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Synthesis of novel N-Heterocyclic Carbenes for chiral complexes and catalysis

Tesi di laurea sperimentale

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Abstract

Scopo del presente lavoro di tesi è la sintesi di nuovi leganti carbene N-eterociclici (NHC) chirali derivanti dal diacido canforico e l'uso di NHC derivanti da precursori imidazolinici per l'immobilizzazione di catalizzatori su supporto di tipo dendrimerico.

La necessità di sviluppare nuovi leganti chirali nasce dal bisogno di ottenere sistemi catalitici enantioselettivi. I leganti sviluppati possono essere facilmente ottenuti partendo dal diacido canforico, una molecola chirale dal basso costo, seguendo diverse vie di sintesi. La via di sintesi studiata permette di ottenere facilmente una funzionalizzazione asimmetrica. Due degli NHC ottenuti sono stati impiegati come leganti per l'alluminio ed il palladio.

Leganti NHC derivati dall'imidazolo sono stati inoltre sfruttati per l'immobilizzazione di complessi di rutenio tetraarilciclopentadienonici su supporti di natura dendritica. Questo approccio è chiamato eterogeneizzazione e mira ad unire i vantaggi della catalisi omogenea a quelli della catalisi eterogenea, principalmente il facile recupero del catalizzatore. I dendrimeri funzionalizzati ottenuti sono stati utilizzati in reazioni di idrogenazione e deidrogenazione. Sono inoltre stati sintetizzati nuovi dendrimeri in cui il legante tetraarilciclopentadienonico è stato sostituito con un ciclopentadienone recante due gruppi trimetilsilanici con l'obiettivo di modificarne la solubilità.

The aim of my training period has been the synthesis of new chiral N-heterocyclic carbene precursors starting from camphoric diacid and the employment of imidazolium salts derived NHC as linker to dendrimers supports for organometallic catalysis.

New chiral ligands are needed to develop new catalytic systems for enantioselective transformations. The new type of ligand described was developed starting from camphoric diacid, a cheap chiral molecule, following different synthetic strategies. Asymmetric functionalized chiral NHCs are readily available by methods developed and two of the precursors obtained were employed in preliminary tests with Aluminium and Palladium.

An NHC derived from imidazolium salt has been investigated as linker to dendrimeric supports for tetraarylciclopentadienone-Ruthenium complexes with the aim to combine advantages of homogeneous catalysis to advantages of heterogeneous one, in particular easy recover of catalyst. The functionalized dendrimers obtained have been used in transfer hydrogenation and dehydrogenation reactions. Moreover a new class of functionalized dendrimer was obtained employing a new tetraarylciclopentadienone-Ruthenium complex with trimethyl silyl groups on cyclopentadienone ligand with the aim to change solubility of the system.

Summary

1. INTRODUCTION

Development of new catalysts to improve reactions yield and to open new synthetic route has a central role in industrial chemistry.

Homogeneous catalysts represent the main tool for chemists when they need to carry out very selective reactions or insert stereo-centres, nonetheless new and very complex reactions are available today thanks to the development of new catalysts.[1] The focus of research in this field is to improve features of already known catalysts and find out new catalytic systems for new type of transformations.

My thesis is on organometallic field of homogeneous catalysis whit a focus on the development of new N-heterocyclic carbene ligands and the development of a new catalytic system which is supported on dendrimers.

1.1. NHCs Ligands

N-heterocyclic carbenes are defined as species which contain the carbene centre directly bonded at least to one nitrogen atom within heterocycle.[2] After 49 years from first N-heterocyclic carbene complexes synthesis by Wanzlick[3] and Öfele[4] (fig. 1.1) and 25 years from first stable free N-heterocyclic carbene isolated by Arduengo[5,6] (fig. 1.1) it can be stated that N-heterocyclic carbenes (NHCs) have had a central role in organometallic chemistry as ancillary ligands.[7–10]

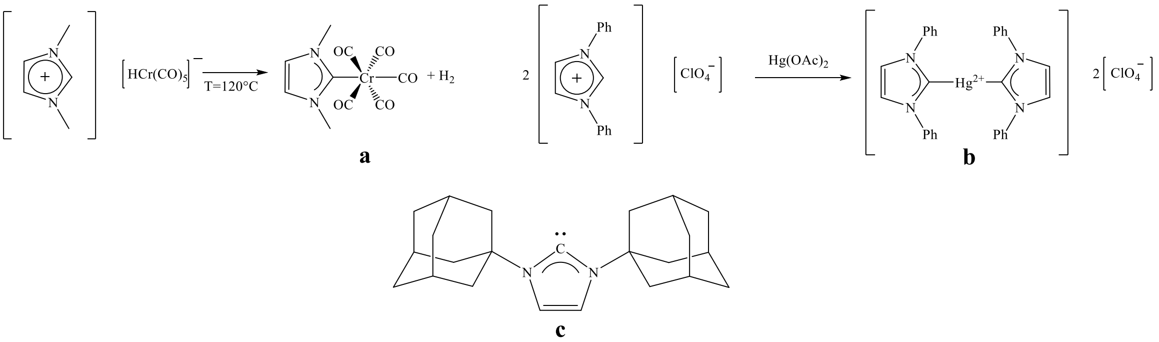


Fig. 1.1*: first examples of complexes containing a NHC by Ofele (**a**) and Wanzlick (**b**); first stable free-NHC isolated by Arduengo (**c**).*

They are one of the best class of ligands because they have very interesting features which can be easily modified by changing substituents on heterocycle and because they are readily available thanks to easy and often cheap synthetic routes developed in organic synthesis. They have unique electronic and steric properties and are very good in stabilizing metal complexes so they have been used as ancillary ligand in a lot of different catalysts.[7–10] All those aspects are being treated in following discussion.

1.2. *Electronic properties of NHCs*

A carbene is a carbon with six electrons in its valence shell. Four of those electrons are used in bonds and two are unpaired. With their valence shell carbenes can have two different ground states depending in which orbital are unpaired electrons. A singlet carbene has its two unpaired electrons in a σ-orbital and has an empty p-orbital while a triplet carbene has one in σ-orbital and one in a p-orbital (fig. 1.2). The ground state of a carbene is determined by the substituents bonded to it and its ground state defines its electronic properties and geometry.

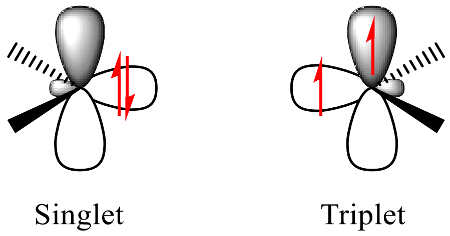
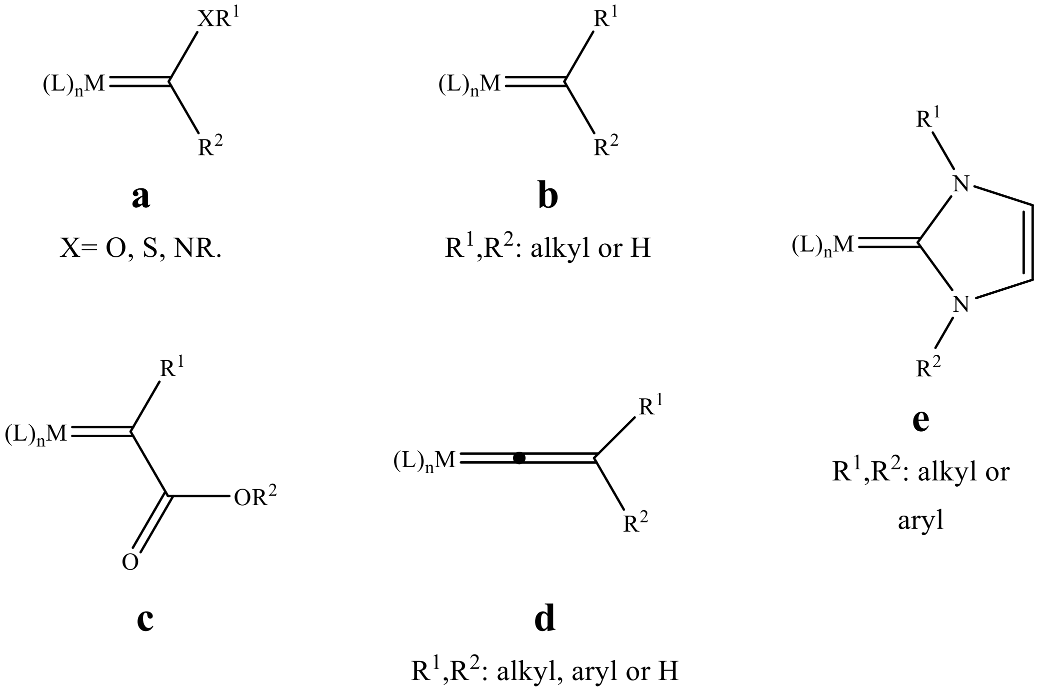


***Fig. 1.2**: orbital models for singlet and triplet carbenes (electrons are represented as red arrow)*

Carbene can be classified into five classes (fig. 1.3):[1]

1) “Fisher Carbenes” that were the first discovered. They are typically electrophilic at carbene carbon and nucleophilic at metal which is usually a low-valent, middle or late transition metal. They contain a π-donating group on carbene; (**a**)
2) “Schrock Carbenes” were the second discovered. They are typically nucleophilic at carbene carbon and electrophilic at metal which is usually a high-valent, early or late transition metal; (**b**)
3) “Carbenoid” or “acceptor-substituted” carbene contain a carbonyl substituent bounded to carbene. This class of carbenes are generated on dinuclear rhodium, ruthenium or copper complexes and are found as intermediate in cyclopropanation; (**c**)
4) “Vinylidene” is an heterocumulene structure in which the metal is one of the two ends of cumulated double bonds. The carbene carbon is electrophilic; (**d**)

5) “N-heterocyclic carbenes” (NHCs) which are the focus of this work. (**e**)



a

X= O, S, NR.

b

R^1,R^2: alkyl or H

e

R^1,R^2: alkyl or aryl

c

d

R^1,R^2: alkyl, aryl or H

Fig. 1.3*: five classes of carbenes.*

N-heterocyclic carbene are singlet carbene due to the presence of nitrogen heteroatoms in the cycle close to carbene carbon. Nitrogen acts in two different way: inductive effect (red arrow, fig. 1.4) and mesomeric effect (blue arrow, fig. 1.4). Thanks to its electronegativity nitrogen withdraw electron density from σ-bone of carbene while using the lone pair in p-orbitals stabilizing the empty p-orbital of carbene. This double effect is very important in carbene stabilizations and is one of the reason why we can isolate this class of carbene as free-carbene.[9]

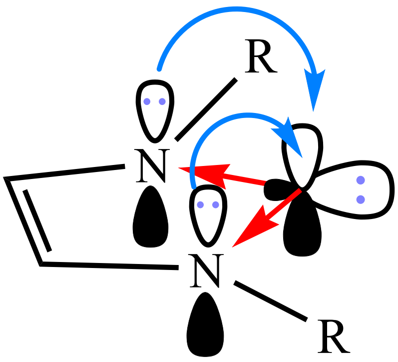


Fig. 1.4*: inductive (red arrows) and mesomeric (blue arrows) effects in a NHCs.*

For long time NHCs where compared with phosphine ligands while both are very good σ-donor.[11] Both experimental and computational studies have been carried to investigate

NHCs electronic proprieties and to compare their donor properties with phosphine ligands. This studies consist in synthesis of standard complexes containing the ligand which is under investigation and carbonyls (like example in fig. 1.5), the σ-donor ability is determined by shifting of carbonyl stretching in IR spectroscopy.[12,13]

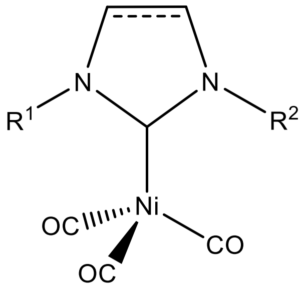


***Fig. 1.5**: example of a metal complexes used to study σ-donor proprieties of NHCs.*

Another electronic propriety long studied is π-interaction with metal centre. NHCs might interact with metal centre using p orbital (see fig. 1.6) but those interactions are not very clear and mainly depend on NHC and metal characteristics.[14,15]

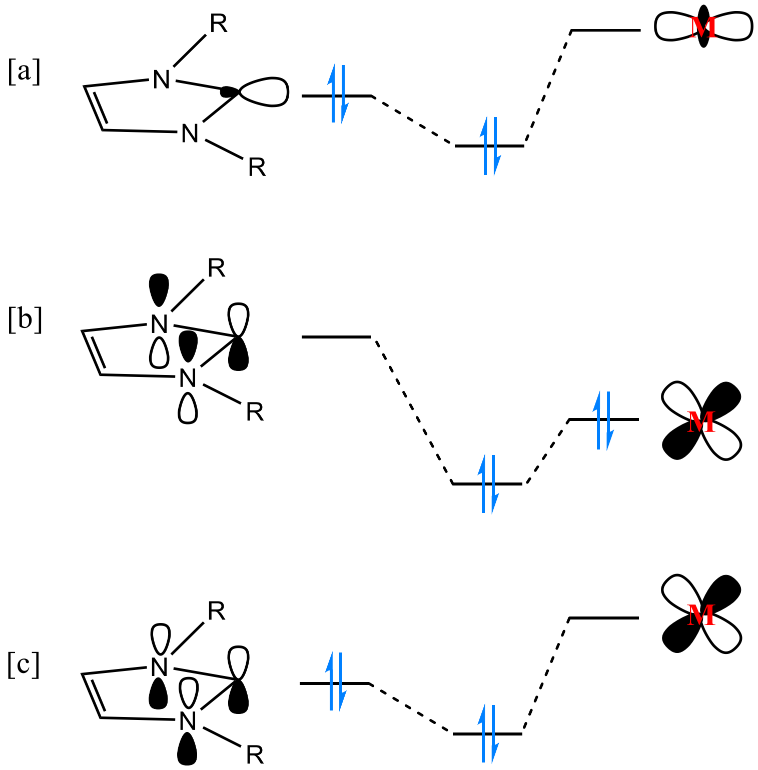


***Fig. 1.6**: [a] NHC → M σ-donation; [b] M → NHC π^*-backdonation; [c] NHC → M π-donation.*

The π-interactions depends by both NHC and metal characteristics as substituents on carbene ring and metal electronic charge.

