-C dihedral angle 123°, 242 kcal/mol at Ru-O-C-C dihedral angle 293° and 196 kcal/mol

at Ru-O-C-C dihedral angle 343° from which the first one was found to be the global minimum.

Since the curve around 123° is the broadest curve of this complex, it can be concluded that for this complex the global minimum was also found to be the most stable minimum.



Graph 5.4: Energy profile of conformer search of **26**.

The global minimum was geometrically optimized again and an energy of 177 kcal/mol was obtained with a Ru-O-C-C dihedral angle of 113° .

After comparing the global minimum with the minimum obtained after geometric optimization without a ruthenium-nitrogen bond (§5.1.5), it was found that these values were not very similar (**Table 5.8**). After optimization without a ruthenium-nitrogen bond the minimum was found at 358° , which was not the global minimum. After optimization of the minimum found by the conformer search, the global minimum was found at 113° . Therefore, for this complex, the optimization without ruthenium-nitrogen bond did not give the global minimum.

Table 5.8: Comparison of total energies, dihedral angles and distances of the found structures

	Optimized structure after the Ru-N bond was removed (§5.1.5)	Optimized structure after conformer search
Total energy (kcal/mol)	196	177
Dihedral angle (°)	358	113
Distance of Ru-N (Å)	2.163	3.784

When the electron density of this complex was overlaid on the LUMO (**Figure 5.75**), it was found that the LUMO around the carbene did not perforate the surface of the electrons. However, because the LUMO around the carbene carbon was found to be very close to perforating the surface of these electrons (indicated by the red circle), this will be the place where the alkene comes in to coordinate to the carbene and start a metathesis reaction.

A difference between this complex, **1** and **68** is that the LUMO of the carbene in this complex is below the carbene group (just like in **25**) whereas the LUMO of **1** as well as **68** is in front of the carbene group. As mentioned before (§5.1.5), this is probably because the R groups of this ligand were more bulky towards the carbene which pushed the phenyl group more towards the NHC ligand. This change in position changed the orientation of the LUMO which made these orbitals more available for metathesis below the carbene group. According to these results, an incoming alkene will start a metathesis reaction with this complex using an associative mechanism whereas **1** as well as **68** used a dissociative mechanism. But because of the steric hindrance of the pyridine group around the carbene, this complex will be less active during a metathesis reaction than **1**.

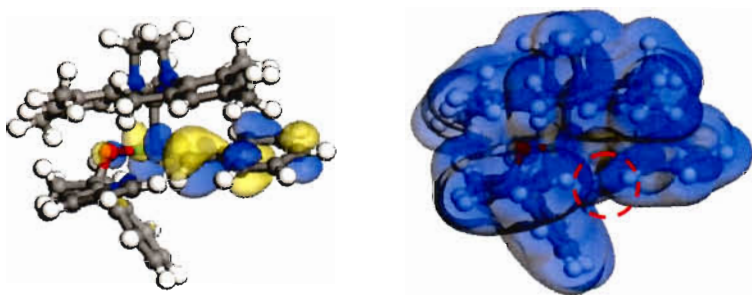


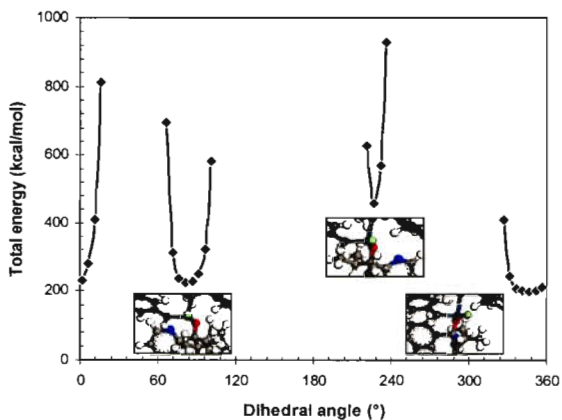
Figure 5.75: LUMO and electron density function of **26**.

- **Complex 27**

When **27** was submitted for a conformer search, several energies were obtained. To see the minima of the complex more clearly the data points with higher energies than 1000 kcal/mol were omitted (**Graph 5.5**).

For this complex it was found that it has five minima: 224 kcal/mol at Ru-O-C-C dihedral angle 82°, 1040 kcal/mol at Ru-O-C-C dihedral angle 162°, 458 kcal/mol at Ru-O-C-C dihedral angle 227°, 2540 kcal/mol at Ru-O-C-C dihedral angle 262° and 200 kcal/mol at Ru-O-C-C dihedral angle 347°, of which the last one was found to be the global minimum.

Since the curve around 347° is the broadest curve of this complex, it can be concluded that for this complex the global minimum was also found to be the most stable minimum.



Graph 5.5: Energy profile of conformer search of **27**.

The global minimum was geometrically optimized again and an energy of 200 kcal/mol was obtained with a Ru-O-C-C dihedral angle of 347°.

After comparing the global minimum with the minimum obtained after geometric optimization without a ruthenium-nitrogen bond (§5.1.5), it was found that these values were similar (**Table 5.9**), which means that the calculation method for

optimization of the structure without ruthenium-nitrogen found a structure close to, but slightly from the global minimum.

Table 5.9: Comparison of total energies, dihedral angles and distances of the found structures

	Optimized structure after the Ru-N bond was removed (§5.1.5)	Optimized structure after conformer search
Total energy (kcal/mol)	409	200
Dihedral angle (°)	327	347
Distance of Ru-N (Å)	2.164	2.164

When the electron density of this complex was overlaid on the LUMO (Figure 5.76), it was found that the LUMO around the carbene did not perforate the surface of the electrons. However, because the LUMO around the carbene carbon was found to be very close to perforating the surface of these electrons (indicated by the red circle), this will be the place where the alkene comes in to coordinate to the carbene and start a metathesis reaction.

A difference between this complex, **1** and **68** is that the LUMO of the carbene in this complex is below the carbene group (just like in **25** and **26**), whereas the LUMO of **1** as well as **68** is in front of the carbene group. As mentioned before (§5.1.5), this is probably because the R groups of this ligand were more bulky towards the carbene which pushed the phenyl group more towards the NHC ligand. This change in position changed the orientation of the LUMO which made these orbitals more available for metathesis below the carbene group. According to these results, an incoming alkene will start a metathesis reaction with this complex using an associative mechanism whereas **1** as well as **68** used a dissociative mechanism. However, because of the steric hindrance of the pyridine group around the carbene, this complex will be less active during a metathesis reaction than **1**.

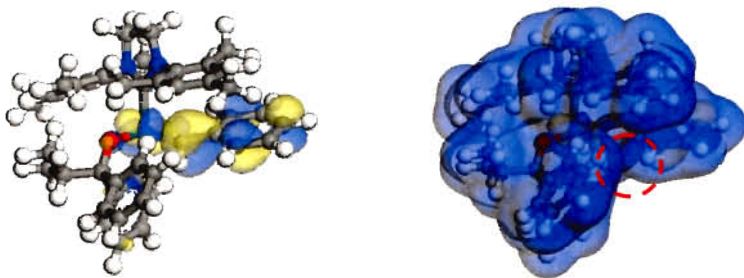


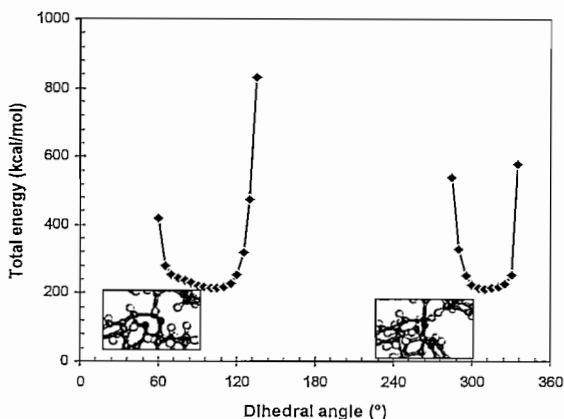
Figure 5.76: LUMO and electron density function of 27.

- **Complex 28**

When **28** was submitted for a conformer search, several energies were obtained. To see the minima of the complex more clearly the data points with higher energies than 1000 kcal/mol were omitted (**Graph 5.6**).

For this complex it was found that it has four minima: 213 kcal/mol at Ru-O-C-C dihedral angle 105°, 3190 kcal/mol at Ru-O-C-C dihedral angle 165°, 13250 kcal/mol at Ru-O-C-C dihedral angle 235° and 212 kcal/mol at Ru-O-C-C dihedral angle 310° of which the last one was found to be the global minimum.

Since the curve around 105° is the broadest curve of this complex, it can be concluded that for this complex a local minimum was found to be the most stable minimum. Therefore, the global minimum is not as stable as one of its local minima.



Graph 5.6: Energy profile of conformer search of 28.

The global minimum was geometrically optimized again and an energy of 206 kcal/mol was obtained with a Ru-O-C-C dihedral angle of -43° (or 317°).

After comparing the global minimum with the minimum obtained after geometric optimization without a ruthenium-nitrogen bond (§5.1.5), it was found that these values were similar (Table 5.10), which means that the calculation method for optimization of the structure without ruthenium-nitrogen found a structure close to, but slightly from the global minimum.

Table 5.10: Comparison of total energies, dihedral angles and distances of the found structures

	Optimized structure after the Ru-N bond was removed (§5.1.5)	Optimized structure after conformer search
Total energy (kcal/mol)	219	206
Dihedral angle ($^\circ$)	320	317
Distance of Ru-N (Å)	2.186	2.200

When the electron density of this complex was overlaid on the LUMO (Figure 5.77), it was found that the LUMO around the carbene did not perforate the surface of the electrons and because the LUMO around the carbene carbon was found not to be

very close to perforating the surface of these electrons, it will be very hard for the alkene to come in and overlap with the HOMO of the alkene in a metathesis reaction.

A difference between this complex, **25**, **26** and **27** is that the LUMO of the carbene in this complex is in front of the carbene group (just like in **1** and **68**), whereas the LUMO of **25**, **26** as well as **27** is below the carbene group. As mentioned before (§5.1.5), this is probably because the R group of this ligand was less bulky towards the carbene. This resulted in the phenyl group of the carbene not changing position and the LUMO looking similar to the LUMO of **1** and **68**. According to these results, an incoming alkene will start a metathesis reaction with this complex using a dissociative mechanism whereas **25**, **26** and **27** used an associative mechanism. However, because the carbene in this complex is less sterically hindered than that of **1** but more so than **68**, this complex will be less active than **1** but more active than **68** during a metathesis reaction. It will guide the incoming alkene more to the carbene.

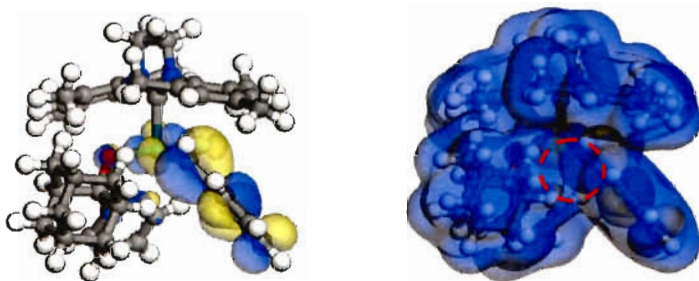


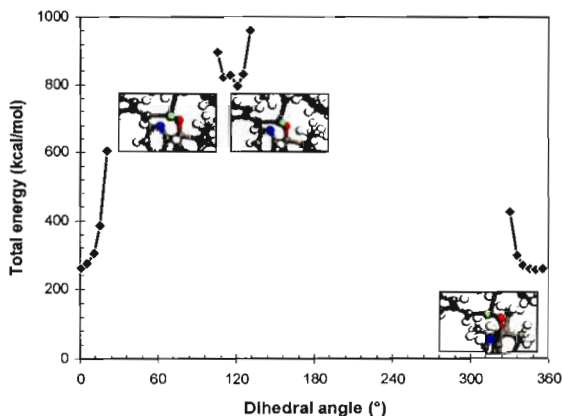
Figure 5.77: LUMO and electron density function of **28**.

- **Complex 29**

When **29** was submitted for a conformer search, several energies were obtained. To see the minima of the complex more clearly the data points with higher energies than 1000 kcal/mol were omitted (**Graph 5.7**).

For this complex, it was found that it has six minima: 12000 kcal/mol at Ru-O-C-C dihedral angle 65°, 823 kcal/mol at Ru-O-C-C dihedral angle 110°, 797 kcal/mol at Ru-O-C-C dihedral angle 120°, 3480 kcal/mol at Ru-O-C-C dihedral angle 190°, 1010 kcal/mol at Ru-O-C-C dihedral angle 275° and 258 kcal/mol at Ru-O-C-C dihedral angle 350° of which the last one was found to be the global minimum.

Since the curve around 350° is the broadest curve of this complex, it can be concluded that for this complex the global minimum was also found to be the most stable minimum.



Graph 5.7: Energy profile of conformer search of **29**.

The global minimum was geometrically optimized again and an energy of 258 kcal/mol was obtained with a Ru-O-C-C dihedral angle of -10° (or 350°).

After comparing the global minimum with the minimum obtained after geometric optimization without a ruthenium-nitrogen bond (§5.1.5), it was found that these values were identical (**Table 5.11**), which means that the calculation method for optimization of the structure without ruthenium-nitrogen, found a structure very close to the global minimum.