1.3. Steric properties of NHCs: Buried Volume

N-heterocyclic carbenes have peculiar steric properties derived from substituents on nitrogen atoms bonded to carbene. While phosphine substituents point away from the metal centre and their steric hindrance is defined by “cone angle” parameter[16], NHCs have a different fashion determined by a fan-like position of their substituent on nitrogen atoms. NHCs steric hindrance point directly to the metal centre and is defined by “buried volume” parameter (fig. 1.7).[15]

“Buried volume” is derived directly by Tolman idea of “cone angle”. NHCs are classified like phosphine ligands using this parameter which is important to rationalize some aspects of metal complexes stability and reactivity and experimental data derived from catalysis studies.[15]

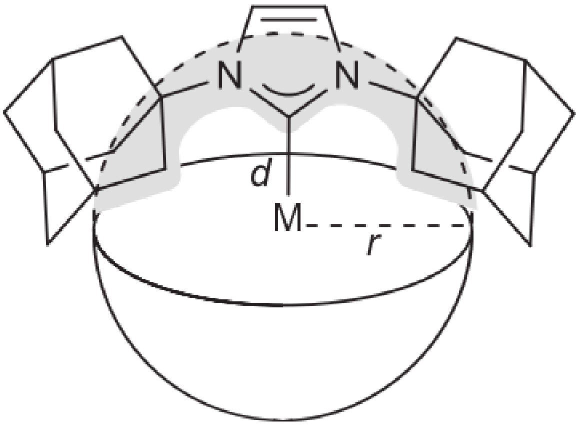


Fig. 1.7*: schematic representation of “buried volume”.*

As electronic properties buried volume is studied starting from experimental data with help from computational simulations.

1.4. *Ligand design of NHCs*

The success of N-heterocycle carbene ligands in catalysis is more than their good abilities to coordinate metals and in stabilizing metal complexes. They are relatively easy to synthesize and in general they are cheap.[17,18] Heterocycles have been studied a lot in organic chemistry and a lot of papers are available. It is generally easy to obtain NHCs of different ring size and bearing different substituents with different functional groups. Looking to a standard NHC structure (represented in fig. 1.8) we can state that NHCs offer a wide range of possibilities to tune their features and the three point of interest for ligand design are represented by substituents on N atoms (red circles), substituent on backbone (blue circles), and backbone itself (green circle).[9]

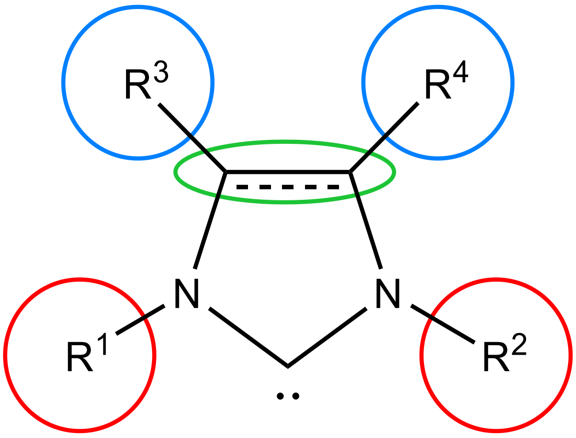


***Fig. 1.8**: schematic representation of NHC structure.*

Substituent on N atoms can influence different aspects:

- Steric proprieties and kinetic stabilization from steric bulk;
- Electronic proprieties of carbene;
- Potential for asymmetric induction;[19,20]
- Generation of chelating or pincer ligand systems inserting arm bearing coordinating groups;[21]
- Potential for immobilizations on support inserting a linker moieties;
- Solubility.

Substituent on backbone:

- Electronic properties which influence stability;
- solubility;
- Potential for immobilizations on support inserting a linker moieties;

- Potential for asymmetric induction.[19,20]

Standard backbone is represented by two sp^2 carbon in imidazolium derived NHCs, but backbone can be formed by different number and type of atoms.[9] It can contain different heteroatom which modify properties of NHCs and it can be saturated or not. With a different number of atoms in backbone we can obtain expanded ring NHCs which have more than five atoms in the cycle. All those different possibilities for the backbone give us NHCs with sensitively different characteristics.

1.5. Synthesis of NHCs precursors

By far the most common class of N-heterocyclic carbenes are five membered rings NHCs and into this class the most common are imidazolium derivatives (fig. 1.9).[7–10]

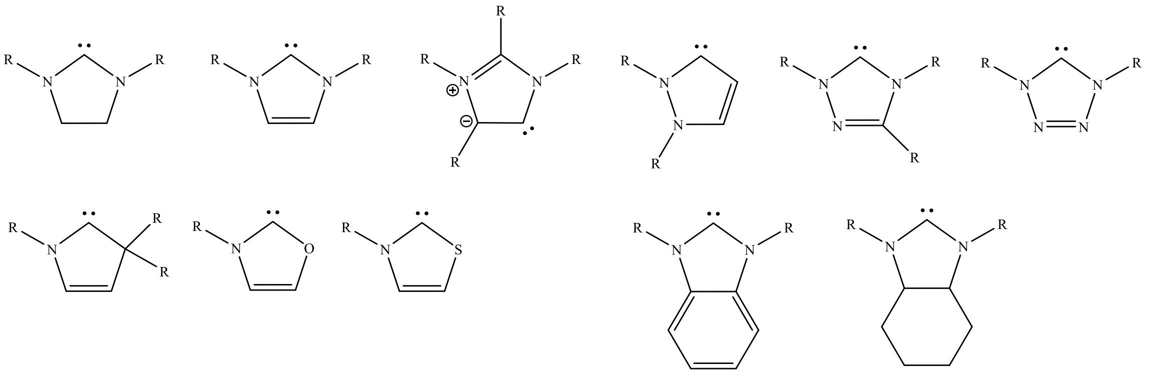


***Fig. 1.9**: common five membered rings NHCs.*

As reported different types of five membered rings are possible.

Salts like imidazolium salts or other heterocyclic salts are often used as NHCs precursor. There are different routes to obtain them: starting from a preformed heterocycle via quaternization of nitrogen or some different ways that have as key step a ring closure reaction. The first way is interesting because synthesis of heterocycle is a broadly studied field in organic chemistry and very available methods are ready to use. The second way is also broadly studied and is more flexible for the synthesis of NHCs functionalized in a more complex fashion.[17,18]

Imidazolium salts derivatives are very easy to obtain following the first route which can be represented by two different synthetic pathways: one starting from imidazole which is first mono-functionalized and then it is turned into an imidazolium salt by the second functionalization (fig. 1.10 **[a]**); second route start from a mono functionalized imidazole easily available from a condensation reaction and the salt is directly obtained by a second alkylation (fig. 1.10 **[b]**).[2]

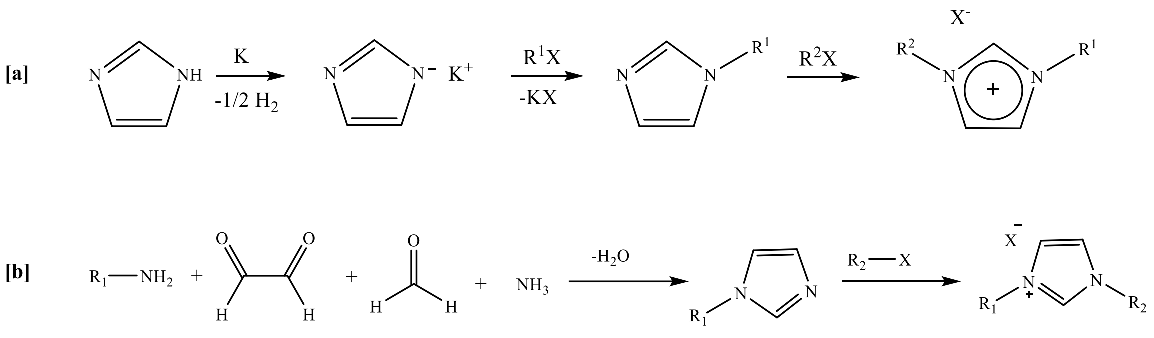


***Fig. 1.10**: synthetic routes to imidazolium salt precursor for NHCs.*

Other five membered ring NHCs precursors are often synthetized in similar way starting from the synthesis of the corresponding heterocycles.

Two very general synthetic strategies which consist of a ring closure reaction are represented below (fig. 1.11). Those ways have been used to obtain NHCs of different ring size like five, six and seven membered rings. It is possible to insert moieties/substituents of interest in the reagent is being transformed in the NHCs backbone and use different substituents on nitrogen. Two different routes are available. The first one follows the synthesis of a N,N-disubstituted formamidine and the following bisalkylation. The second consist in the synthesis of a diamine which is reacted with triethyl orthoformate. Both pathways are very flexible because N,N’-disubstituted formamidine and diamine can be synthetized by different reaction.[17]

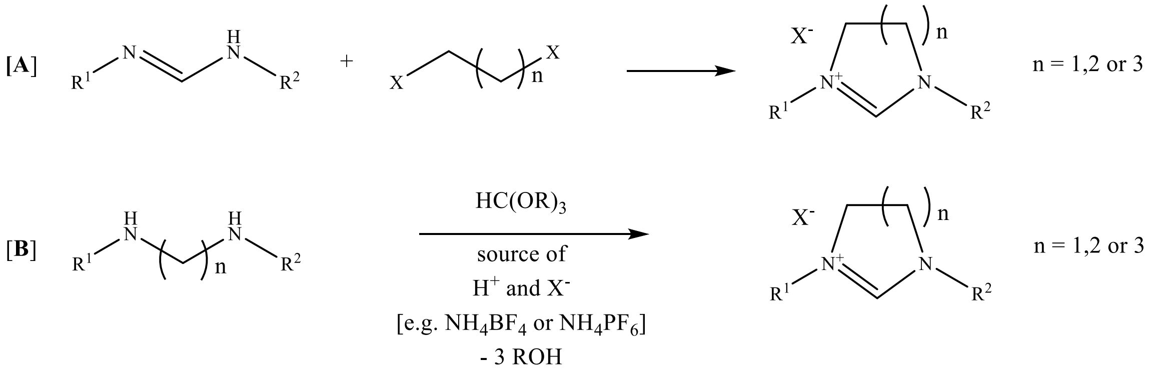


***Fig. 1.11**: ring closure synthetic routes to NHCs precursors: [**A**] bisalkylation of N,N’- disubstituted formamidine; [**B**] cyclization of diamine by trialkyl orthoformate.*

Synthesis of chiral NHC precursors have been achieved using different synthetic strategies. They are often designed starting from privileged[22] structure already used for different types of ligand and some examples are reported below. Those examples use a synthetic pathway via a ring closure reaction.

Starting from a cycloesan diamine a N-heterocyclic carbene can be obtained after the alkylation of amines to insert the nitrogen substituent of final NHC via a Buchwald-Hartwig reaction then the cycle is obtained via a ring closing reaction using triethyl orthoformate (fig. 1.12). The alkyl groups on nitrogen should contain bulky substituents with aims to transfer chirality effects from backbone to metal centre. The first example were reported by Grubbs et al.[23]

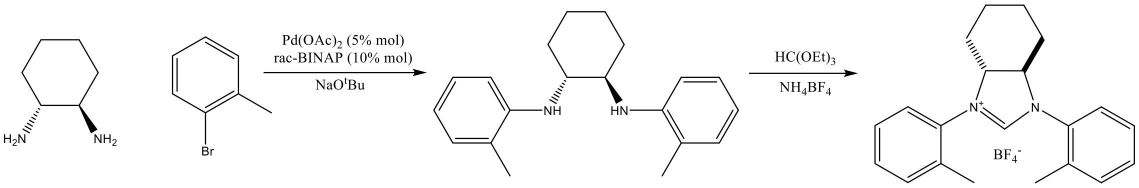


Fig. 1.12

Stahl et al. have developed the synthesis of seven membered ring starting from 2,2’-diaminobiphenyl or from 2,2’-diaminobinaphthyl. Seven membered NHCs have showed a torsional twist angle that results in axially chiral rings with C_2 symmetric structures. As reported in fig. 1.13 the synthesis starts from enantiopure BINAM through reductive amination to insert alkyl groups on nitrogen atoms followed by ring closing reaction using triethyl orthoformate. As mentioned above bulky R substituent have been used to help transferring chirality from backbone to metal centre.[24]

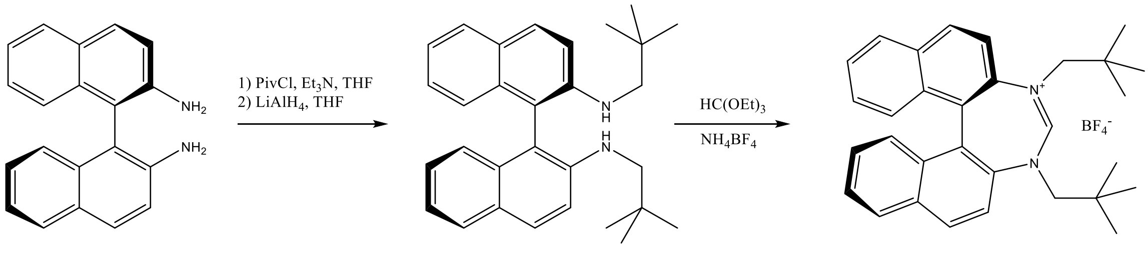


Fig. 1.13

1.6. NHCs precursors activation and coordination

The most used class of NHCs precursor are imidazolium and imidazolium-like salts and complexes bearing NHCs can be synthetized by different ways of activation of those precursors (fig. 1.14).[18,25]

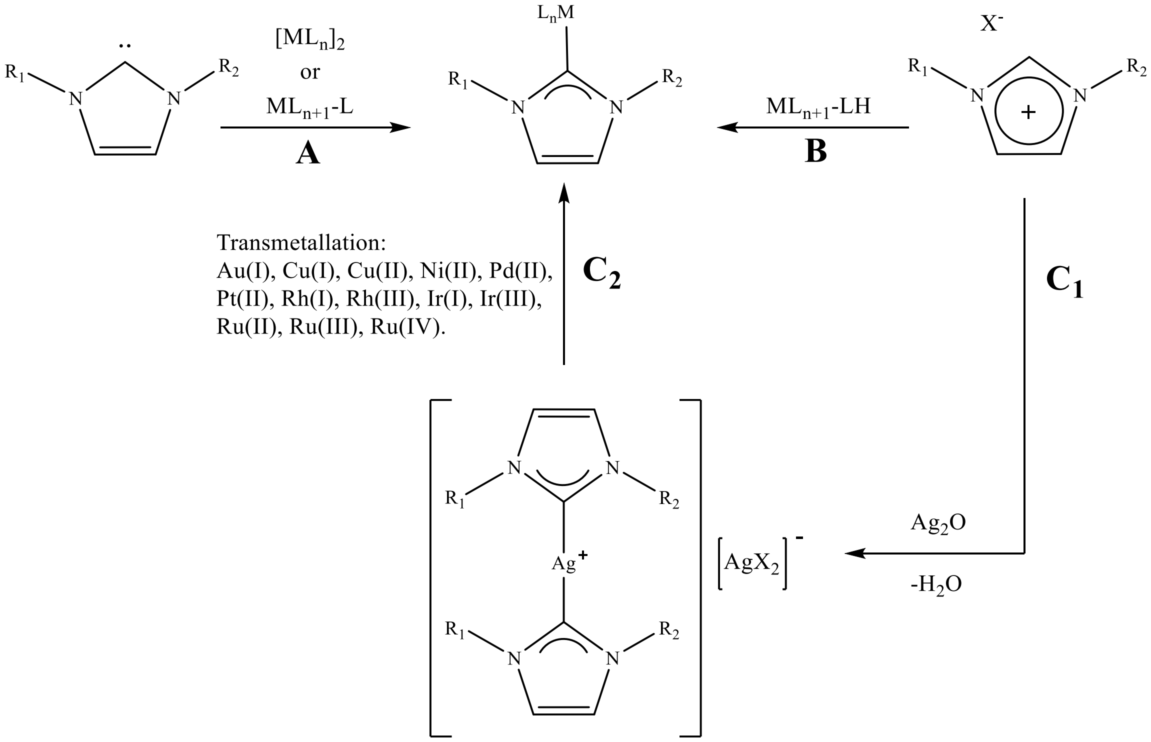


Fig. 1.14

1) Salt is deprotonated by a strong base then free-carbene coordinates to a metal (method **A**)
2) A metal precursor with a basic ligand is used (method **B**). In this case ligand acts as the base of routes A and leave the complex;
3) Direct reaction of salt with Ag_2O directly lead to Silver-NHC complexes (method **C1**)
4) Silver-NHC complexes are used as transmetallating agents (method **C2**). Different metal precursor can be used with silver-NHC complexes.[26]

More complex routes are available for activation but less used because they are more complex.

1.7. Newman’s seven membered ring chiral NHCs

Above expanded N-heterocyclic ligands a particular type has been developed by Newman and his group. This novel class of NHCs have a bicyclic and chiral backbone. They are expanded ring NHCs with the main cycle formed by seven atoms. While most of six and seven membered ring NHCs have showed an enhanced basicity/σ-donor ability and greater steric demand respect to five membered countrepart, this new class of bicyclic expanded ring N-heterocyclic carbenes has showed properties more close to five membered type.

The synthetic route developed by Newman group (fig. 1.15) start from camphoric diacid which is a very cheap chiral molecule. It is transformed in diamine by a Schmidt reaction followed by functionalization of amines and the ring closing reaction via triethyl orthoformate. The strategy studied is very flexible and asymmetric functionalized NHCs are easily obtained nonetheless it is an interesting example of development of chiral ligand via a ring closing strategy like above mentioned in paragraph 1.5 starting from a chiral pool reagent.[27]

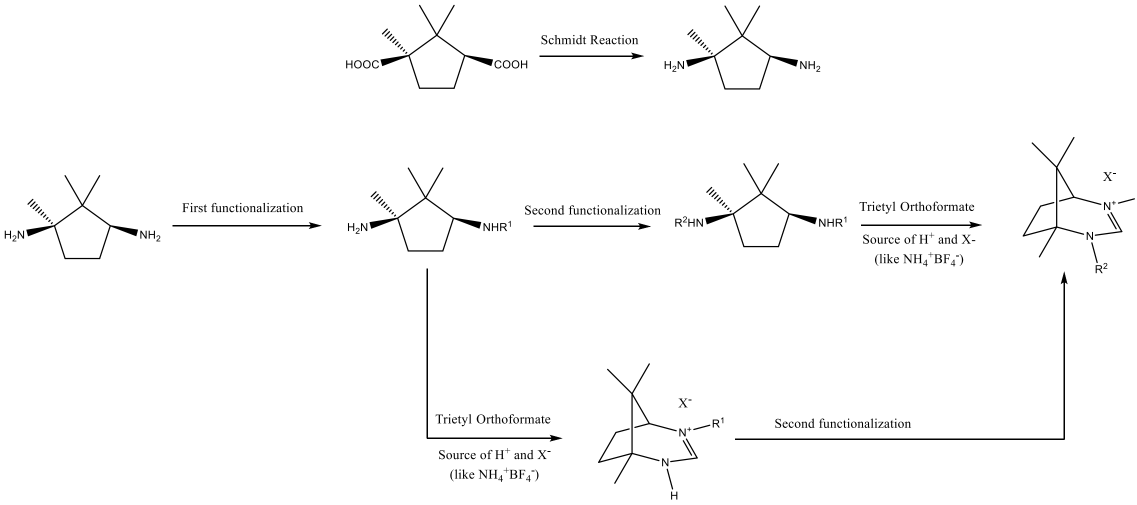


Fig. 1.15

They were used to obtain some chiral complexes with different transition metals.[28,29]

The first example (fig 1.16) reported is a pincer PCP ligand. Both (**a**) and (**b**) have been used in cross coupling reaction which is unusual for trans phosphine palladium complexes. The same ligand was used with different metals to obtain different (κ^3-P,C,P’) complexes with a central NHC carbon donor which have been very few studied.[28]

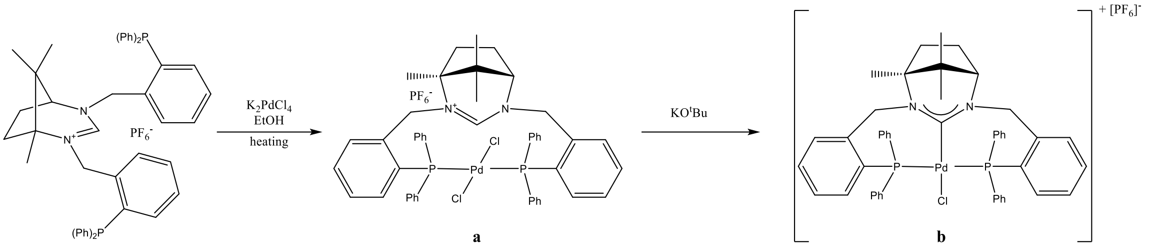


Fig. 1.16: examples of Pd-NHC complexes have been synthetized by Newman.

The second is a pincer NCN ligand coordinated to Nickel (fig. 1.17). The reaction represents a unique example of the oxidative addition of a saturated or large ring NHC to a metal center, confirming the unusual properties of these bicyclic structures. Oxidative addition is more typical of the unsaturated five-membered imidazolium salts, while the proton in C2 of azolium salts of saturated five, six and seven membered NHCs is generally not acidic enough. The complex (**a**) obtained by oxidative addition of NHC ligand and concerted formal isomerization from 1,5 to 1,3 of COD decomposes to (**b**) when dissolved in $CHCl_3$ in air.[29]

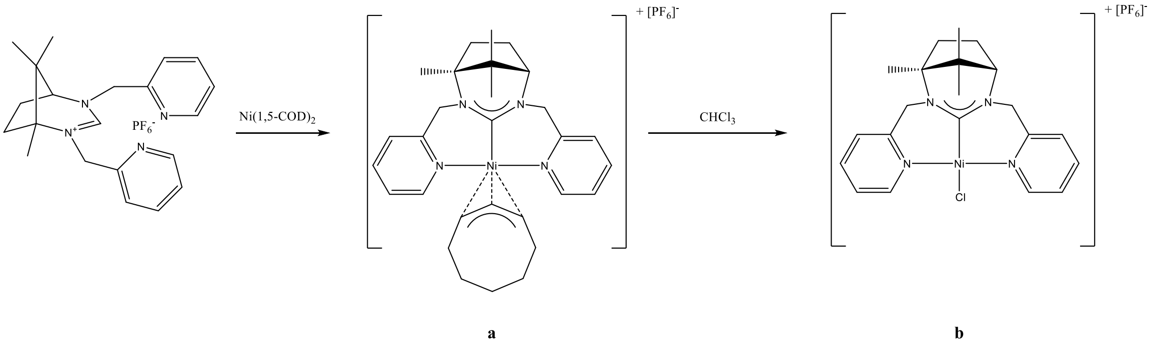


Fig. 1.17

1.8. Complexes containing NHCs

NHC ligands have been used in a lot of different complexes to develop new catalysts. They have represented a new and innovative class of ligand due to their features. Some examples are reported below:

- Transfer hydrogenation[30]

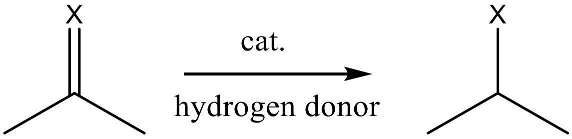


Fig. 1.18

Hydrogenation reactions are important transformation in chemistry where an unsaturated bond is reduced by adding hydrogen. Transfer hydrogenation reactions (fig. 1.18) are a class of hydrogenation reaction where the source of hydrogen is not represented by H_2 but different hydrogen donors are used like isopropanol which is converted in acetone. This approach to hydrogenation is interesting because no dangerous high pressure gas is needed and good selectivity is reached. It was discovered by Knoevenagel[31] by more than a century and NHCs give new perspective to this catalysis thanks to their properties as ligand. Some example of catalysts developed by Gade[32] which contain a chelating NHC and Kühn[33] which contain abnormal NHC are reported below in fig. 1.19.