Table 5.11: Comparison of total energies, dihedral angles and distances of the found structures

	Optimized structure after the Ru-N bond was removed (§5.1.5)	Optimized structure after conformer search
Total energy (kcal/mol)	258	258
Dihedral angle (°)	350	350
Distance of Ru-N (Å)	2.147	2.147

When the electron density of this complex was overlaid on the LUMO (Figure 5.78), it was found that the LUMO around the carbene did not perforate the surface of the electrons. However, because the LUMO around the carbene carbon was found to be very close to perforating the surface of these electrons (indicated by the red circle), this will be the place where the alkene comes in to coordinate to the carbene and start a metathesis reaction.

A difference between this complex and the complexes **1** and **68** is that the LUMO of the carbene in this complex is below the carbene group (just like in **25**, **26** and **27**), whereas the LUMO of **1** as well as **68** is in front of the carbene group. As mentioned before (§5.1.5), this is probably because the R groups of this ligand were more bulky towards the carbene which pushed the phenyl group more towards the NHC ligand. This change in position changed the orientation of the LUMO which made these orbitals more available for metathesis below the carbene group. According to these results, an incoming alkene will start a metathesis reaction with this complex using an associative mechanism whereas **1** as well as **68** used a dissociative mechanism. However, because of the steric hindrance of the pyridine group around the carbene, this complex will be less active during a metathesis reaction than **1**.

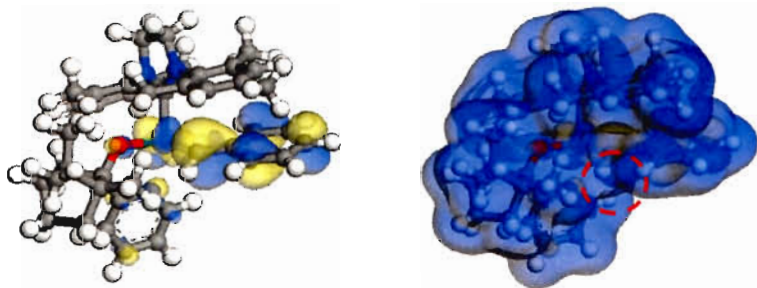


Figure 5.78: LUMO and electron density function of **29**.

5.1.7 Pre-liminary modelling of dissociation step of 25 and 26 in the activation cycle of the mechanism

To obtain the angle whereby the hemilabile ligand open up a conformer search was done (§5.1.6). An additional conformer search was done to find the conformer with the least sterically hindered carbene group by changing the orientations of the hemilabile ligand as well as the phenyl substituent on the carbene group. In order to investigate whether a ligand behaves as a hemilabile ligand, the dissociation step of the activation cycle (Figure 2.13) was investigated. Due to lack of time, only 25 and 26 were investigated.

The geometrically optimized structures of both complexes, which were obtained after the conformers searches in §5.1.6, were used for this conformer search (Figure 5.80).

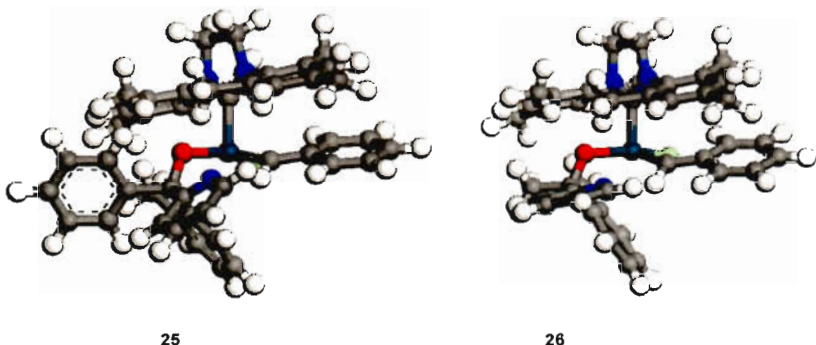
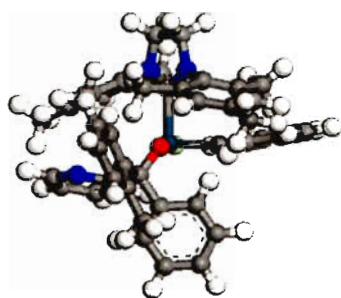
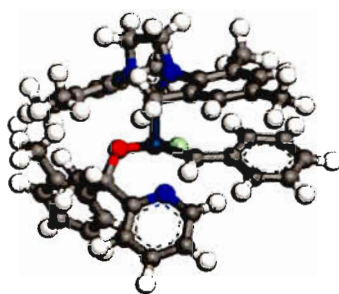


Figure 5.80: Optimized structures of 25 and 26 which were obtained after the first conformer search.

The above mentioned conformer search where conducted by first doing the geometry optimization of the NHC ligand together with the chlorine atom and obtaining the structure with the lowest energy. Then a conformer search was done by changing the dihedral angles of H-C=Ru-O and Ru-O-C-C(pyridine). The setting for the calculation method was the same as in §5.1.6. It was important that this conformer has a minimum in energy so that this structure remains almost the same after geometry optimization. The conformers which were obtained for each complex are shown in Figure 5.81.



25



26

Figure 5.81: Optimized structures of **25** and **26** which were obtained after the second conformer search.

The angles, bond distances and energies that were obtained for both complexes are shown in **Table 5.12**. It was found that the conformer with the least steric hindered carbene group was a local minimum, the energy was higher than after the first conformer search which was found to be the global minimum. The bond distances and angles did not change that much from the conformer found after the first conformer search but the dihedral angles did.

Table 5.12: Angles ($^{\circ}$), bond distances ($\text{\AA}$) and energies (kcal/mol) of **25** and **26** after the first and second conformer search

	25		26	
	Optimized structure after 1 st conformer search	Optimized structure after 2 nd conformer search	Optimized structure after 1 st conformer search	Optimized structure after 2 nd conformer search
Total energy (kcal/mol)	111	333	177	301
Ru-O	2.1	2.0	2.1	2.1
N-Ru	3.8	4.1	3.8	3.1
Ru-O-C	112.5	111.9	115.6	118.0
O-C-C	110.1	112.7	105.8	112.1
Ru-O-C-C	106.3	-35.8	113.4	62.9
O-C-C-N	-24.7	-109.0	-53.9	-0.5
O-Ru-C-C	-157.6	-177.2	-154.9	-167.8

For **25** the nitrogen of the pyridine ring was found not coordinated to the ruthenium atom any more after the minimum with the least steric hindered carbene was found. A reason for that is that **25** undergo a metathesis reaction using a dissociative mechanism, the hemilabile ligand will open up followed by an overlap of the HOMO of the alkene with the LUMO of the ruthenium atom. The nitrogen atom of **26** was still coordinated to the ruthenium atom after the local minimum was found, which means that this hemilabile ligand will open up after the HOMO of an incoming alkene will start to overlap with the LUMO of the ruthenium, better known as an associative mechanism.

By obtaining these conformers, the first step in the activation cycle (A to B) of the metathesis mechanism as shown in Figure 2.13 was obtained.

After the second conformer search, the total energies of both complexes **25** and **26** are much higher than after the first conformer search. The pyridine ring of the complexes would rather stay coordinated to the ruthenium as shown in Figure 5.80. As discussed in §5.1.6, these complexes have a space below the carbene from where an incoming alkene can start a metathesis reaction with the complex. For this reason, the pyridine ring does not opens up to start a dissociative metathesis reaction. Therefore, the N[^]O ligands of complexes **25** and **26** seemed to undergo an associative mechanism during the 1-octene metathesis reaction, the pyridine ring opens up after the incoming alkene overlapped with the LUMO of the carbene.

5.2 Synthesis of ligands and complexes

5.2.1 Introduction

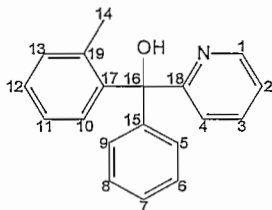
After the modelling was done, the 5 alcohols which were chosen to be investigated experimentally were synthesized. First the alcohols (§5.2.2) and then the lithium salts of the alcohols were synthesized (§5.2.3). Lastly, the lithium salts were coordinated to **4** (§5.2.4).

5.2.2 Preparation of the alcohols

All alcohols, except **19**, were obtained in a good yield (see Tables 4.1 - 4.3) and the GC-MS showed pure products for each. In the case of **19** a yield of not higher than 16% was obtained and the product was not 100% pure. Purification of this product as well as attempts to improve the yield was unsuccessful.

The structures of the alcohols were verified as discussed in the analysis of products in Chapter 4 by GC-MS, MS, IR, ¹H NMR and ¹³C NMR analysis. These results are discussed below (spectra can be found in Appendices III-VI):

- Alcohol 15^[2]



The MS spectrum showed a molecular ion (M^+) of 275 g/mol which indicates the same molecular mass as this alcohol and corresponds with literature.^[2]

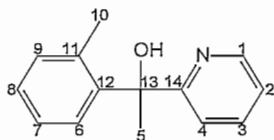
The IR spectrum showed an alcohol peak at 3432.4 cm^{-1} , a C-H stretch of the aromatic rings at 3046.8 cm^{-1} and a stretch of the C=C and C=N double bonds between $1588.4\text{--}1569.9\text{ cm}^{-1}$.

The ^1H NMR spectrum showed a signal from the H_1 atom at 8.599 ppm. Due to the coupling of this H atom with the H_2 atom the signal is splitted into a doublet. A doublet of doublets from H_3 was found between 7.640 and 7.559 ppm due to the coupling with H_2 and H_4 . Between 7.398 and 7.107 ppm a multiplet was found for the $\text{H}_5\text{--H}_{13}$ atoms and the signal from H_4 was found between 7.073 and 7.001 ppm which showed to be a doublet due to the coupling with the H_3 atom. The H_2 atom showed a signal between 6.992 and 6.920 ppm which was splitted twice into a doublet of doublets due the coupling with H_1 and H_3 . Between 6.245 and 6.146 ppm a singlet was found for the H of the OH group and the methyl H atoms of C_{14} were found at 2.119 ppm as a singlet.

The ^{13}C NMR spectrum showed a singlet at 163.69 ppm for the C_{18} atom which was not coupled to any H atoms and a doublet at 147.841 ppm for the C_1 atom which was coupled to one H atom. At 146.305, 144.016 and 139.183 ppm three singlets were found for C_{15} , C_{17} and C_{19} which were not coupled to any H atoms. Due to the coupling with one H atom the signal at 136.246 ppm is a doublet which comes from the C_3 atom and the doublet at 132.555 ppm comes from the C_5 atom. For the same reason the C_{13} , C_6 , C_{12} , C_7 , C_4 and C_2 atoms showed doublets at 128.955, 128.020, 127.676, 127.088, 123.251 and 122.166 ppm. At 81.813 ppm a singlet from C_{16} was found and at 21.700 ppm C_{14} showed a quartet due to the coupling with the three H atoms that are attached to this atom.

From all this data together with the measured melting point of 103°C which showed to be similar to the melting point as mentioned in literature^[2], it can be concluded that the correct product was obtained. The yield of the synthesized alcohol was 52% which was found to be much lower than the 82% which was reported in literature.^[2] A reason for this difference is that the alcohol was synthesized using method C instead of method B from where they have synthesized this alcohol in literature.^[2] The reason for using method C was because the chemicals which had to be used for method B were not available.

• Alcohol 16^[3]



The MS spectrum showed a molecular ion (M^+) of 213 g/mol which indicates the same molecular mass as this alcohol and corresponds with literature.^[3]

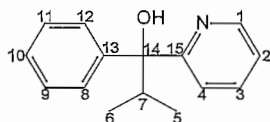
The ^1H NMR spectrum showed a signal from the H_1 atom at 8.544 ppm. Due to the coupling of this H atom with the H_2 atom the signal is splitted into a doublet. A doublet of doublets from H_3 was found between 7.620 and 7.608 ppm due to the coupling with H_2 and H_4 . The signal from H_4 was found between 7.548 and 7.520 ppm which showed to be a doublet due to the coupling with the H_3 atom. Between 7.220 and 7.059 ppm a multiplet was found for the H_6 - H_9 atoms. The H_2 atom showed a signal between 6.924 and 6.911 ppm which was splitted twice into a doublet of doublets due to the coupling with H_1 and H_3 . At 5.454 ppm a singlet was found for the H of the OH group and the six H atoms of the C_5 and C_{10} methyl groups were found at 1.921 and 1.861 ppm both as singlets.

The ^{13}C NMR spectrum showed a singlet at 165.88 ppm for the C_{14} atom which was not coupled to any H atoms and a doublet at 147.26 ppm for the C_1 atom which was coupled to one H atom. At 142.92 and 138.21 ppm two singlets were found for C_{12} and C_{11} which were not coupled to any H atoms. Due to the coupling with one H atom the signal at 136.83 ppm is a doublet which comes from the C_3 atom. For the same reason the C_9 , C_8 , C_7 , C_6 , C_4 and C_2 atoms showed doublets at 132.39, 127.78, 126.86, 125.34, 121.74 and 120.27 ppm. At 76.21 ppm a singlet from C_{13} was found

and at 31.63 and 21.08 ppm C₅ and C₁₀ showed both a quartet due to the coupling with the three H atoms that are attached to these atoms.