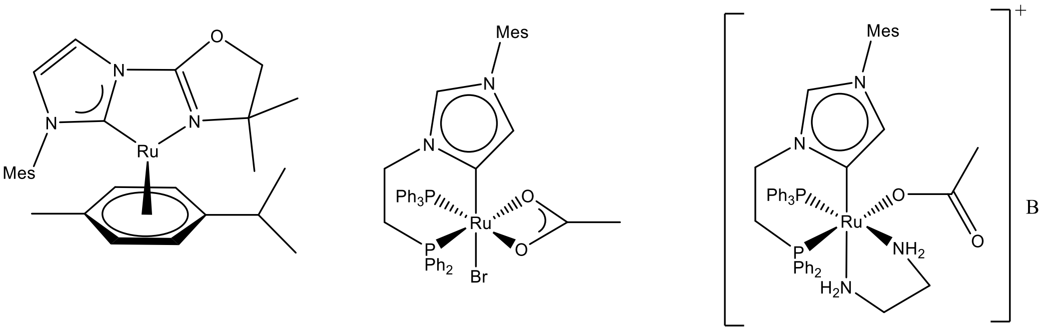


Fig. 1.19

The research group where I have worked in Bologna is developing new hydrogen transfer catalysts based on ruthenium complexes which contain tetraarylcyclopentadienone and NHC ligands (fig. 1.20 **Ru-n**). They have also developed the protonated species of those complexes (fig. 1.20 **Ru-n[X]**) by protonation with strong acids like triflic acid. Both types have been studied in transfer hydrogenation reactions. They have been used for transfer hydrogenation of polar double bond, mainly chetones, and transfer dehydrogenation of alcohols.[34]

Ru-1 $R_1 = R_2 = CH_3$;
Ru-2 $R_1 = CH_3$, $R_2 = CH_2CH_2CH_2CH_3$;
Ru-3 $R_1 = CH_3$, $R_2 = CH_2CH_2OH$;
Ru-4 $R_1 = CH_2CH_2CH_2CH_3$, R_2 = 2-pyridine.

Ru-1[X] $R_1 = R_2 = CH_3$; $X = CF_3SO_3$, Cl, BF_4;
Ru-2[X] $R_1 = CH_3$, $R_2 = CH_2CH_2CH_2CH_3$; $X = CF_3SO_3$;
Ru-3[X] $R_1 = CH_3$, $R_2 = CH_2CH_2OH$; $X = CF_3SO_3$;
Ru-4[X] $R_1 = CH_2CH_2CH_2CH_3$, R_2 = 2-pyridine. $X = CF_3SO_3$, Cl, BF_4.

Fig. 1.20

- Coupling reaction[35]

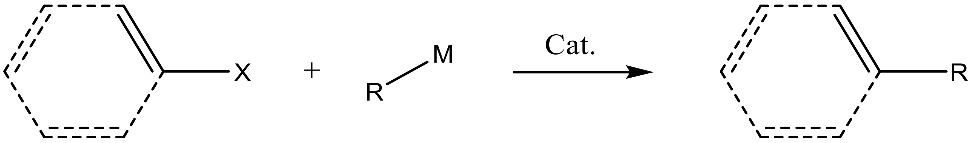


Fig. 1.21

Cross-coupling reactions have often been used in synthesis of very complex molecules to obtain new C-C and C-heteroatom bond (fig. 1.21). In cross coupling reactions aryl and vinylic halides or sulfonates react with different organo-reagents. Different class of cross coupling reactions have been developed by using different type of organo-reagents like organomagnesium, organotin, organosilicon and organoboron, even olefin can be used for this scope. Cross-coupling reactions good tolerate functional groups on reagents and are very selective. They can be used to obtain chiral product using chiral catalytic systems which contain chiral ligands. Catalysts for cross-coupling reaction are improved by NHCs: oxidative addition is favoured by more electron rich NHC based catalysts; reductive elimination is favoured by steric hindrance and buried volume of NHCs pointing to catalytic site so also this step is accelerated. Two example reported below are a PEPPSI (pyridine enhanced precatalyst preparation, stabilization and initiation) Pd-NHC[36] and a nickel complexes with tetra-chelating NHC ligand (fig. 1.22).[37]

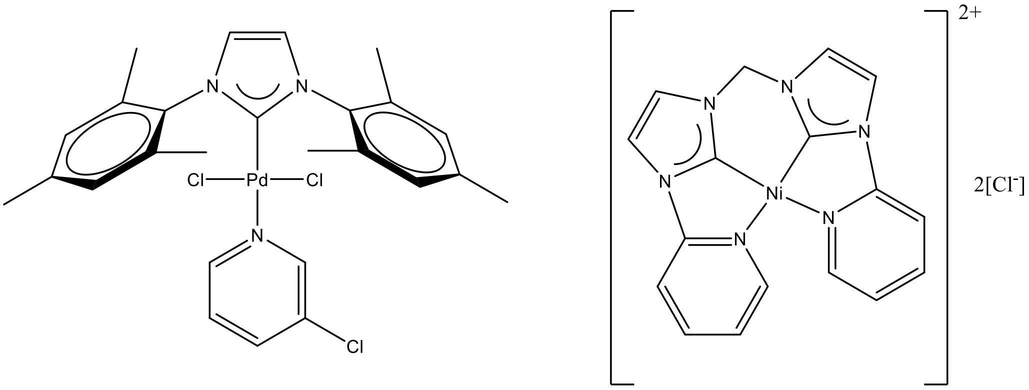


Fig. 1.22

- Polymerization

Polymerizations is one of the most important transformation in industrial chemistry. Homogeneous catalysts are widely studied for polymerization reaction. N-heterocycle ligands have been used to develop new catalytic system for polymerization like catalysts reported below. Pd-NHC is used for the direct synthesis of polycarbonate from carbon monoxide and bisphenol A[38] and Fe-NHC for atom transfer radical polymerization (fig 1.23).[39]

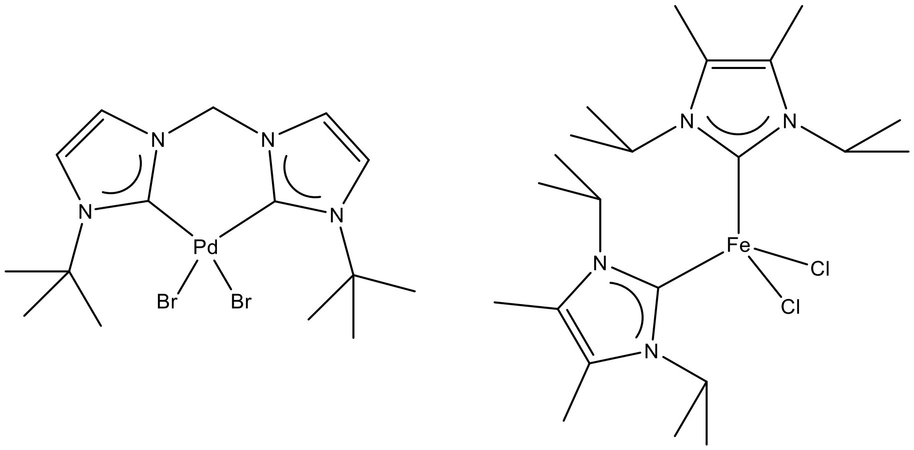


Fig. 1.23

- Metathesis[40]

  The main goal of NHCs is represented by the development of the second generation of “Grubbs Catalyst” for metathesis of olefin. This reaction has been a breakthrough in catalysis and NHCs have improved its importance by the possibility of increase catalyst performance.

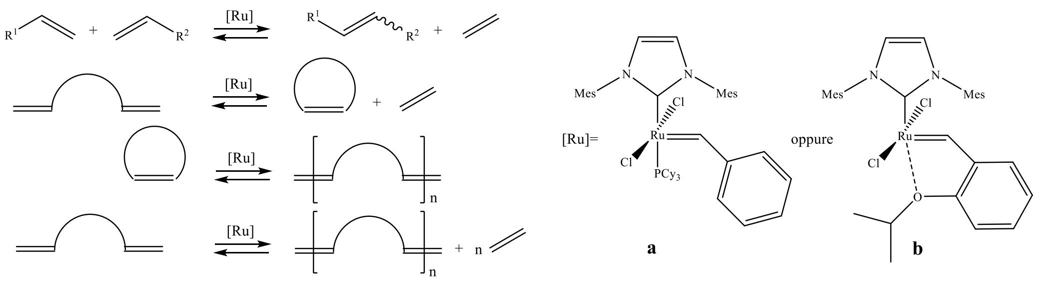


***Fig. 1.24**: general examples of metathesis reactions and second generations of Grubbs Catalyst (**a**) and Hoveyda-Grubbs Catalyst (**b**).*

Both complexes reported are derived by first generation catalysts by replacement of one phosphine ligand with an NHC ligand (fig. 1.24). Using specific designed

NHCs chemists can tune catalyst feature to reach desired properties and improve reactivity toward desired metathesis pathway.

1.9. *Immobilizations of Catalysts*

Most of homogenous catalyst based on transition metals are very expensive both for metals and ligands cost. Organometallic catalysts are based on expensive metals like ruthenium, iridium, rhodium, etc. and ligands can also be very expensive. It is not surprising that one of the focus of researches in this field is being recover of catalyst after a reaction to reuse it in more batches. Different approaches are possible and one of most investigated is immobilization of catalysts on different types of supports. This approach is called "heterogenization" by the meaning that an homogeneous catalyst will be easy recoverable like an heterogeneous one.[41]

The heterogenization is mainly achieved using a ligand designed to link metal complex to a support. N-heterocyclic carbene ligands are good candidates to this approach. They can be easily designed for this function inserting a linker functionality in the substituents on nitrogen atoms or in the backbone (fig. 1.25). They also give a good stability to the catalyst which is needed to be recovered. Without stable catalysts this approach will fail for leaching phenomena.

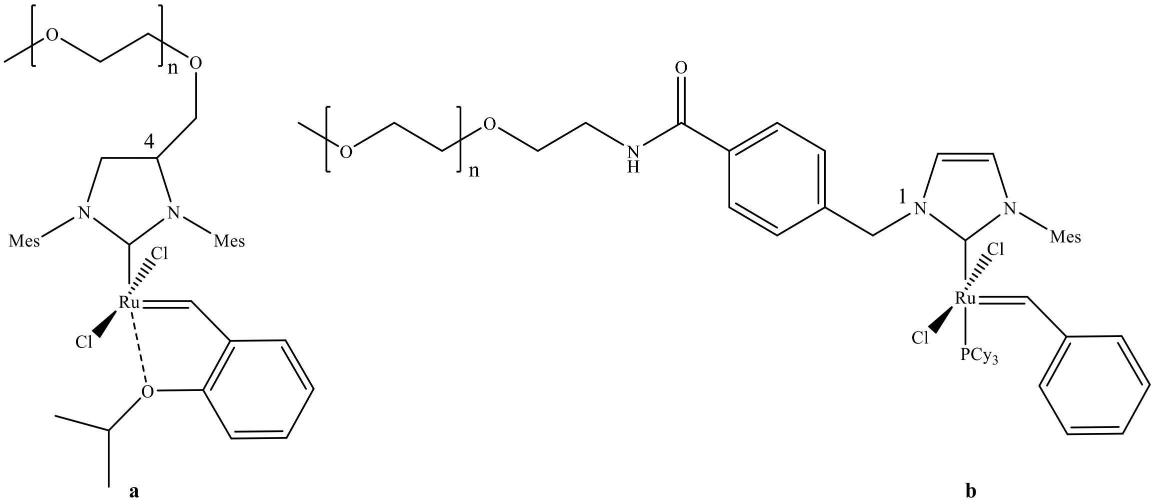


***Fig. 1.25**: Hoveyda-Grubbs catalyst linked by C-4 of NHC [**a**] and 2nd generation Grubbs catalyst linked by N-1 substituent [**b**] to PEG through a linker functionality inserted on NHC.*

Different types of supports have been studied and developed in searching of a good catalytic system with desired features:

- Polymers

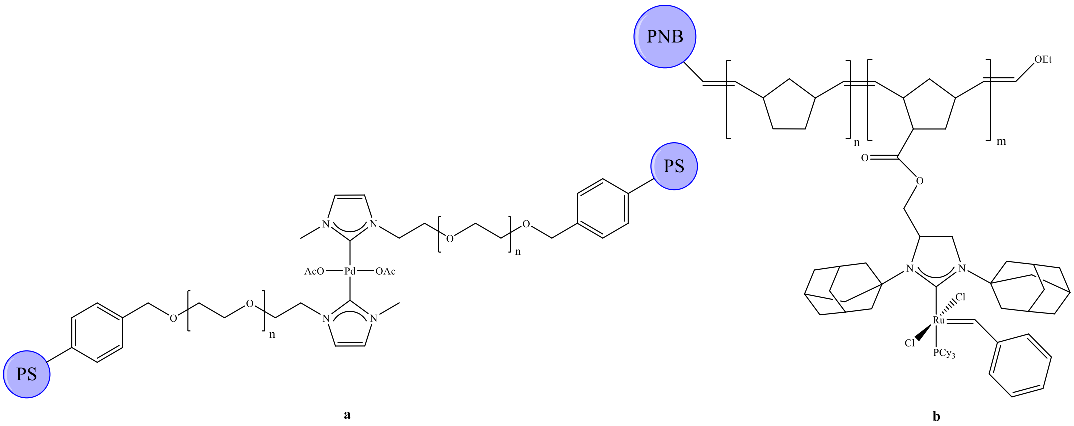


Fig. 1.26

- Inorganic supports like silica[42]

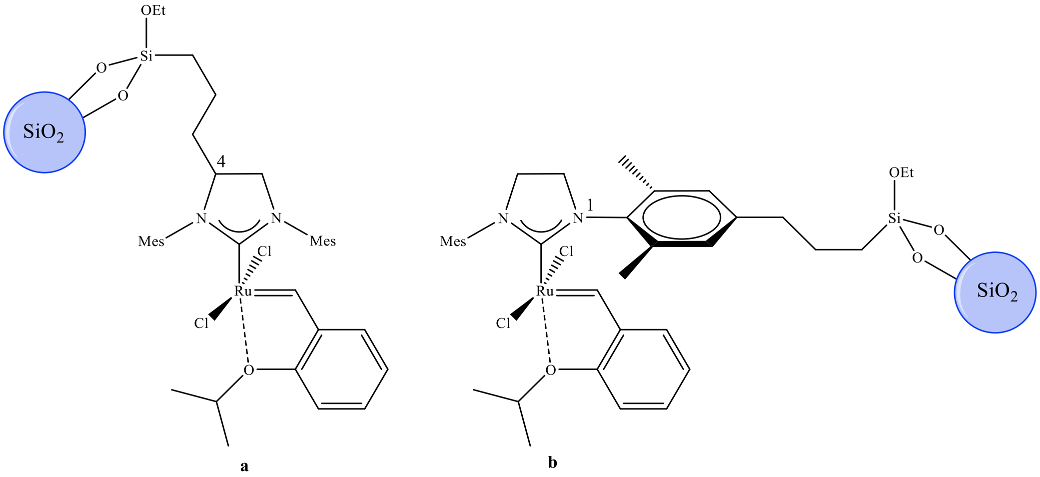


Fig. 1.27

- Dendrimers

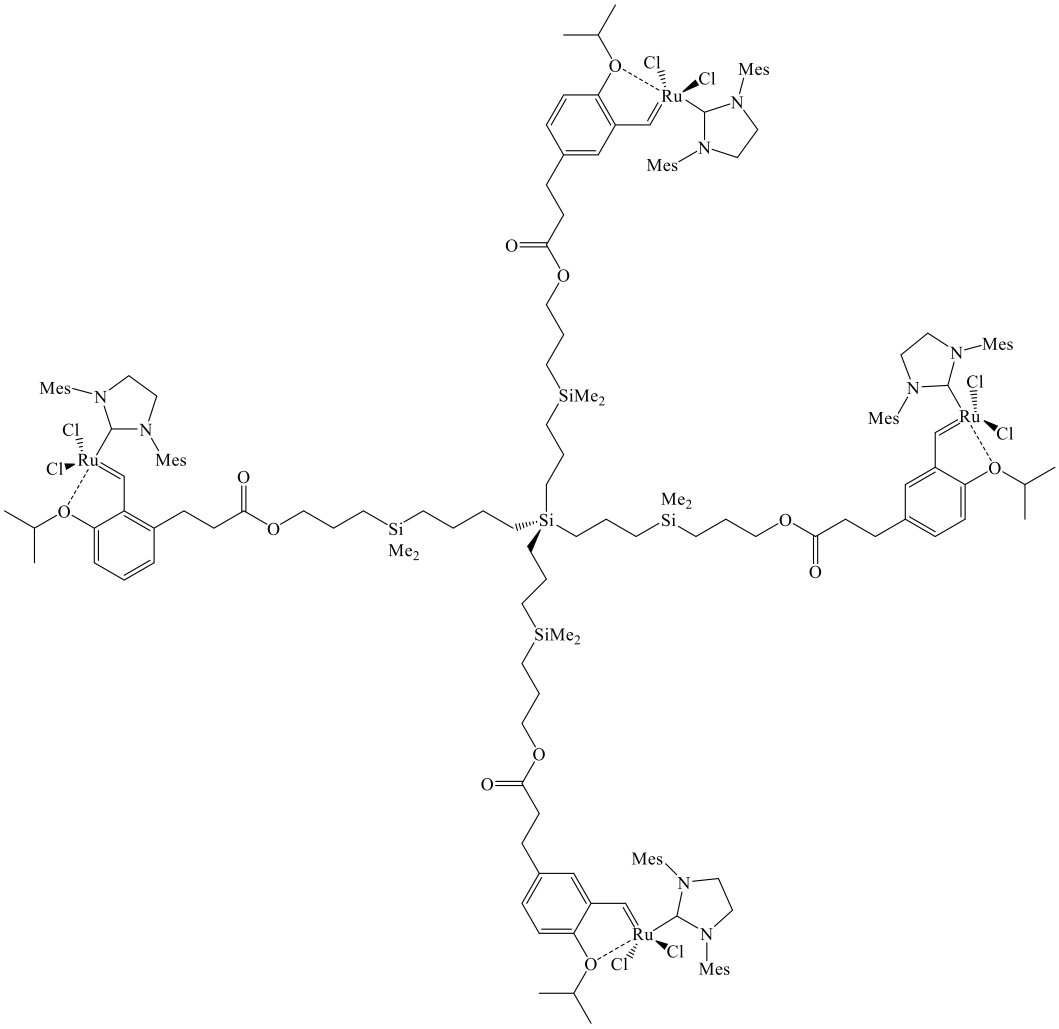


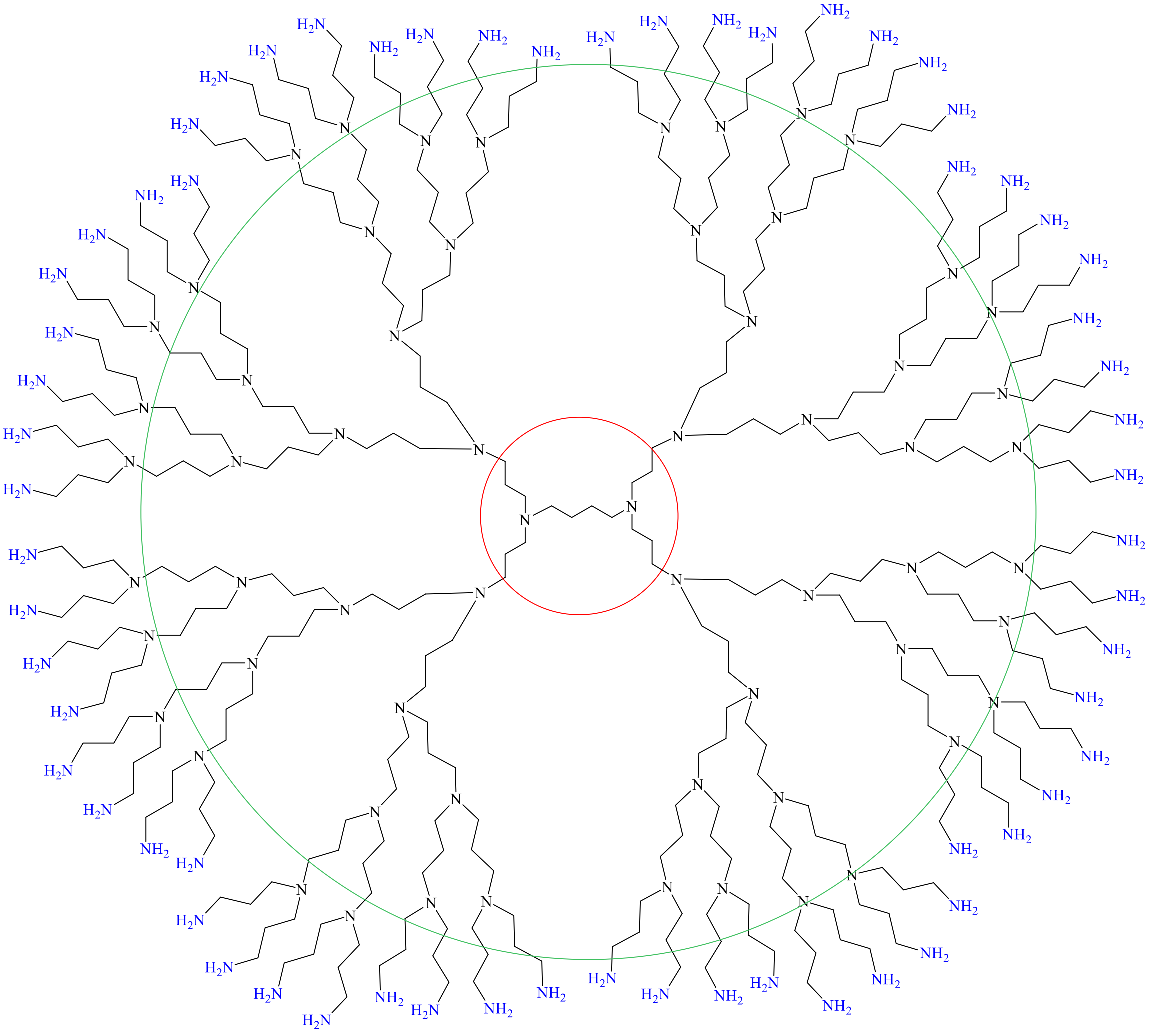
Fig. 1.28

As showed (fig. 1.26, 1.27, 1.28) supports studied range from organic to inorganic. System whit different solubility can be obtained by changing the type of polymer so a system soluble in the target solvent can be developed by using a specific polymer. Water soluble supported catalyst can be obtained using inorganic type of supports like silica or polymer like PEG while dendrimer systems can be tailored to obtain a lot of different characteristics. The main objective is to find a system which is good both in catalysis and in recycling features.[41] Functionalized dendrimers could actually represent both the characteristics of homogeneous and heterogenous catalysts: easy recover by means of membranes and easy availability due to solubility.