From all this data together with the measured melting point of 89-91°C which showed to be similar to the melting point as mentioned in literature^[3], it can be concluded that the correct product was obtained. The yield of 47% was much higher than the 21% obtained in literature, this is probably because the butyl lithium was used as purchased and not synthesized as described in literature.^[3]

- Alcohol 17^[3]



The MS spectrum showed a molecular ion (M⁺) of 227 g/mol which indicates the same molecular mass as this alcohol and corresponds with literature.^[3]

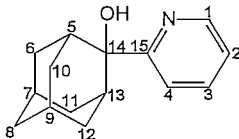
The IR spectrum showed an alcohol peak at 3291.3 cm⁻¹, a C-H stretch of the aromatic rings at 3049.9 cm⁻¹, a C-H stretch of the aliphatic isopropyl group at 2967.8-2865.1 cm⁻¹ and a stretch of the C=C and C=N double bonds at 1596.6 cm⁻¹.

The ¹H NMR spectrum showed a doublet from the H₁ atom at 8.446 ppm. Due to the coupling of this H atom with the H₂ atom the signal is splitted into a doublet. Between 7.637 and 7.588 ppm a multiplet was found for the H₉-H₁₁ atoms. A doublet of doublets from H₃ was found between 7.446 and 7.433 ppm due to the coupling with H₂ and H₄ and the multiplet from the H₈ and H₁₂ atoms was found between 7.296 and 7.270 ppm. The signal from H₄ was found between 7.170 and 7.146 ppm which showed to be a doublet due to the coupling with the H₃ atom. The H₂ atom showed a signal between 7.103 and 7.082 ppm which was split twice into a doublet of doublets due the coupling with H₁ and H₃. At 5.887 ppm a singlet was found for the H of the OH group and the H₇ atom was found as a multiplet between 2.840 and 2.796 ppm. The C₅ and C₆ methyl groups of the isopropyl group were found between 0.954 and 0.943 ppm and between 0.746 and 0.734 ppm, both leaving quartets due to the coupling of the three H atoms of the one methyl group with the H atoms of the other methyl group.

The ^{13}C NMR spectrum showed a singlet at 163.921 ppm for the C_{15} atom which was not coupled to any H atoms and a doublet at 146.928 ppm for the C_1 atom which was coupled to one H atom. At 146.440 ppm a singlet was found for C_{13} which was not coupled to any H atoms. Due to the coupling with one H atom the signal at 136.849 ppm is a doublet which comes from the C_3 atom. For the same reason the C_{10} , C_{12} , C_{11} , C_4 and C_2 atoms showed doublets at 128.130, 126.481, 126.064, 121.675 and 120.466 ppm. At 79.610 ppm a singlet from C_{14} was found and at 36.119 ppm C_7 showed a doublet due to the H atom which was attached. Two quartets were found at 17.188 and 16.735 ppm due to the coupling with the three H atoms that are attached to both C_8 and C_5 atoms.

From all this data together with the measured melting point of 67-70°C which showed to be similar to the melting point as mentioned in literature^[3], it can be concluded that the correct product was obtained. The yield of 67% was much higher than the 44% obtained in literature, this is probably because the butyl lithium which was used as purchased and not synthesized as suggested in literature.^[3]

- Alcohol 18^[4]



The MS spectrum showed a molecular ion (M^+) of 229 g/mol which indicates the same molecular mass as this alcohol and corresponds with literature.^[4]

The IR spectrum showed an alcohol peak at 3395.0 cm^{-1} , a C-H stretch of the aliphatic adamantane group between 2932.7 and 2855.6 cm^{-1} and a stretch of the C=C and C=N double bonds at 1592.7 cm^{-1} .

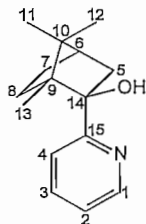
The ^1H NMR spectrum showed a signal from the H_1 atom at 8.567 ppm. Due to the coupling of this H atom with the H_2 atom the signal is splitted into a doublet. A doublet of doublets from H_3 was found between 7.660 and 7.634 ppm due to the coupling with H_2 and H_4 . The signal from H_4 was found between 7.475 and 7.462 ppm which showed to be a doublet due to the coupling with the H_3 atom. The H_2 atom showed a signal between 7.138 and 7.119 ppm which was split twice into a doublet of doublets due the coupling with H_1 and H_3 . A multiplet from H_{11} - H_{12} was found between 2.649

and 2.425 ppm and at 2.054 ppm a singlet was found for the H of the OH group. The H_{13} atom was found as a singlet at 1.889 ppm and the 9 H atoms (H_8-H_{10}) of the adamantane group were found between 1.775 and 1.665 ppm as a multiplet.

The ^{13}C NMR spectrum showed a singlet at 164.547 ppm for the C_{15} atom which was not coupled to any H atoms and a doublet at 149.235 ppm for the C_1 atom which was coupled to one H atom. Due to the coupling with one H atom the signal at 136.448 ppm is a doublet which comes from the C_3 atom. For the same reason the C_4 and C_2 atoms showed doublets at 121.987 and 120.158 ppm. At 77.210 ppm a singlet from C_{14} was found and at 37.923 ppm C_5 showed a doublet due to the H atom which was attached. Two triplets were found at 35.310 and 34.993 ppm due to the coupling with the two H atoms that are attached to both C_6 and C_8 atoms. The C_7 atom was found as a doublet at 33.071 ppm due to the coupling with one H atom and due to the coupling with two H atoms C_{12} showed a triplet at 27.569 ppm. At 27.229 ppm the C_{13} atom showed a doublet due to the coupling with the one H atom that is attached.

From all this data together with the measured melting point of 109°C and the yield of 72% which showed to be the same as the yield as mentioned in literature^[4], it can be concluded that the correct product was obtained.

- Alcohol 19^[5]



The MS spectrum showed a molecular ion (M^+) of 231 g/mol which indicates the same molecular mass as this alcohol and corresponds with literature.^[5]

The IR spectrum showed an alcohol peak at 3446.2 cm^{-1} , a C-H stretch of the aliphatic camphor group between 2958.5 and 2928.3 cm^{-1} and a stretch of the C=C and C=N double bonds between 1571.4 and 1590.4 cm^{-1} .

The ^1H NMR spectrum showed a signal from the H_1 atom at 8.507 ppm. Due to the coupling of this H atom with the H_2 atom the signal is splitted into a doublet. A doublet of doublets from H_3 was found between 7.636 and 7.624 ppm due to the coupling with H_2 and H_4 . The signal from H_4 was found between 7.410 and 7.397 ppm which showed to be a doublet due to the coupling with the H_3 atom. The H_2 atom showed a signal between 7.144 and 7.141 ppm which was splitted twice into a doublet of doublets due to the coupling with H_1 and H_3 . At 5.240 ppm a singlet was found for the H of the OH group and the three methyl groups of H_{11} - H_{13} were found between 0.983 and 0.803 ppm as a multiplet. The 7 H atoms of H_5 - H_8 were found between 1.394 and 1.250 ppm as a multiplet.

The ^{13}C NMR spectrum showed a singlet at 163.54 ppm for the C_{15} atom which was not coupled to any H atoms and a doublet at 147.36 ppm for the C_1 atom which was coupled to one H atom. Due to the coupling with one H atom the signal at 135.52 ppm is a doublet which comes from the C_3 atom. For the same reason the C_4 and C_2 atoms showed doublets at 121.56 and 120.58 ppm. At 82.64 ppm a singlet from C_{14} was found and at 57.67 ppm C_9 showed a singlet. The C_{10} atom was found as a singlet at 46.76 ppm and at 43.27 ppm a triplet from C_5 was found due to the coupling with the two H atoms that are attached. The C_6 atom was found as a doublet at 43.03 ppm due to the coupling with one H atom and due to the coupling with two H atoms C_8 showed a triplet at 29.89 ppm and C_7 at 27.02 ppm. At 19.75, 19.12 and 9.22 ppm, the C_{12} , C_{11} and C_{13} atoms showed all three quartets due to the coupling with 3 H atoms that are attached.

At first a 5% yield was obtained for this alcohol which was improved to 16% by adding a more diluted camphor solution over 30 minutes instead of adding it in a higher concentration in a few minutes. Even when the reaction was stirred twice as long, at higher temperature as they mentioned in literature^{[5][6]}, the yield did not improve. No further improvement could be obtained, although literature reported a 83% yield.^[6] Due to impurities the melting point of 56-67°C could also not be obtained. In an effort to identify the reason for the inability to obtain the pure product in high yields, the camphor and pyridine were analyzed with the GC-MS and large peaks were obtained. About 90% of the impurities in the product were identified as camphor. The (+)-enantiomer of camphor, which showed to be 99% pure, showed a similar low yield. For this reason it can be concluded that the impure product is not as a result of using impure camphor.

After 2-bromopyridine and n-butyl lithium were reacted in the first part of the reaction, the reaction mixture turned red, just as mentioned in literature.^[9] So most probably the lithium pyridine intermediate was formed. Because camphor as well as the lithium

pyridine intermediate, which are the two starting materials of the second part of this reaction, showed to be present in the reaction mixture, it should be possible that the desired alcohol was obtained. The fact that this reaction occurs in a very low yield has to be related to other factors than the starting materials. Some of these factors can be the solvent, the ratio and order of the chemicals added, this was however not investigated further.

It was found impossible to purify this alcohol, because after recrystallization only a small amount of the camphor was removed. During flash chromatography using a silica column the camphor moved through the column, but for **19** it was not possible to pass through the column, the alcohol remained on the column.

5.2.3 Preparation of the lithium salts

All lithium salts were obtained in a good yield (see Table 4.4), except **24** which showed to be only 18%. The reason for the low yield of **24** is due to the fact that the impure alcohol (**19**) was used to make the lithium salt. All the impurities of the alcohols were removed during the washing with the pentane. During the preparation of lithium salt **24** the pentane solution became dark red after the two hours of stirring, but when the salt was washed with pentane just like the other lithium salts were washed, a white powder was obtained. Due to the sensitivity to air, no further characterization or purification was done on the lithium salts.

5.2.4 Preparation of the complexes

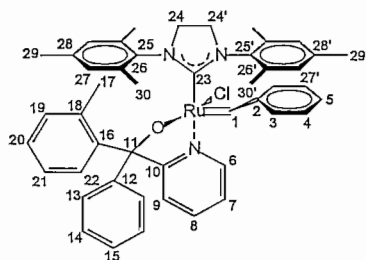
The reaction mixtures containing **25**, **26** and **27**, were stirred for about 2 days while monitored by TLC. Reaction mixtures containing **28** and **29** had to be stirred for a week until the green spot on TLC, which represents the prepared complex, did not change. This was probably due to the sterical hindrance of the last mentioned complexes which makes it harder for the lithium salt to coordinate to **4** (§4.5.2).

For **25**, **26** and **27**, it was necessary to repeat the washing procedure twice to get a pure product. These complexes were obtained in moderate yields (see Tables 4.5 - 4.6) which is probably a result of their intensive purification procedure (§4.5.2). The synthesized complexes **25**, **26** and **27** were verified by ^1H NMR and MALDI TOF analysis. It is important that the synthesized complexes show just one carbene peak on ^1H NMR. Because **4** contains a PCy_3 group, it is also useful to get a ^{31}P NMR spectrum, when all the unreacted **4** is washed out of the complex, the spectrum would not show any phosphorus peak.^[7]

Complexes 28 and 29 did not show a carbene peak on the ^1H NMR spectra and no signals of the bulky R-groups were observed either. Because the green spots on the TLC indicated that the products were present before the washing procedure, it can be concluded that these complexes decomposed during the washing procedure. They were probably not as stable as 25, 26 and 27.

The NMR and MALDI TOF results of the synthesized complexes 25, 26 and 27 will be discussed below (spectra can be found in Appendices III and V).

- Complex 25



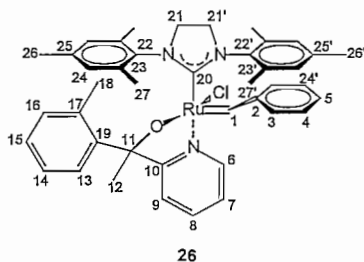
25

MALDI TOF MS showed that this complex has a molecular weight of 807 g/mol which indicates the correct molecular weight of this complex.

The ^1H NMR spectrum showed a signal from the carbene H_1 atom at 17.327 ppm. A doublet from H_8 was found between 9.758 and 9.527 ppm due to the coupling with H_7 and the signal from H_5 and H_6 was found between 7.096 and 7.084 ppm which showed to be a doublet of doublets. The H_{13} - H_{15} , H_{18} - H_{22} , H_{27} and $\text{H}_{27'}$ atoms showed a multiplet between 7.084 and 6.987 ppm and between 6.676 and 6.551 ppm a triplet from the H_4 and H_7 atoms was found. The H_9 atom was found as a doublet between 6.444 and 6.355 ppm due to the coupling with the H_8 atom and a doublet from H_3 was found between 6.355 and 6.164 ppm. Between 3.728 and 3.466 ppm a multiplet from the H_{24} and $\text{H}_{24'}$ atoms was found. The 18 H atoms of the 6 methyl groups of the NHC ligand were found as three singlets between 2.494 and 1.834 ppm. The methyl group of C_{17} was found as a singlet at 1.235 ppm.

From this data, it can be concluded that the correct product was obtained.