1.10. Dendrimers

Dendrimers are perfect monodisperse macromolecules with a regular and highly branched three-dimensional architecture developed by Vögtle in 1978.[43]

Dendrimers contain three distinct architectural regions (Fig. 1.29): first one is the core (inside red circle), second one are layers which contain branching centres and are bounded to the core (inside green circle) and the third is the surface which is formed by end groups (the blue amino groups). Dendrimers are characterized by branching point and the dendrimer generation increases with the number of branching centres it contains. The core is than the "zero generation". As their generation increase their properties are dominated by the nature of ending groups.[44]



DAB-dendr-$(NH_2)_{64}$ (**G5**)

Fig. 1.29

Two different synthetic strategies have been developed: divergent and convergent approaches (fig. 1.30). In divergent strategies growth start from the central core by successive stepwise addition and activation steps. This approach lead to a rapid increase of the dendrimers but it need high yield reactions and present problems in purification because each batch must be perfect to use it in the following reaction. Convergent approach start from the synthesis of dendrons followed by dendrons attachment to the core. Dendrons can be synthetized starting both from the centre or periphery in a stepwise fashion of addition and activation. The convergent strategy lead to more easy synthesis and purification than divergent strategy. Convergent approach is also more flexible and dendrimers with very complex architecture can be synthetized by this strategy.[45,46]

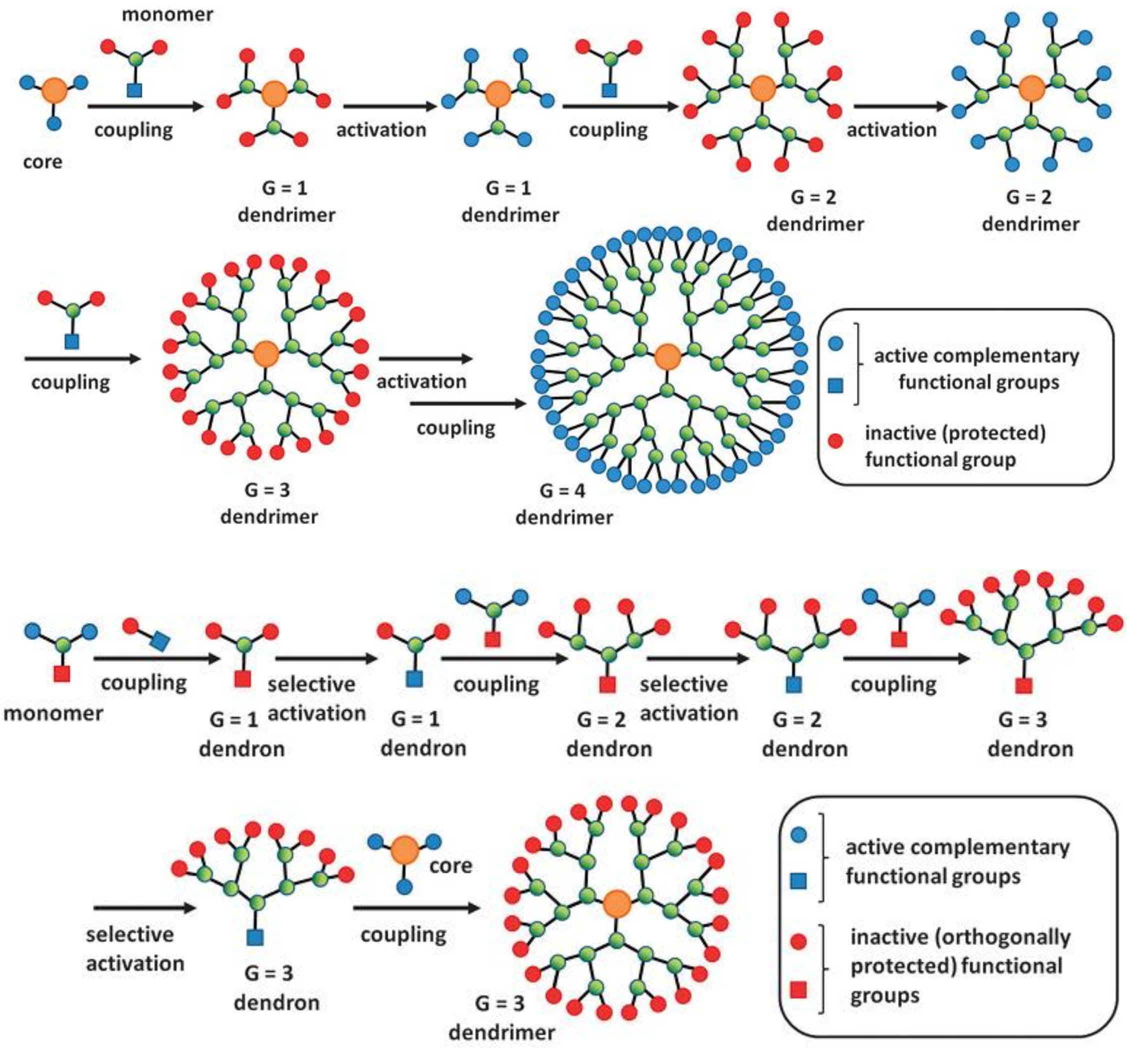


***Fig. 1.30**: divergent (first one) and convergent (second one) synthetic strategies.*

The poly(propylene imine) dendrimers used in my work are synthetized by divergent approach in a large scale synthesis by a sequence of double Michael addition of acrylonitrile to primary amines, followed by the heterogeneously catalysed hydrogenation of nitriles resulting in doubling of the number of end primary amines (fig. 1.31).[47]

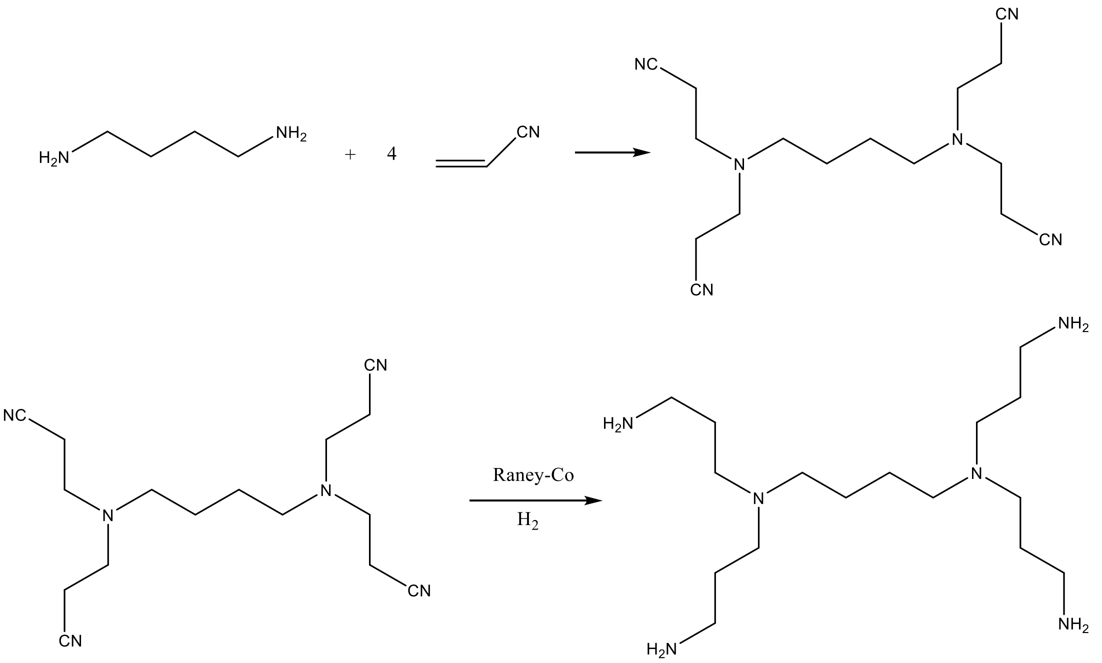
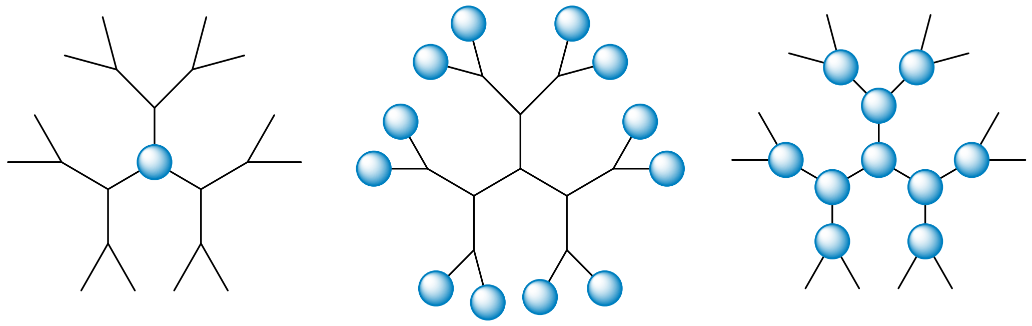


Fig. 1.31

Dendrimes employed for heterogenization strategies lead to the synthesis of metallodendrimers. Metals can be inserted as core, as branching centres or as termini in the dendridic structure giving three different classes of metallodendrimers represented in fig. 1.32. All of those three classes were developed as catalytic system for heterogenization strategy and to investigate new catalysts.[48]



Metals as Core **Metals as termini** **Metals as branching centers**

Fig. 1.32

Metal complex can be the core of the metallodendrimer, so the dendrimer can be designed as ligand like the following example in which substituents on nitrogen atoms of an NHC are two dendrons (fig. 1.33). This approach give a catalytic centre covered by dendrimer and insert it in a new chemical-physical habit that can be modified by changing dendrimer type.

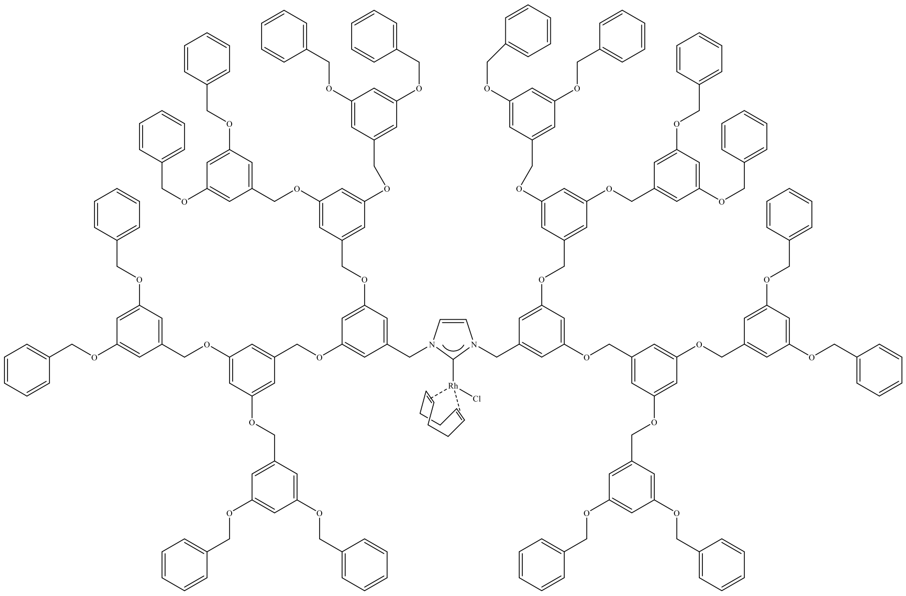


Fig. 1.33

If metal complexes are needed as termini, dendrimer ending groups are designed as ligands as in example reported below where the ending groups are N-heterocyclic carbenes (fig. 1.34). Dendrimers can be designed to change the solubility of the catalytic system to influence catalysts performances.

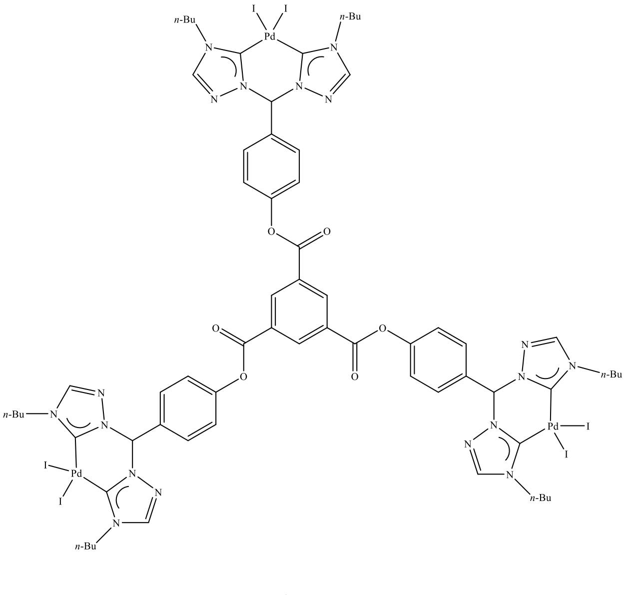


Fig. 1.34

1.11. AIM OF THE THESIS WORK

My training period was developed in different research groups. I have had the opportunity to work under the supervision of Professor Paul Newman at Cardiff University (Wales). His group is developing new type of expanded ring N-heterocyclic carbenes which are chiral and synthetized starting from camphoric diacid. I was involved in synthesis of NHCs and in preliminary study of their reactivity with following aims:

- Synthesis of expanded ring NHCs bearing different substituents in an asymmetric fashion;
- Preliminary studies on their reactivity with aluminium precursors;
- Preliminary studies on their reactivity with palladium.

I have also worked under the supervision of Prof. Rita Mazzoni at Alma Mater Studiorum – Università di Bologna (Italy). As showed above (paragraph 1.8) her group works on novel ruthenium catalysts for transfer hydrogenation containing N-heterocyclic carbene ligands.