• Complex 26

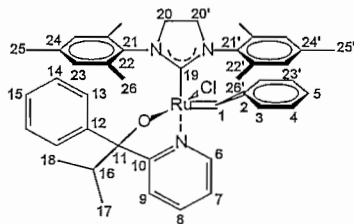


MALDI TOF MS showed that this complex has a molecular weight of 745 g/mol which indicates the correct molecular weight of this complex.

The ^1H NMR spectrum showed a singlet signal from the carbene H_1 atom at 17.318 ppm. A doublet from H_6 was found between 9.871 and 9.463 ppm due to the coupling with H_7 and the signal from H_3 was found between 7.436 and 7.261 ppm which showed to be a doublet due to the coupling with the H_4 atom. The H_5 and H_8 atoms showed a triplet between 7.125 and 6.990 ppm. A multiplet from the H_{13} - H_{16} , H_{24} and $\text{H}_{24'}$ atoms was found between 6.965 and 6.719 ppm and between 6.701 and 6.574 ppm a triplet from the H_4 and H_7 atoms was found. The H_9 atom was found as a doublet between 6.333 and 6.000 ppm due to the coupling with the H_8 atom and a triplet from the H_{21} and $\text{H}_{21'}$ atoms was found between 4.239 and 3.777 ppm. A multiplet of the 18 H atoms of the 6 methyl groups of the NHC ligand were found between 2.601 and 2.364 ppm. The methyl groups of C_{12} and C_{18} were found as a singlet and a doublet at 1.571 ppm and between 1.406 and 1.086 ppm.

From this data, it can be concluded that the correct product was obtained.

- Complex 27



27

MALDI TOF MS showed that this complex has a molecular weight of 758 g/mol which indicates the correct molecular weight of this complex.

The ^1H NMR spectrum showed a singlet signal from the carbene H_1 atom at 17.332 ppm. A doublet from H_6 was found between 9.393 and 9.384 ppm due to the coupling with H_7 and the doublet from H_5 was found between 7.291 and 7.266 ppm. The 3 H atoms of H_{13} - H_{15} were found as a multiplet at 7.034 ppm and the H_9 and H_8 atoms showed a multiplet at 6.940 ppm. A multiplet from the H_{23} and $\text{H}_{23'}$ atoms was found between 6.868 and 6.835 ppm and between 6.592 and 6.567 ppm a triplet from the H_4 and H_7 atoms was found. A triplet from the H_{20} and $\text{H}_{20'}$ atoms was found between 4.082 and 4.002 ppm. Three singlets of the 18 H atoms of the 6 methyl groups of the NHC ligand were found between 2.716 and 2.122 ppm. The 6 H atoms of C_{17} and C_{18} were found as a multiplet between 1.278 and 1.235 ppm and a multiplet between 0.649 and 0.638 ppm. Between 1.549 and 1.342 ppm a triplet from H_{18} was found.

From this data, it can be concluded that the correct product was obtained.

After complexes 25, 26 and 27 were synthesized and showed a single carbene peak on the ^1H NMR spectrum around 17.3 ppm and no phosphorus peak on the ^{31}P NMR spectrum during characterization, they were tested for a 1-octene metathesis reaction.

5.3 Metathesis

5.3.1 Introduction

During the metathesis reactions, the decrease of 1-octene, the increase of primary metathesis products (PMP), the formation of isomerisation products (IP) and secondary metathesis products (SMP) were monitored by GC (§4.7). For a metathesis reaction with 1-octene the PMP are ethylene (C_2) and 7-tetradecene (C_{14}) (*trans* and *cis*), the IP are 2-octene ($C_2=C_8$), 3-octene ($C_3=C_6$) and 4-octene ($C_4=C_4$) and the SMP that were obtained were nonene (C_9), decene (C_{10}), undecene (C_{11}), dodecene (C_{12}), tridecene (C_{13}), pentadecene (C_{15}) and hexadecene (C_{16}).

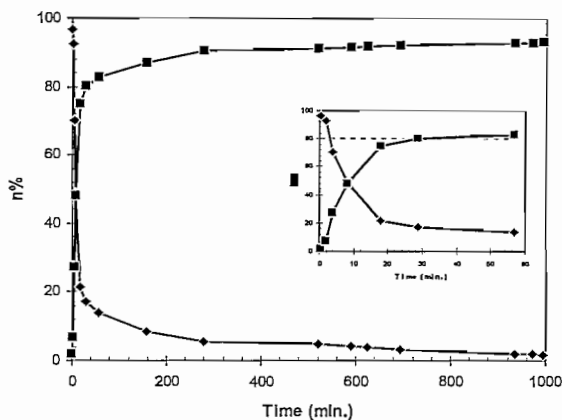
The metathesis results of the three Grubbs 2 type complexes **25**, **26** and **27** were compared with the metathesis results of complex **1** and will be discussed in the following paragraphs.

5.3.2 Metathesis reaction with complex 1

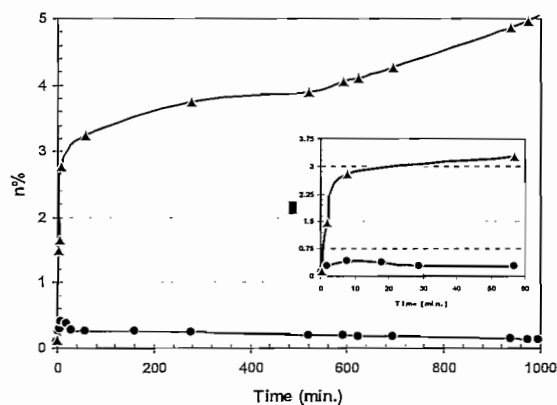
Before the new complexes were tested, complex **1** was studied in a 1-octene metathesis reaction at 60°C, with a molar ratio ruthenium : 1-octene of 1 : 9000. These conditions were chosen because in a previous study it was found to be the optimal conditions for this complex.^[1] To discuss the activity and selectivity of a catalyst it is important to look at the decreasing 1-octene and the formation of PMP, SMP and IP. The graphs of the decrease of 1-octene and the formation of PMP, SMP and IP with complex **1** are shown in Graph 5.8 and 5.9.

It was found that this catalyst has a very high activity, because in the first hour 83% PMP (Graph 5.8) was formed where according to the literature complex **4** showed not be that active.^[1] After 1 hour, the formation of PMP slowed down because the concentration of 1-octene decrease in the reaction mixture. The slope of the graph became 0 after about 16.5 hour (995 min.) where 93% PMP was formed. At that time only 0.1% IP was formed, but in the first 15 minutes of the reaction the IP increased to 0.4% after which it decreased to 0.1% which is probably due to cross metathesis of the IP to form SMP (Graph 5.9). After 16.5 hours 5% SMP was formed which resulted together with the 93% PMP in a selectivity of 95%.

The overall efficiency of a catalyst can also be described by the turnover number (TON), the number of 1-octene molecules that were converted to metathesis products by one molecule of pre-catalyst, which was found to be 8373 for complex **1**.



Graph 5.8: The decrease of 1-octene [♦] and the formation of PMP [■] during metathesis with complex 1 at 60°C and a molar ratio complex : 1-octene of 1 : 9000 (Enlarged inset of the first 60 min.)

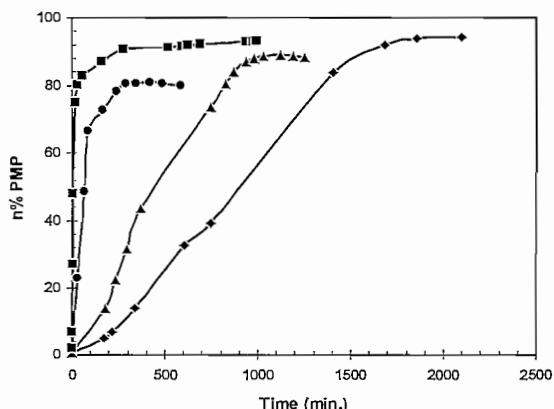


Graph 5.9: The formation of IP [●] and SMP [▲] during metathesis with complex 1 at 60°C and a molar ratio complex : 1-octene of 1 : 9000 (Enlarged inset of the first 60 min.)

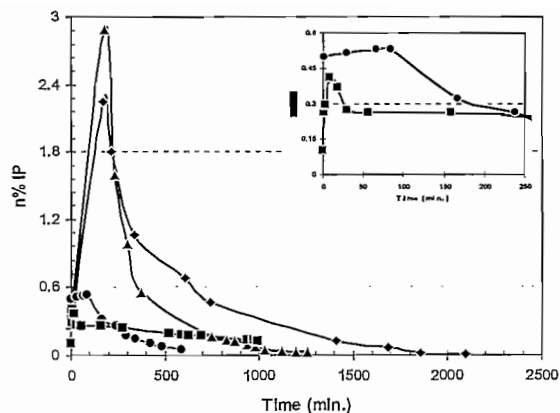
5.3.3 Comparison of activity and selectivity of synthesized complexes with complex 1

To compare the synthesized complexes 25, 26 and 27 to complex 1, the metathesis reactions were carried out under the same conditions, at 60°C and with a ruthenium : 1-octene molar ratio of 1 : 9000. The graphs of the formation of PMP, IP and SMP during these metathesis reactions are shown in Graphs 5.10, 5.11 and 5.12.

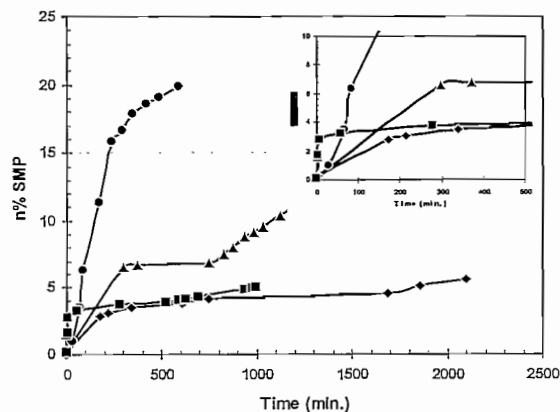
For the determination of which complex was more active, the increase of PMP within a certain time was compared for each complex. After about 170 min. complex 1 formed 87% PMP, where the synthesized complexes formed 5% (25), 73% (26) and 14% (27) PMP. From this it could be concluded that complex 1 is the most active complex. But it was also found that this complex is very active in the first few hours of the metathesis reaction but after about 90% PMP was formed the activity decreased and the maximum amount of PMP was only obtained after about 16.5 hours (995 min.). For complexes 25, 26 and 27, a proportional distributed decrease in activity was observed from the start of the reaction till the maximum PMP was formed. For this reason 26 formed the maximum amount of PMP in half the time that 1 formed it (421 min.). Complexes 25 and 27 reached their maximum PMP after 2098 min. (25) and 1121 min. (27) which showed to be longer than that of complexes 26 and 1. Of the synthesized complexes, complex 26 was found to be the most active complex and 25 showed to be the least active complex.



Graph 5.10: The formation of PMP during metathesis with 1-octene in the presence of complex 1 [■] and the synthesized complexes 25 [◆], 26 [●] and 27 [▲] at 60°C and a molar ratio complex : 1-octene of 1 : 9000.



Graph 5.11: The formation of IP during metathesis with 1-octene in the presence of complex 1 [■] and the synthesized complexes 25 [★], 26 [●] and 27 [▲] at 60°C and a molar ratio complex : 1-octene of 1 : 9000 (Enlarged inset of the first 250 min.)



Graph 5.12: The formation of SMP during metathesis with 1-octene in the presence of complex 1 [■] and the synthesized complexes 25 [★], 26 [●] and 27 [▲] at 60°C and a molar ratio complex : 1-octene of 1 : 9000 (Enlarged inset of the first 500 min.)

For the determination which complex is more selective, the formula as shown in §4.7.3 was used to calculate the selectivity towards PMP (%S) (Table 5.13). It was found that none of the synthesized complexes showed a better selectivity than complex 1. For each complex the same curve was observed for the formation of IP in comparison to that of complex 1. For complex 1 the maximum IP was found after about 10 min. where that of complex 26 was found after 90 min. and that of complexes 27 and 25 after about 175 min. The IP undergo metathesis to form SMP and it was found that the more active the complex is, the earlier the maximum IP was formed and the more SMP was formed (Table 5.13). Because complex 1 showed to be very active in the first few hours of the reaction and less active after that, also the formation of SMP slowed down. This resulted in a low amount of SMP which was comparable to the SMP when the least active synthesized complex was used, 25. Where complexes 1 and 25 showed to have an SMP of about 5% at the end of the metathesis reaction, complexes 26 and 27 showed 19.9% and 10.6% SMP which is much higher because the activity of these complexes will not decrease during the metathesis reaction like that of complex 1. The formation of SMP will continue which will result in a higher amount of SMP of complexes 26 and 27. For this reason the selectivity of complex 25 was similar to that of complex 1 and the selectivity of complexes 26 and 27 showed to be less.

Table 5.13: Selectivity of the synthesized Grubbs 2-type of complexes in comparison to 1.

Pre-catalyst	%PMP	%IP	%SMP	%S	Reaction time (min.)	TON
1	93.0	0.1	5.1	94.8	995	8373
25	94.0	0	5.5	94.5	2098	8464
26	80.0	0.1	19.9	80.1	421	7267
27	88.2	0	11.5	88.5	1121	7939

So in conclusion, the synthesized complexes were less active and less selective than complex 1, but the TON of complex 25 was found to be better than complex 1 which means that this catalyst will convert more 1-octene molecules into PMP.