During the part of the training which I developed in Bologna I was involved in the preparation of functionalized dendrimers employed as hydrogen transfer catalysts with following aims:

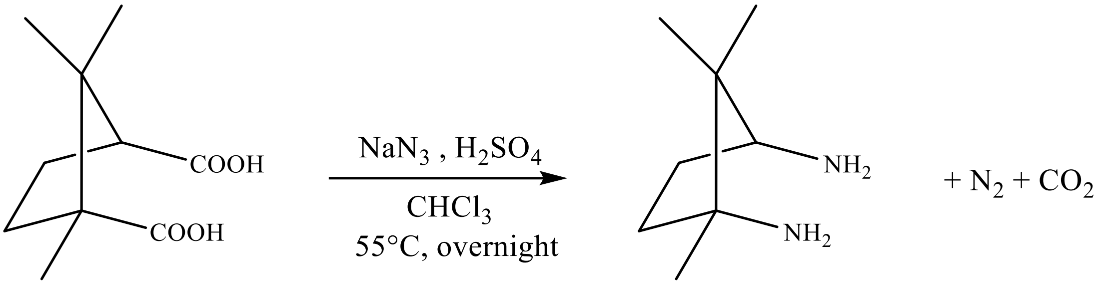
- Synthesis of polycationic functionalized dendrimers by protonation of DAB-dendr-$[NH(O)CO(NHC)Cp{=}ORu(CO)_2]_n$ {n=4; NHC=[-CH_2CH_2-5-CH_3-imidazol-2-ylidene]; Cp-OH =[3,4-$(CH_3O\text{-}C_6H_4)_2$-2,5-$Ph_2(\eta^4\text{-}C_4CO)$]};
- Catalytic tests in transfer hydrogenation and dehydrogenation of functionalized dendrimers;
- Synthesis of DAB-dendr-$[NH(O)CO(NHC)CpRu(CO)_2]_4$ {NHC=[-CH_2CH_2-5-CH_3-imidazol-2-ylidene]; Cp=[2,4-bis(trimethylsilyl)bicyclo[3.3.0]nona-1,4-dien-3-one]}.

2. RESULTS AND DISCUSSION

2.1. Synthesis of N-heterocyclic ligands precursors

The synthetic strategies for bicyclic expanded ring N-heterocyclic carbenes developed by Newman's Group start from the synthesis of diamine by camphoric diacid via a Schmidt reaction as mentioned above in paragraph 1.7. The diamine is going to become the chiral bicyclic backbone of NHCs synthetized. The following step is the first functionalization which in my case exploited a Buchwald-Hartwig C-N coupling reaction in order to link the first substituent on the less hindered nitrogen, then the second substituent is inserted via a reductive amination employing an aldehyde. Once both substituents are inserted the key step is a neat ring closing reaction in triethyl orthoformate. Another studied route passes through a ring closing reaction after the insertion of the first substituent followed by the alkylation of the second nitrogen.

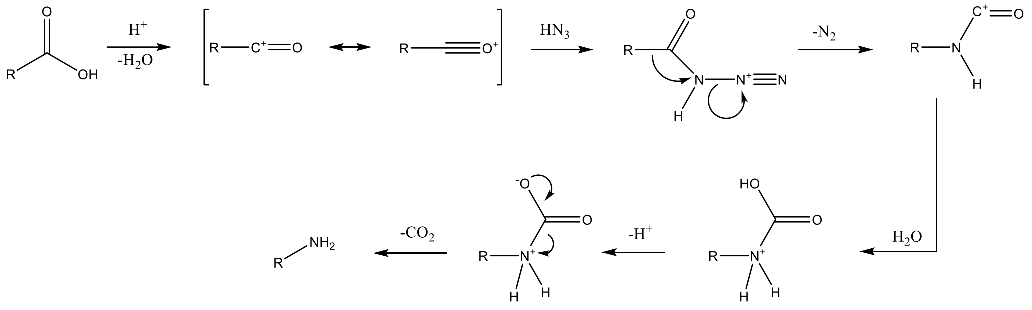
2.2. Synthesis of (1R,3S)-1,3-Diamino-1,2,2-trimethylcyclopentane (R,S-tmcp) (1)



1

Scheme 2.1

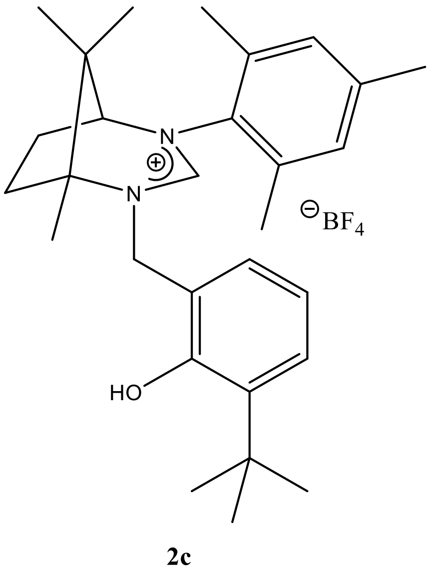
The first stage is the synthesis of R,S-tmcp (**1**) starting from camphoric diacid via a Schmidt reaction (scheme 2.1). It is a very easy and cheap way to obtain an amine starting from a carboxylic acid and using camphoric diacid a very interesting chiral backbone is obtained. The Schmidt reaction is a rearrangement carried out with a strong acid and sodium azide. The strong acid is needed both for formation of azidic acid and to catalyse the reaction (scheme2.2).



Scheme 2.2*: Reaction mechanism of Schmidt rearrangement.*

The synthesis is carried out using a procedure reported in literature[49] and the product, obtained in 63% yield after the purification as a yellow solid, is characterized by ^{1}H-NMR (see experimental section).

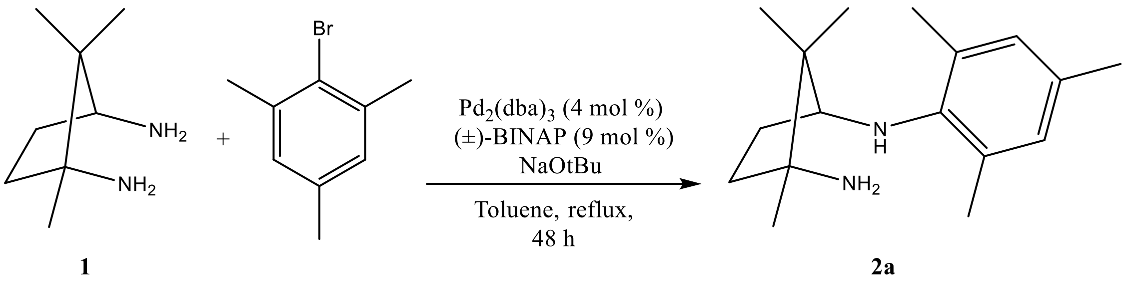
2.3. Synthesis of (1R-5S)-N^2-(3-(tert-butyl)-2-hydroxybenzyl)-N^4-mesityl-1,8,8-trimethyl-2,4-diazabicyclo[3.2.1]oct-2-en-2-ium tetrafluoroborate (2c)



2c

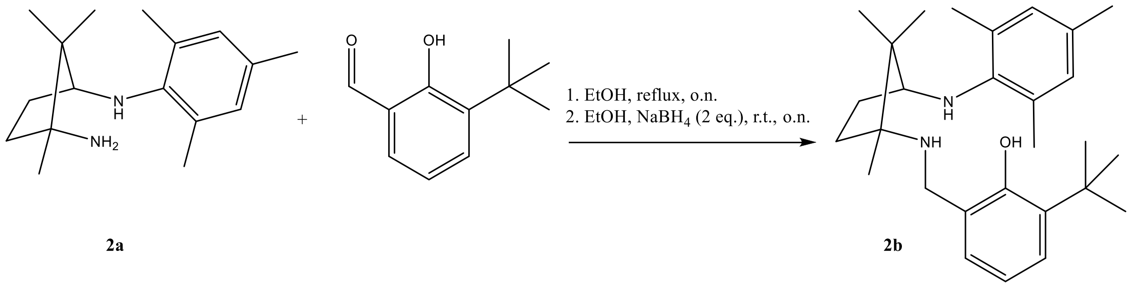
Fig. 2.1*: Structure of ligand* ***2c****.*

The ligand **2c** (fig. 2.1) is a bicyclic chiral NHC and is asymmetrically functionalized. It is obtained starting from R,S-tmcp via the three steps described below.



Scheme 2.3

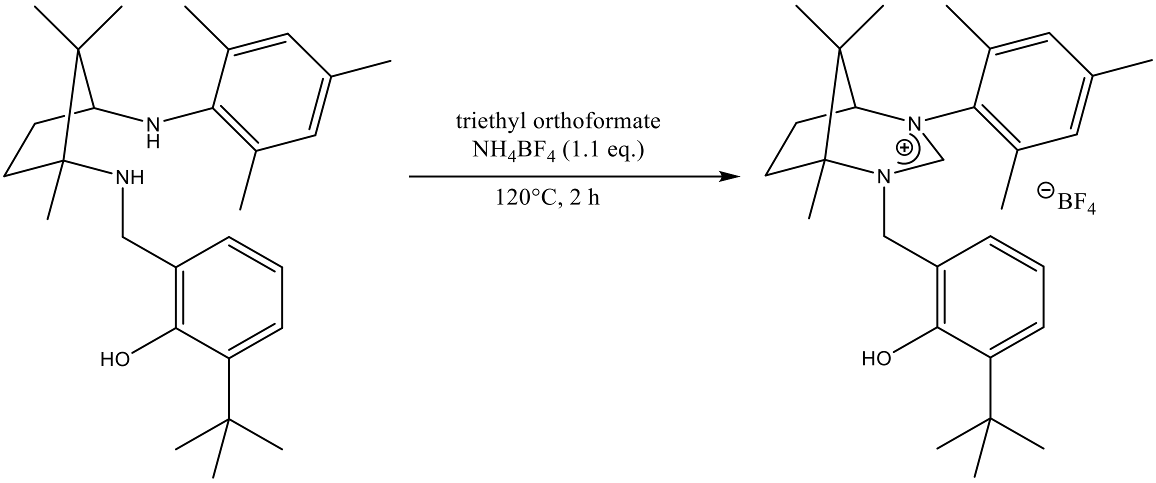
The first functionalization is a Buchwald-Hartwig cross coupling[27] between R,S-tmcp (**1**) and 2-bromo-1,3,5,trimethylbenzene catalysed by $Pd_2(dba)_3$ (4 mol %) in toluene with adding of rac-BINAP (9 mol %) and sodium tert-butanoate (scheme 2.4). The synthesis was already reported in literature and after 48 hours of reaction at reflux and the purification a yellow oil is obtained in 70% yield. Product (1S, 3R)-N^1-mesityl-2,2,3-trimethylcyclopentan-1,3-diamine (**2a**) is characterized by ^{1}H-NMR where mesityl substituent resonances are at 6.78 ppm the two equivalent aromatic protons, at 2.25 ppm the two meta-CH_3 and 2.21 ppm the para-CH_3. Moreover the signals of camphor structure are slightly shifted and are identified. Diagnostic signals are methyls at 1.11, 1.08 and 0.94 ppm.



Scheme 2.4

The second functionalization is a reductive amination of **2a** using 3-tert-butylsalicylaldehyde (scheme 2.4). The aldehyde reacts with the primary amine to give an enamine. The reaction runs overnight at reflux in ethanol and reaction mix colour change from yellow to bright orange. Reaction mix is cooled down to room temperature and the imine formed is directly reduced by using two equivalents of sodium borohydride overnight at room temperature. After work-up a yellow sticky oil is obtained in 90% yield and it is identified as (1R, 3S)-N^1-(3-(*tert*-butyl)-2-hydroxybenzyl)-N^3-mesityl-1,2,2-trimethylcyclopentan-1,3-diamine (**2b**) by ^{1}H-NMR. Resonances for new substituents are at 7.20, 6.89 and 6.73 ppm for aromatic protons, at 3.94 ppm for CH_2 linker and at 1.43

ppm for tert-butyl. Diagnostic signals of camphor structure are found like 1.20, 1.09 and 1.08 ppm which are resonances of methyl. Another evidence is proven by ESI-TOF where is shown a signal at 423 m/z that corresponds to $[M+H]^+$.



2b **2c**

Scheme 2.5

The last stage is the ring closing reaction where **2b** is dissolved in triethyl orthoformate with 1.1 equivalents of ammonium tretrafluoroborate at 120°C (scheme 2.5). The product is a dark orange oil which came out from solution, so triethyl orthoformate is evaporated. **2c** is characterized by NMR and ESI-TOF. In ^{1}H-NMR (fig. 2.2) we can observe the new signal of ring closed product at 7.69 ppm which correspond to proton between nitrogen atoms, the signals of substituents are slightly shifted and diagnostic signals of methyls of camphor skeleton are found at 1.32, 1.31 and 1.16 ppm.