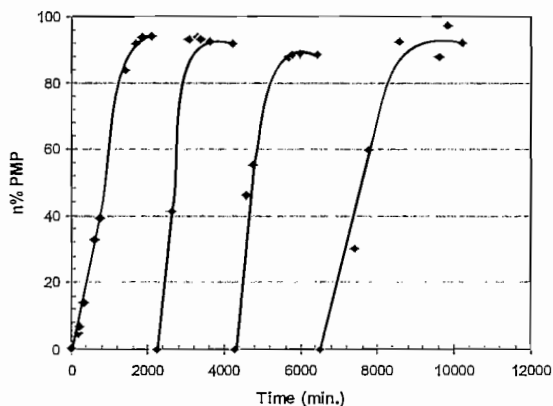
5.3.4 Lifetime of the synthesized complexes

To determine the lifetime of the synthesized complexes, 20 mL 1-octene was added when most of the 1-octene was converted, as explained in §4.8.4.

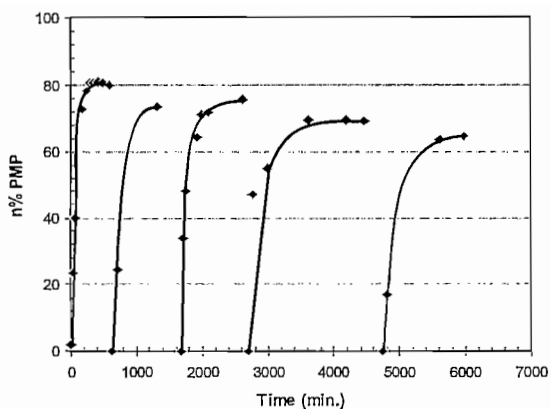
The graphs of the PMP during this investigation are shown in Graphs 5.13, 5.14 and 5.15. Table 5.14 shows the time it takes for the complexes to convert the 1-octene to max. PMP, SMP and IP. In general it was found that the activity as well as the TON of the complexes decrease after each new addition of 1-octene. A reason for this observation is the fact that the

catalyst loading gets lower every time a sample is taken. For the same reason the selectivity also gets lower, the maximum amount of PMP after new 1-octene is added is lower than the earlier reached maximum. After the last addition 1-octene, complex 25 showed a higher max. PMP than the earlier maxima which can be because it gets harder to find the internal standard nonane peak in the GC-spectrum as a result of the dilution of nonane.

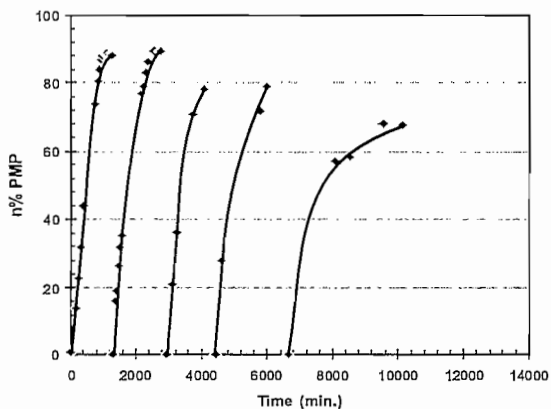
However the complexes were still active when the investigation was terminated, so it can not be concluded which complex has the longest life time. When the investigation was stopped, complex 25 was active for 7 days (10325 min.), complex 26 for 4 days (5976 min.) and complex 27 for 8 days (11827 min.). Since complex 1 showed to be active for about 2 days according to literature^[8] and the synthesized complexes were still active after the investigation was stopped, it can be concluded that all three synthesized complexes have improved lifetime.



Graph 5.13: The formation of PMP during metathesis with four additions of 1-octene in the presence of complex 25 at 60°C and a complex : 1-octene molar ratio of 1 : 9000



Graph 5.14: The formation of PMP during metathesis with five additions of 1-octene in the presence of complex 26 at 60°C and a complex : 1-octene molar ratio of 1 : 9000



Graph 5.15: The formation of PMP during metathesis with five additions of 1-octene in the presence of complex 27 at 60°C and a complex : 1-octene molar ratio of 1 : 9000

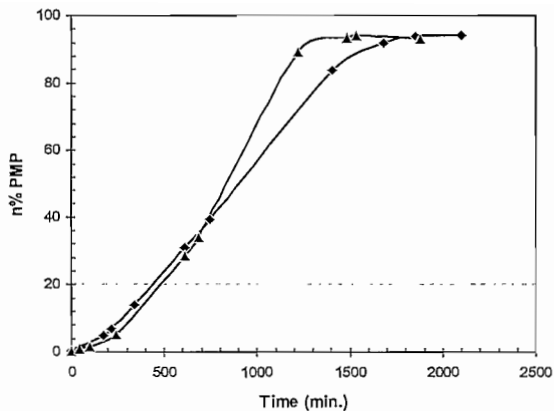
Table 5.14: Conversion time of complexes 25, 26 and 27 after every addition of 1-octene

Pre-catalyst		Addition 1	Addition 2	Addition 3	Addition 4	Addition 5
25	t (min.) =	2190	2067	2246	3822	-
	max. PMP (%) =	94,3	91,8	88,8	92,2	-
	SMP (%) =	5,6	8,2	11,1	7,6	-
	IP (%) =	0	0	0	0	-
	S (%) =	94,4	91,8	88,9	92,4	-
	TON =	8487	8259	7989	8297	-
26	t (min.) =	630	1039	1024	2036	1247
	max. PMP (%) =	80,0	73,4	75,5	69,1	64,6
	SMP (%) =	19,9	26,1	23,8	30,6	33,6
	IP (%) =	0,1	0,2	0,2	0,2	0,7
	S (%) =	80,1	73,8	76,0	69,3	65,8
	TON =	7196	6607	6799	6222	5810
27	t (min.) =	1298	1632	1484	2246	5167
	max. PMP (%) =	88,2	89,5	78,2	71,7	78,8
	SMP (%) =	11,5	9,4	13,8	6,2	9,8
	IP (%) =	0	0,1	0,5	0,4	0,2
	S (%) =	88,5	90,5	85,0	92,0	88,9
	TON =	7939	8059	7036	6455	7091

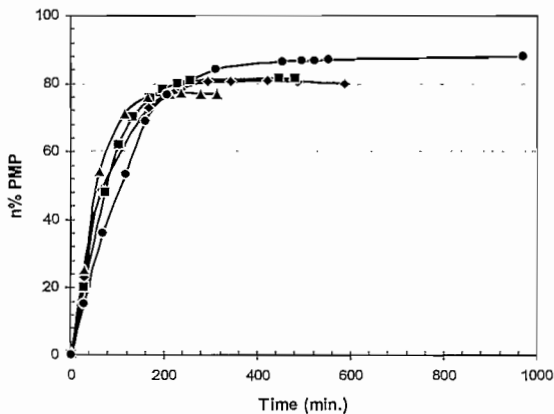
5.3.5 Variation of molar ratio complex : 1-octene

When the synthesized complexes were used at different molar ratios the graphs as shown in **Graphs 5.16, 5.17 and 5.18** were obtained. The same trend was observed for all three complexes (**Table 5.15**); when the molar ratio is increased, the catalyst concentration in the reaction mixture decrease and the number of effective collisions during the reaction decreased which results in a lower activity. A low activity results in a high percentage PMP and a low percentage SMP, as explained in §5.3.3. As a result of the lower activity at higher molar ratio, the reaction time increase. Together with the reaction time also the TON increase, which means more 1-octene are converted into PMP.

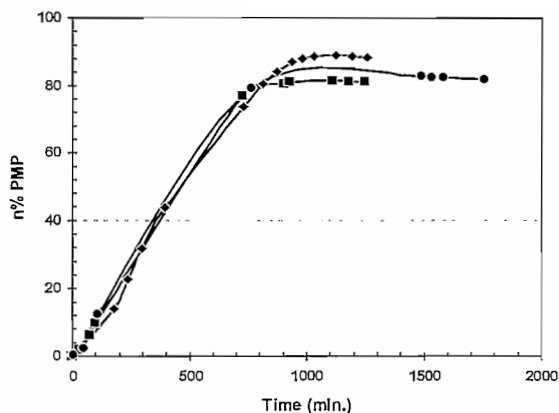
The increase of PMP in the first hour(s) of the reaction is similar for different molar ratios, all the curves of one complex follow the same trend. This means that the different molar ratios do not influence the initiation step of the reaction.



Graph 5.16: The formation of PMP during metathesis with 1-octene in the presence of complex 25 in a complex : 1-octene molar ratio of 1 : 6500 (▲) and 1 : 9000 (◆) at 60°C.



Graph 5.17: The formation of PMP during metathesis with 1-octene in the presence of complex 26 in a complex : 1-octene molar ratio of 1 : 4500 (▲), 1 : 9000 (◆), 1 : 10700 (■) and 1 : 12000 (●) at 60°C.



Graph 5.18: The formation of PMP during metathesis with 1-octene in the presence of complex 27 in a complex : 1-octene molar ratio of 1 : 9000 (♦), 1 : 12000 (■) and 1 : 14000 (●) at 60°C.

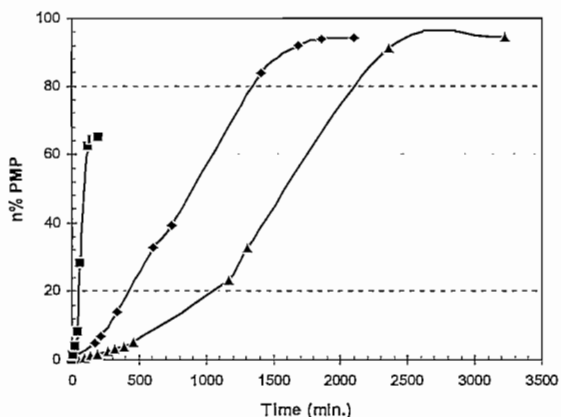
Table 5.15: % PMP and SMP after metathesis with 25, 26 and 27 at different molar ratios (mr) complex : 1-octene

	25		26				27		
mr	6500	9000	4500	9000	10700	12000	9000	12000	14000
t (min.)	1875	2098	313	595	481	970	1265	1244	1752
%PMP	93.2	94.0	77.0	80.0	81.6	88.0	88.2	81.0	81.9
%SMP	6.7	5.5	20.6	19.9	17.1	11.1	11.5	18.1	18.0
TON	6062	8460	3465	7196	8728	10555	7939	9723	11460

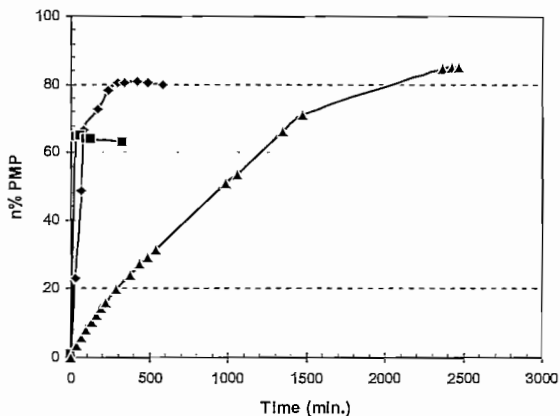
5.3.6 Variation of temperature

When the metathesis reactions were done at different temperatures the graphs as shown in Graphs 5.19, 5.20 and 5.21 were obtained. A trend was observed for all three complexes (Table 5.16); when a metathesis reaction was done at higher temperatures, the kinetic energy of the molecules increased creating more movement which leads to more effective collisions during the reaction and an higher activity. When the activity as well as the amount of SMP increased, the percentage PMP decreased, as explained in §5.3.3. As a result of the higher activity at higher temperatures, the reaction time decrease. Together with the reaction time also the TON decrease, which means that less 1-octene are converted into PMP.

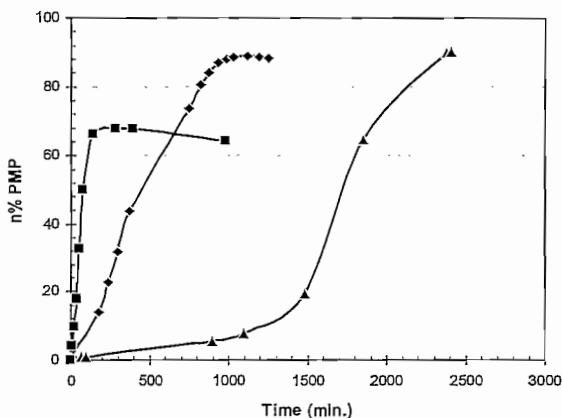
The increase of PMP in the first hour(s) of the reaction is different at different temperatures, all the curves of one complex do not follow the same trend. This means that the different temperatures have a great influence in the initiation step of the reaction. For complex 27, the initiation of the catalyst took about 1400 minutes at 40 °C (Graph 5.21).



Graph 5.19: The formation of PMP during metathesis with 1-octene in the presence of complex 25 at 40°C (▲), 60°C (+) and 80°C (■) and a complex : 1-octene molar ratio of 1 : 9000



Graph 5.20: The formation of PMP during metathesis with 1-octene in the presence of complex 26 at 40°C (▲), 60°C (◆) and 80°C (■) and a complex : 1-octene molar ratio of 1 : 9000



Graph 5.21: The formation of PMP during metathesis with 1-octene in the presence of complex 27 at 40°C (▲), 60°C (◆) and 80°C (■) and a complex : 1-octene molar ratio of 1 : 9000

Table 5.16: % PMP and SMP after metathesis with 25, 26 and 27 at different temperatures

	25			26			27		
T (°C)	40°C	60°C	80°C	40°C	60°C	80°C	40°C	60°C	80°C
t (min.)	3224	2098	203	2463	595	323	2410	1265	981
%PMP	95.4	94.0	64.9	85.2	80.0	63.1	90.2	88.2	64.4
%SMP	3.6	5.5	34.4	10.5	19.9	35.6	9.4	11.5	35.4
TON	8582	8460	5845	7670	7196	5678	8118	7939	5797

5.4 Comparison of modelling and experimental results

In molecular modelling (§5.1) first calculations were done to predict the ability of several alcohols to coordinate as a ligand to complex 4 followed by calculations to predict the activity of these complexes during a metathesis reaction. By synthesizing 5 ligands (§5.2) and coordinate them to complex 4 (§5.3), it was possible to investigate the value of molecular modelling by comparing the modelling results with the experimental results. This chapter can be divided into two subdivisions, the preparation of the complexes and their activity in the metathesis reactions.

5.4.1 Preparation of the complexes

According to molecular modelling, alcohols 15, 16 and 17 showed to have similar electronic properties as well as a similar size and orientation of the R groups as 9 which will result in a similar ease in synthesis. The HOMO around the nitrogen and oxygen atoms will therefore overlap easy with the LUMO of the Grubbs 2 pre-catalyst. In comparison to the experimental results, the same observation was made, it is easy to synthesize these complexes.

The alcohols 18 and 19 were not chosen because of their similar electronic properties to 9 or 36, but because of their differences in enantioselectivity or bulkiness. The bulky R groups of these alcohols will result more difficult synthesis in comparison to 9. Therefore it will be difficult for the HOMO around the nitrogen and oxygen atoms to overlap with the LUMO of the Grubbs 2 pre-catalyst. Since the difference in bulkiness between the R group of 19 and that of 18 is not much, it would not show a difference in the ease to synthesize. In comparison to the experimental results, the same observation was made, it was difficult to synthesize complexes 18 and 19.

5.4.2 Activity in metathesis reactions

According to molecular modelling, complexes **25**, **26** and **27** showed similar electronic properties than that of complex **1**. These three complexes show slightly different steric hindrance around the carbene due to their different R groups. This differences will then result in differences in the ease of the metathesis reaction. Because complex **25** is the most sterical hindered complex, it will be more difficult for its LUMO around the carbene to overlap with the HOMO of an incoming alkene. Therefore, for complex **26**, it will be more easy to overlap, since this is the least sterical hindered complex. In comparison to the experimental results, the same observation was made, complex **26** is the least active complex during a metathesis reaction, followed by complex **27** and complex **25** from which the last one is the most active complex. In comparison to **1**, all three synthesized complexes are less active since the carbene phenyl of this complex is orientated in another position which guides the incoming alkene more to the carbene.

Unfortunately, the modelling results of complexes **28** and **29** could not be compared to experimental results due to instability of the complexes.

So in conclusion molecular modelling gave in this project a good indication about how the ligand would coordinate to **4** as well as how this synthesized complex would behave in a metathesis reaction.

5.5 References

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Chapter 6: Conclusion and recommendations

6.1 Introduction

The main aim of this study was to improve activity as well as lifetime of Grubbs-type of catalysts, which was done by investigating several aromatic N⁺O hemilabile ligands, their Grubbs derivatives and their behaviour in a 1-octene metathesis reaction. Earlier work was done by Jordaan^[1], who investigated several types of hemilabile ligands when coordinated to a Grubbs 2-type of catalyst. She found that the pre-catalyst with an aromatic N⁺O hemilabile ligand (Puk-Grubbs 2) seemed to increase the activity and lifetime during a metathesis reaction in comparison to Grubbs 2 as well as pre-catalysts with non-aromatic hemilabile ligands.

6.2 Molecular modelling of hemilabile ligands and their complexes

Earlier investigations found that GGA/PW91/DNP in DMol³ (DFT) of the modelling program Material Studio showed a good correlation with experimental results for catalysts with hemilabile ligands.^{[1][2]} It was possible to compare the HOMO, LUMO and Fukui functions of the hemilabile ligand of the Puk-Grubbs 2 pre-catalyst (1) with 202 possible hemilabile ligands, with the use of DFT calculations. This screening process was done on a visual comparison of the orbitals.

From the 202 investigated ligands, it was found that the position and size of the R groups attached to the ligand had a large influence on the orientation of the HOMO and LUMO orbitals. Bulky aliphatic substituents like those of ligands 18 and 19, can influence the chemistry of these ligands in such a way that these ligands do not act as a hemilabile ligand but as monodentate ligands. It is then impossible for the N atom to coordinate with ruthenium metal centre. Ligands 15-17 contain two different R substituents from which one or two (for ligand 15) is aromatic. This is different from the one aliphatic R group of ligands 18 and 19. The two R substituents of ligands 15-17 gives the ligand more freedom of movement. This implies that the lower the energy the more stable the ligands will be depends on the orientation of the substituents on the ligands. Also the electron withdrawing or electron donating R groups of the ligands have a great influence on the HOMO and LUMO orbitals of the ligands because an electron donating R group will possibly result in a larger HOMO around the nitrogen and oxygen atoms. This will result in an easier overlap with the Grubbs 2 type catalyst.

After modelling the dissociation step of complexes **25** and **26**, it was found that these ligands would possibly not undergo a dissociative mechanism because their hemilabile ligands seemed to stay coordinated to the nitrogen atom. They probably attend an associative mechanism.

In this study, no mechanistic study was done on the chosen complexes.

6.3 Synthesis of hemilabile ligands and coordination to Grubbs 2

All 5 ligands chosen from molecular modelling were synthesized according to literature methods.^[9-16] For the two bulky ligands **18** and **19**, it was more difficult to synthesize them, something which was expected from modelling results. Ligand **19** was obtained in very low yield (16%). Since the starting materials of the second reaction step were found to be present in the reaction mixture, although the lithium salt of 2-Bromopyridine was formed in the first reaction step. A possible reason for this low yield is the solvent, the ratio or order of chemicals added.

The methods for synthesizing these ligands were all based on the same procedure, which was used by Herrmann^[7] who used these type of ligands for the fine tuning of molybdenum catalysts. After Grubbs^{[9][10]} found that ruthenium based catalysts were more suitable for alkene metathesis reactions, Herrmann coordinated these ligands to Grubbs 2 (**4**) which showed to be a great improvement on alkene metathesis catalysts.^[10] After coordination of ligands **15-19** to Grubbs 2 (**4**), only complexes **25-27** could be synthesized in relatively good yield (**25** = 16%, **26** = 27% and **27** = 49%). These complexes contained the least steric hindered ligands and because these ligands contain two substituents (R_1 = phenyl, *o*-tolyl and propyl, R_2 = *o*-tolyl, methyl and phenyl), it is possible for them to move both substituents in order to obtain the most stable complex. For this reason, ligands **15-17** did not influence the position of the orbitals around the nitrogen and oxygen atoms. Complexes **28** and **29**, which contain the bulky ligands **18** and **19**, could not be synthesized. Since TLC showed that the complexes were present in the reaction mixture, however these complexes decomposed during the purification step. A possible reason for this decomposition was that these ligands **18** and **19** behaved like monodentate ligands instead of bidentate ligands due to their bulky R groups. Several research teams^{[11][12]} proved that bidentate hemilabile ligands increased the stability of the catalyst. So the decomposition of complexes **28** and **29** during the washing procedure could be explained by the fact that the ligands **18** and **19** behave like monodentate ligands which resulted in less stable complexes.

Although the model which was obtained for molecular modelling was based on visual results, it showed a good correlation with experimental results.

6.4 Metathesis reaction with synthesized complexes

Herrmann's ligands coordinated to Grubbs 2 (**4**) increased the activity of **4** during metathesis reactions (§2.2).^[10] After Jordaan changed the substituents of this ligand into two phenyl groups, the activity as well as the lifetime of the catalyst was increased.^[1] After testing the synthesized complexes **25-27** for 1-octene metathesis, all three were found to be active. As expected from modelling results, the activity of the synthesized complexes was found to be lower than that of the Puk-Grubbs 2 (**1**) catalyst. This could be the result of a different mechanism that is used during the reaction, an associative mechanism instead of a dissociative mechanism which was proved to be responsible for the metathesis reaction of 1-octene with the Puk-Grubbs 2 catalyst (**1**). Only complex **25** showed a similar selectivity to that of **1**. The synthesized complexes **25-27** proved to have a much longer lifetime (stability) as well as a higher turnover number. The aim of many research teams is to develop catalysts with a longer lifetime and TON for industrial needs. For this reason, these catalysts are a great improvement in the field of alkene metathesis.

When the reaction temperature was increased or when lower complex : 1-octene molar ratios were used, complexes **25-27** showed an increase in activity. After Jordaan^[1] optimized the reaction conditions of the Puk-Grubbs 2 catalyst, she found similar results. It was also found that with a higher activity, the selectivity of the synthesized complexes decreased.

6.5 Recommendations

Further investigation in this field is necessary. Some recommendations from this study are listed below:

- Since most of the hemilabile ligands are still not investigated, it would be useful to investigate some more possible hemilabile N⁺O ligands.
- The molecular modelling model which is used in this study is based on visual results. To link these results to values, more investigation needs to be done.
- After molecular modelling of the dissociation step of complexes **25** and **26**, they seemed to undergo an associative mechanism. Since the Puk-Grubbs 2 catalyst proved to undergo a dissociative mechanism, it will be interesting to investigate the dissociation/association step of these types of complexes thoroughly.
- The metathesis mechanisms of synthesized complexes **25-27** were not investigated in this study so a mechanistic investigation using molecular modelling as well as experiments would be useful.

- During the second reaction step of the synthesis of ligand **19**, both starting materials were present in the reaction mixture but the ligand was only obtained in a poor yield. An investigation to improve this yield must be done.
- Since the complexes **28** and **29** decomposed during the purification step, it will be interesting to see how these complexes would behave while using other purification procedures and solvents.
- The synthesized complexes **25-27** are only tested for 1-octene metathesis reactions. Metathesis reactions for ROMP, RCM and other 1-alkenes will have to be investigated experimentally as well as through molecular modelling.
- During this study, everything was compared to Jordaan's Puk-Grubbs 2 catalyst. For this reason, the same reaction conditions were used. Optimization of complexes **25-27** for different reaction conditions, like temperature, catalyst load and solvent must be done.

6.6 References

- [1] Jordaan, M., *Experimental and Theoretical investigation of New Grubbs-type Catalysts for the Metathesis of Alkenes*, PhD-thesis, (North-West University), 2007
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- [10] Denk, K., Fridgen, J. and Hermann, W.A., *Adv. Synth. Cat.*, 2002, **344**, 666
- [11] Kingsbury, J.S., Harfity, J.P.A., Bonitatebus, P.J., Jr. and Hoveyda, A.H., *J. Am. Chem. Soc.*, 1999, **121**, 791
- [12] de Clercq, B. and Verpoort, F., *Tetrahedron Lett.*, 2002, **43**, 9101

Appendix I

Modelling of 202 alcohols

Can be found on the inclosed cd (bl. 177-246)

Appendix II

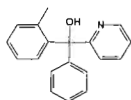
Modelling of 43 ligands when coordinated to a simplified catalyst

Can be found on the Inclosed cd (bl. 247-262)

Appendix III

Copies of MS/Maldi ToF MS spectra

Phenyl-[2-pyridyl-o-tolyl] methanol (15)



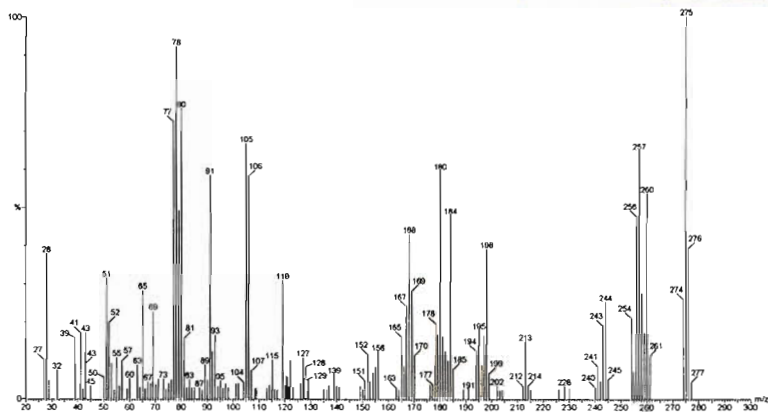
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MS

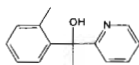
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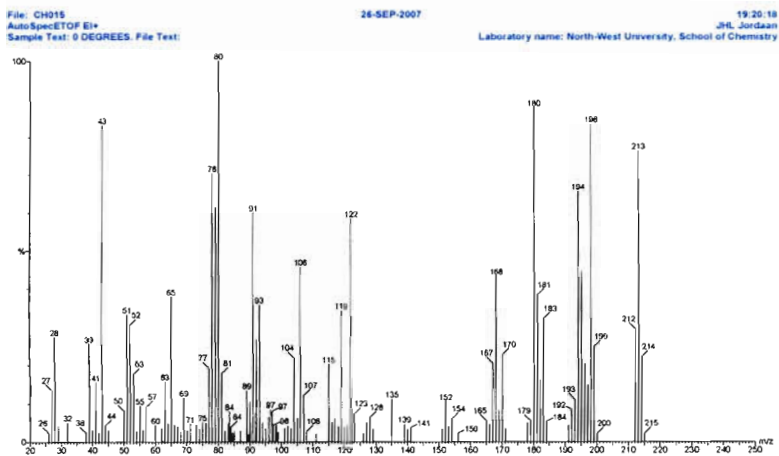


1-[2]-pyridyl-1-o-tolyl ethanol (16)

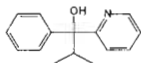


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MS

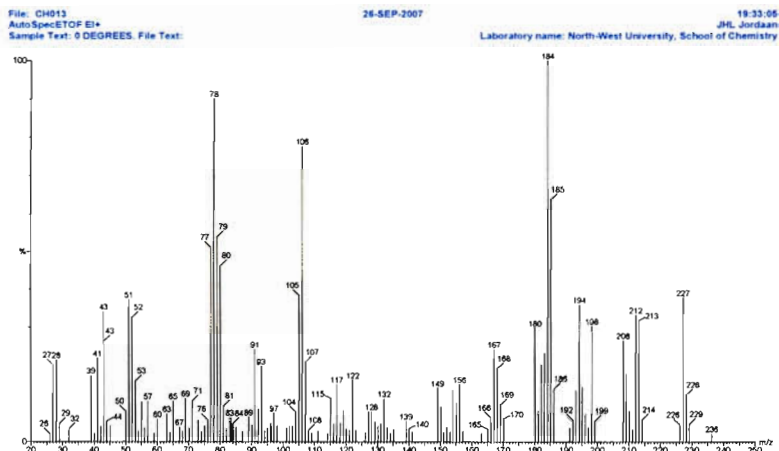


2-methyl-1-phenyl-1-pyridin-2-yl-propan-1-ol (17)

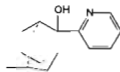


Mw = 227 g/mol

MS

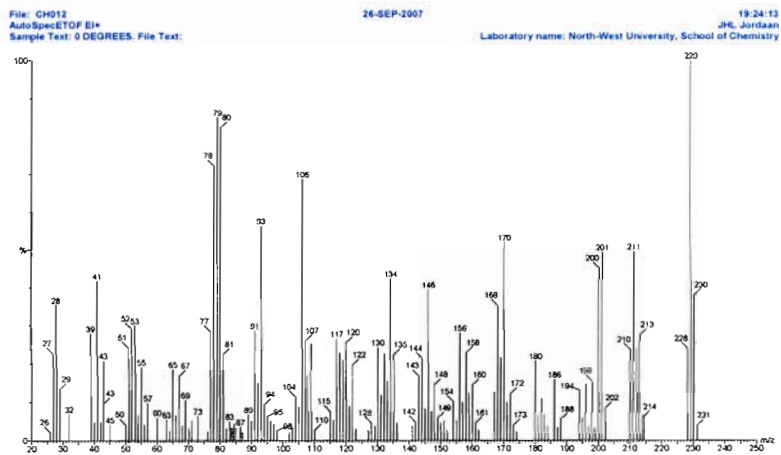


2-(2-pyridinyl)-2-adamantanol (18)

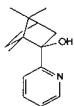


Mw = 229 g/mol

MS

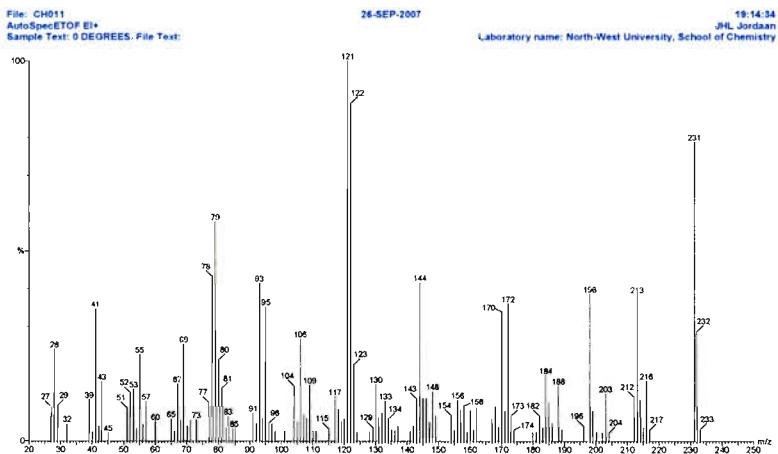


1,1,7-trimethyl-2-(2'-pyridyl)-bicyclo[2.2.1] heptan-2-ol (racemate) (19)

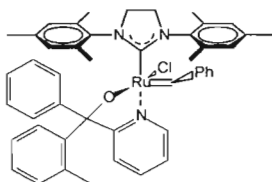


Mw = 231 gmol

MS

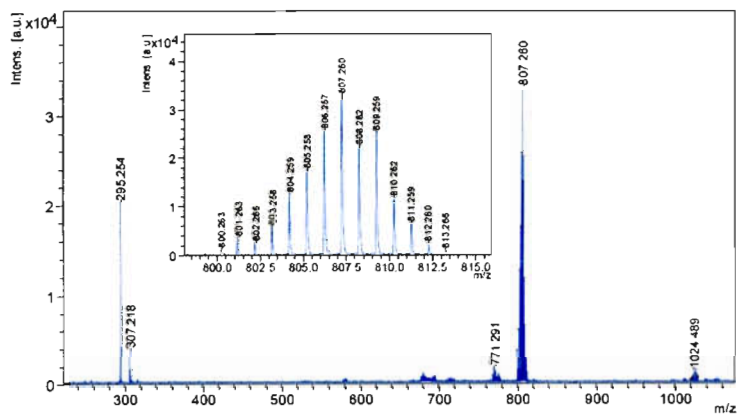


Complex 25

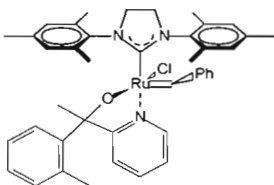


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Maldi-Tof MS

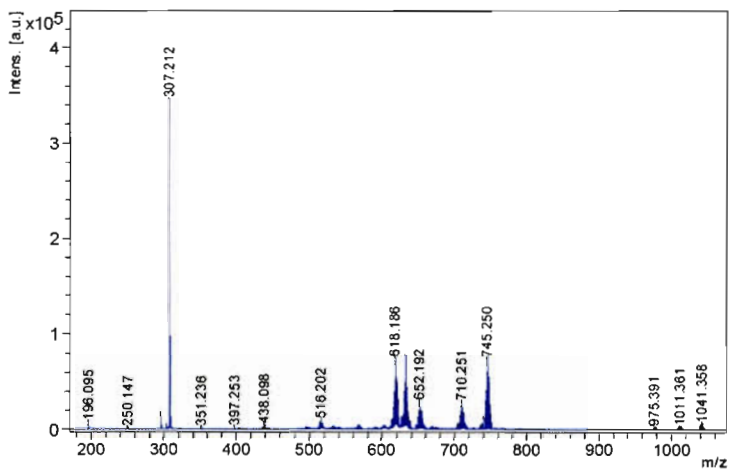


Complex 26

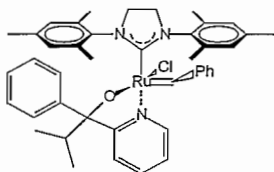


Mw = 745 g/mol

Maldi-Tof MS

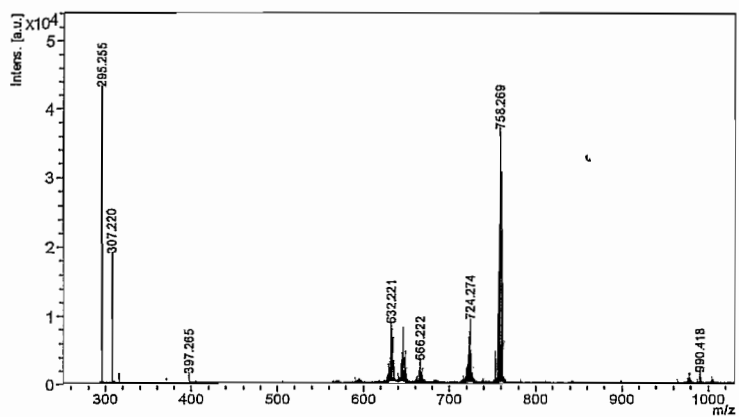


Complex 27



Mw = 758 g/mol

Maldi-Tof MS

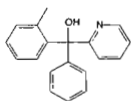


Appendix IV

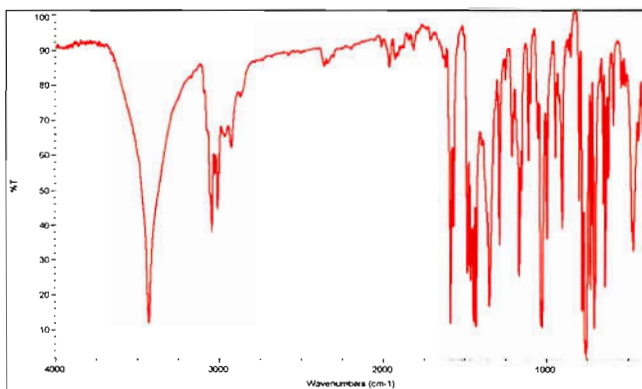
Copies of IR spectra

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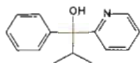
Phenyl-[2]-pyridyl-o-tolyl methanol (15)



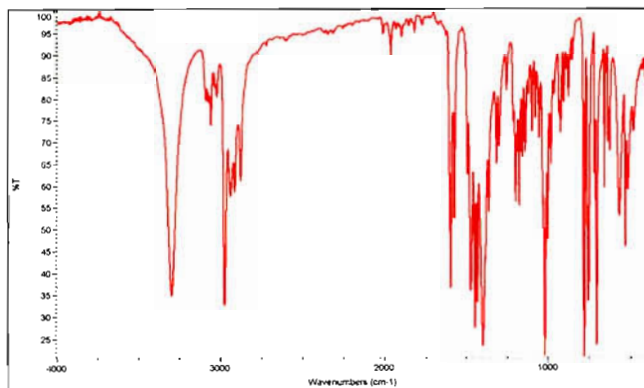
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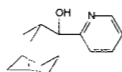
2-methyl-1-phenyl-1-pyridin-2-yl-propan-1-ol (17)



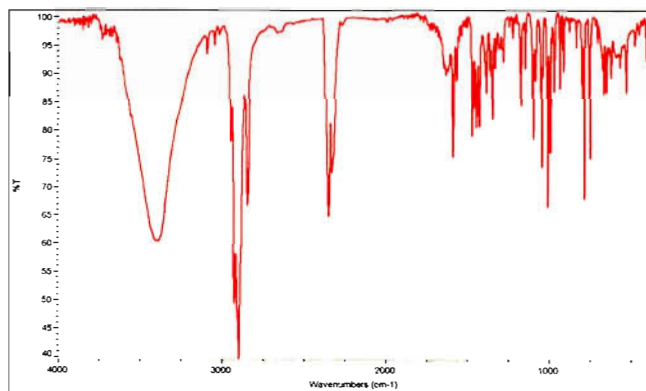
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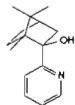
2-(2-pyridinyl)-2-adamantanol (18)



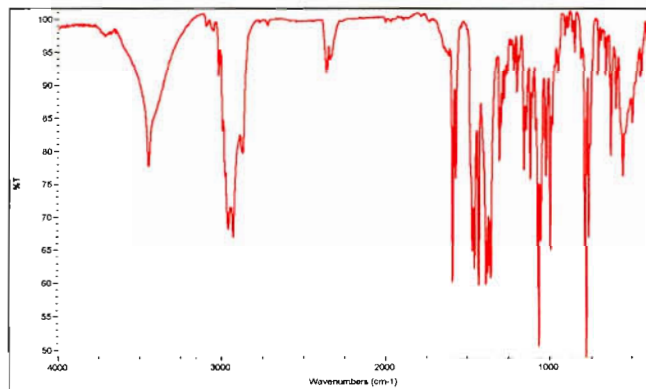
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1,7,7-trimethyl-2-(2'-pyridyl)-bicyclo[2.2.1] heptan-2-ol (racemate) (19)



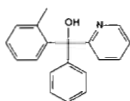
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Appendix V

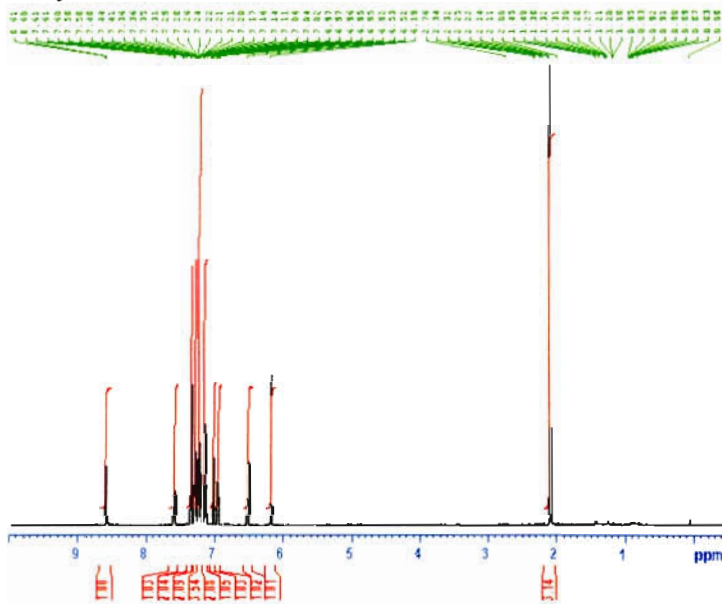
Copies of ^1H NMR spectra

Phenyl-[2]-pyridyl-o-tolyl methanol (15)

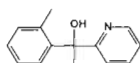


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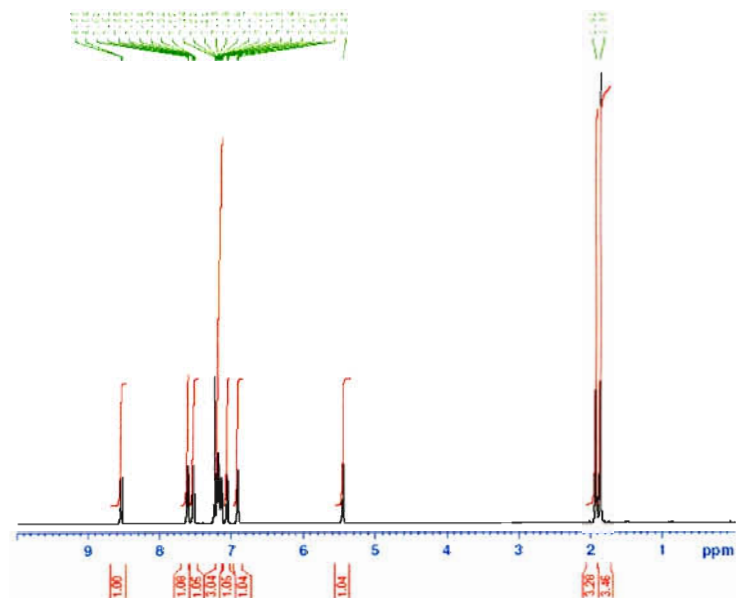
C Huijsmans



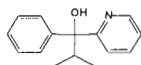
1-[2]-pyridyl-1-o-tolyl ethanol (16)



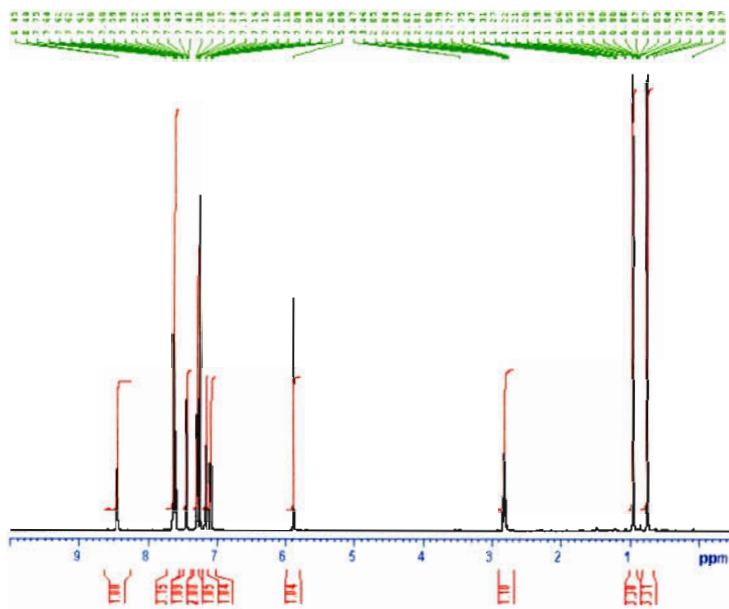
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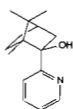
2-methyl-1-phenyl-1-pyridin-2-yl-propan-1-ol (17)



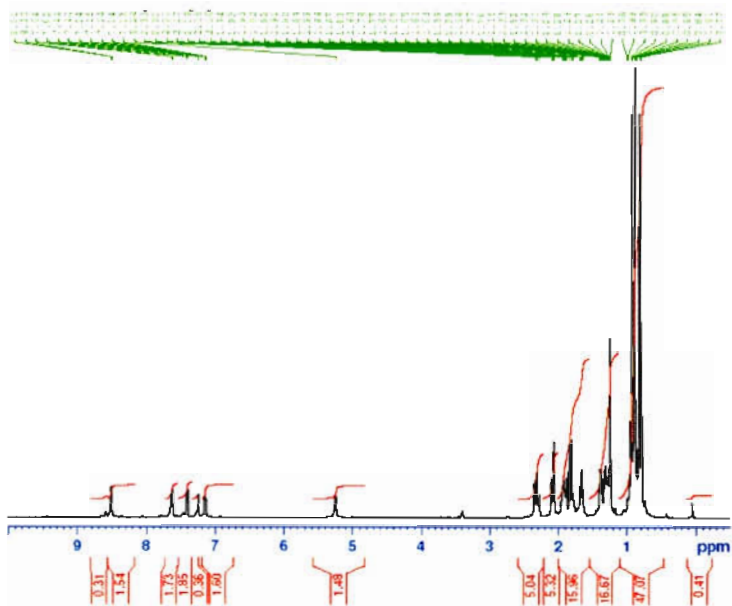
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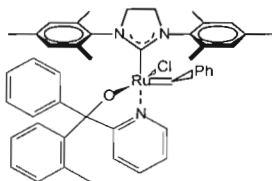
1,7,7-trimethyl-2-(2'-pyridyl)-bicyclo[2.2.1] heptan-2-ol (racemate) (19)



^1H NMR

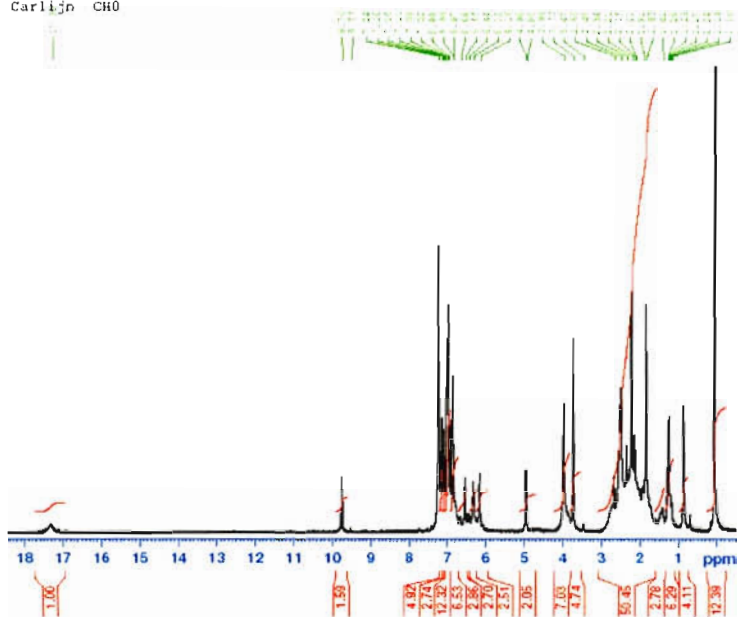


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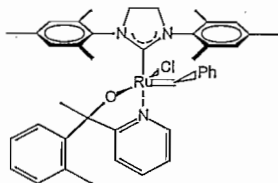


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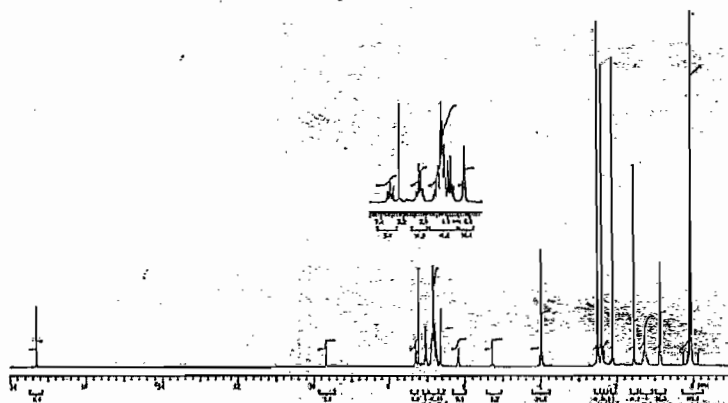
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Complex 26



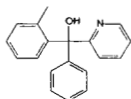
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Appendix VI

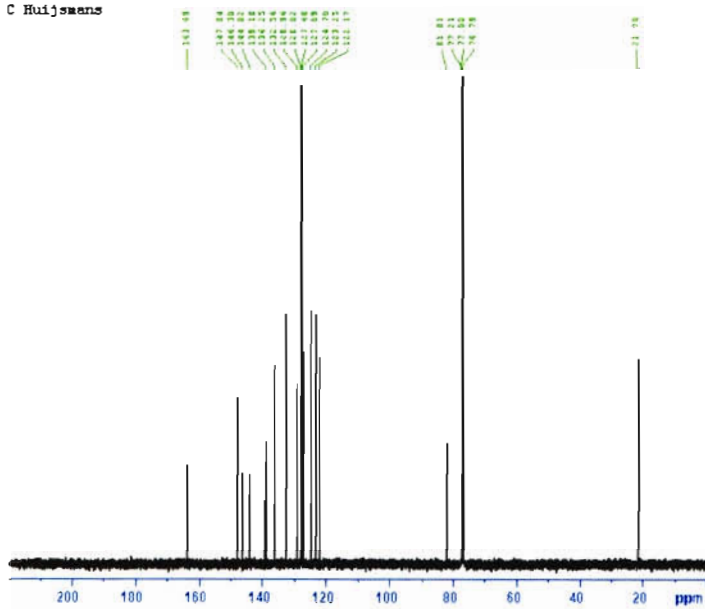
Copies of ^{13}C NMR spectra

Phenyl-[2]-pyridyl-o-tolyl methanol (15)

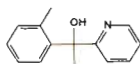


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C Hujsmans

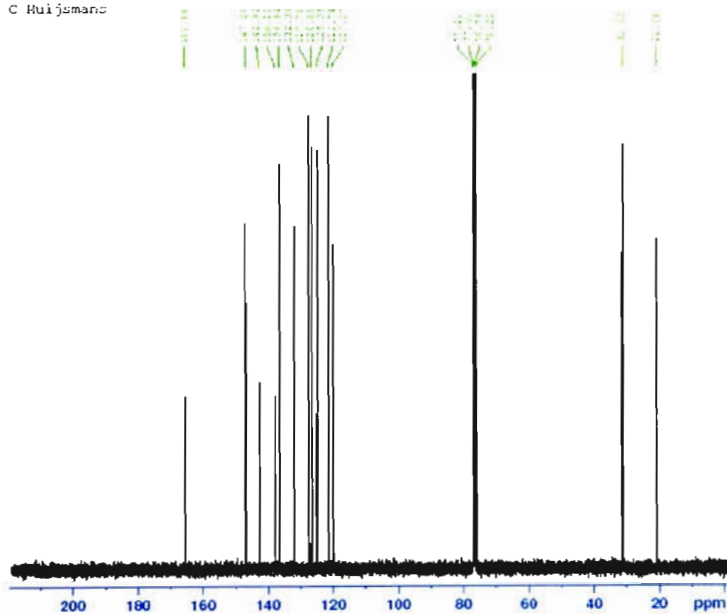


1-[2]-pyridyl-1-o-tolyl ethanol (16)

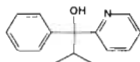


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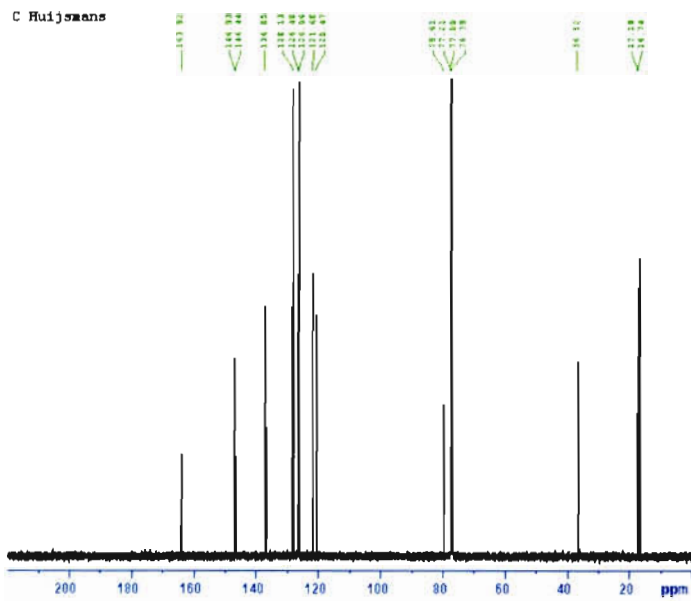
C. Huijsmans



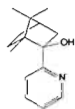
2-methyl-1-phenyl-1-pyridin-2-yl-propan-1-ol (17)



^{13}C NMR



1,7,7-trimethyl-2-(2'-pyridyl)-bicyclo[2.2.1] heptan-2-ol (racemate) (19)



^{13}C NMR