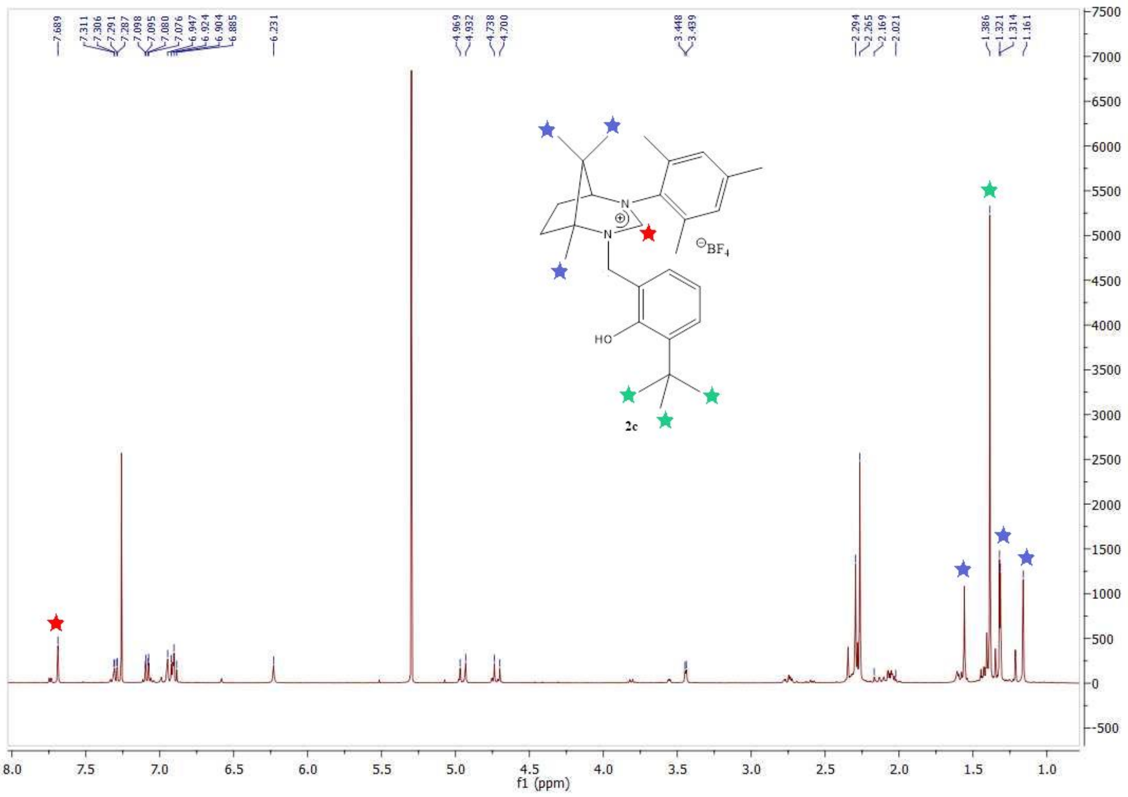


***Fig. 2.2**: ^{1}H-NMR of **2c**.*

In ^{19}F-NMR a signal is found at -148.19 ppm that correspond to counterion. Another evidence for **2c** is proven by ESI-TOF (fig. 2.3) where is showed a signal at 433 m/z that corresponds to $[M]^+$.

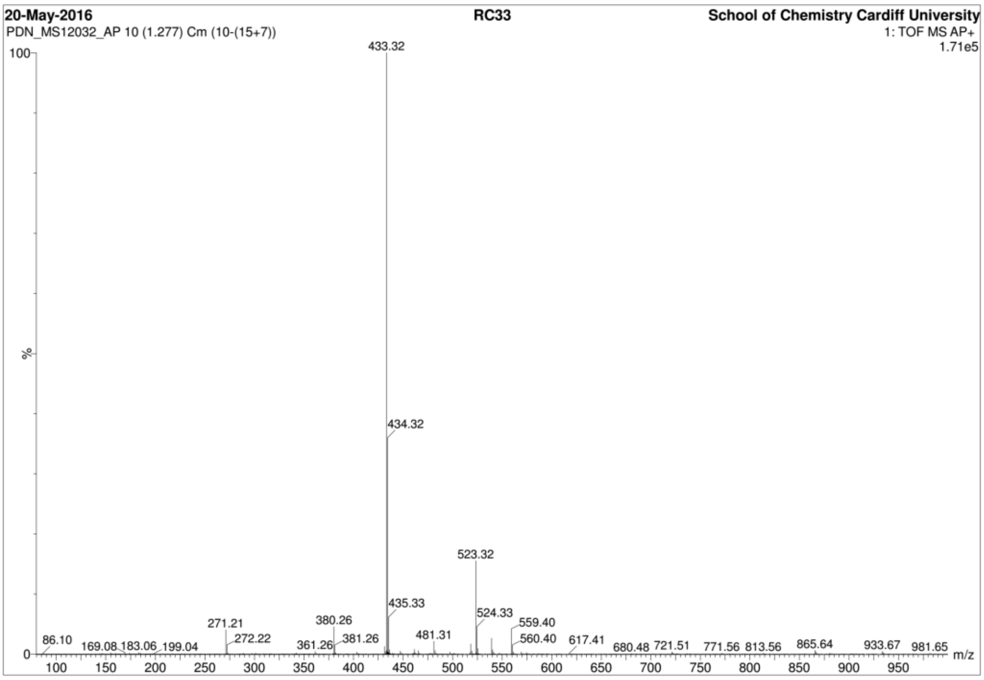
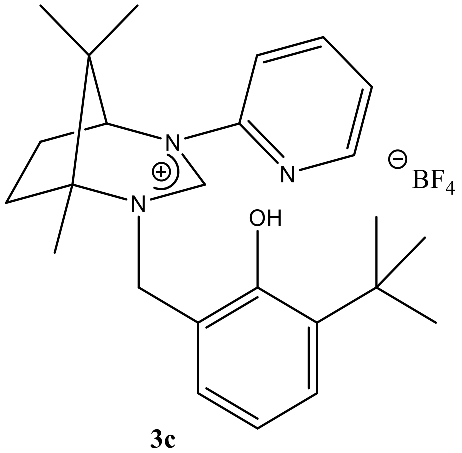


***Fig. 2.3**: ESI-TOF of **2c**.*

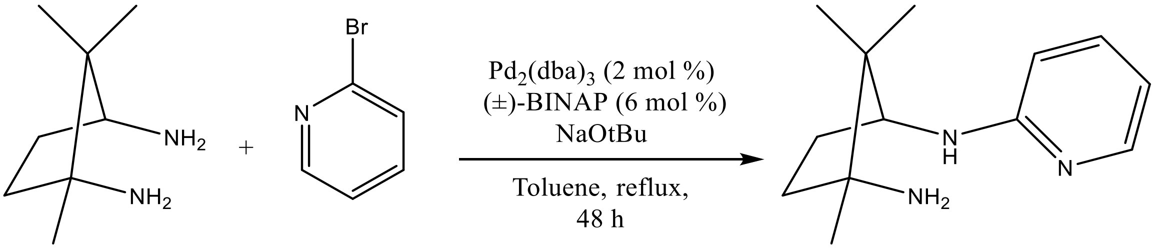
2.4. Synthesis of (1R-5S)-N^2-(3-(tert-butyl)-2-hydroxybenzyl)-N^4-pyrid-2-yl-1,8,8-trimethyl-2,4-diazabicyclo[3.2.1]oct-2-en-2-ium tetrafluoroborate (3c)



3c

***Fig. 2.4**: structure of ligand **3c**.*

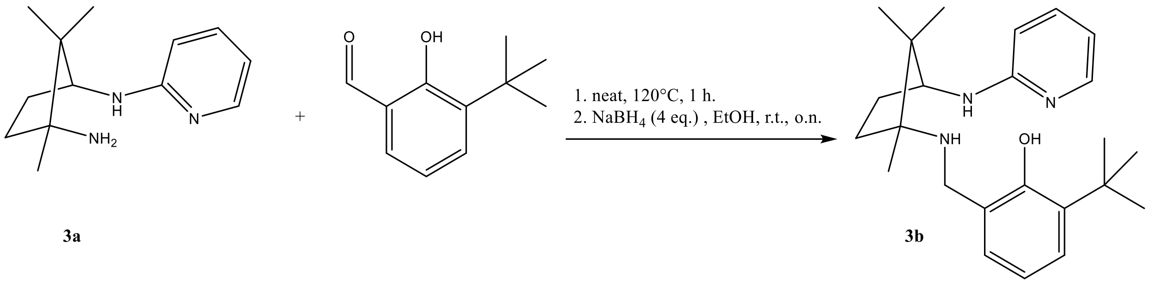
In order to insert a basic nitrogen functionality on ligand the mesityl has been substituted by pyridine to obtain ligand **3c** by following the same pathway used for **2c**.



1 **3a**

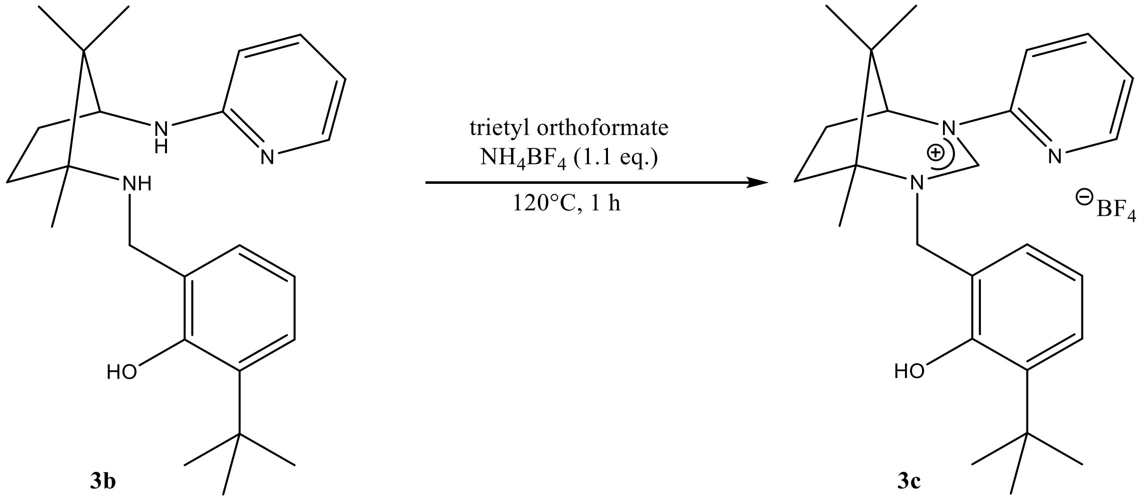
Scheme 2.6

The first functionalization is carried out using the same procedure used to obtain **2a** for the Buckwald-Hartwig cross coupling[27] but using 2-bromopyridine (scheme 2.6). After 48 hours of reaction a yellow oil is obtained in 90% yield. Product (1S, 3R)-N^1-pyrid-2-yl-2,2,3-trimethylcyclopentan-1,3-diamine (**3a**) is characterized by ^{1}H-NMR where pyridyl pattern is easily identified as resonances at 8.01, 7.30, 6.43 and 6.31 ppm. Moreover signal of camphor structure are identified like diagnostic methyls signals at 1.55, 1.11 and 0.91 ppm.



Scheme 2.7

The second functionalization of **3a** is a reductive amination using 3-tert-butylsalicylaldehyde (scheme 2.7). The reaction between aldehyde and diamine is carried out in neat condition at 120°C for one hour, then it is cooled down and crude product is dissolved in ethanol. The imine is reduced by reacting with 4 equivalents of sodium borohydride overnight. After work-up a yellow sticky oil is obtained in 70% yield. The product (1R,3S)-N^1-(3-(*tert*-butyl)-2-hydroxybenzyl)-N^3-pyrid-2-yl-1,2,2-trimethylcyclopentan-1,3-diamine (**3b**) is characterized by ^{1}H-NMR. Resonances for new substituents are at 7.24, 6.93 and 6.77 ppm for aromatic protons, at 3.98 ppm for CH_2 linker and at 1.48 ppm for tert-butyl. Diagnostic signals of camphor structure are found like 1.31, 1.04 and 1.00 ppm for methyls. In ESI-TOF is found a signal at 381 m/z that corresponds at $[M+H]^+$.



Scheme 2.8

The NHC precursor **3c** is then obtained by the same way already used to obtain **2c**, so a ring closing reaction is the final step (scheme 2.8). **3b** is dissolved in triethyl orthoformate with 1.1 equivalents of ammonium tetrafluoroborate at 120°C. After one hour of reaction an orange oil came out from solution, the solvent is removed and after work-up a yellow oil is isolated in quantitative yield. **3c** is characterized by ^{1}H-NMR and ESI-MS. In ^{1}H-

NMR (fig. 2.5) we can observe the new signal of ring closed product at 8.91 ppm which corresponds to proton between nitrogen atoms, the signals of substituents are shifted and diagnostic signals of methyl are found at 1.33, 1.25 and 1.20 ppm.

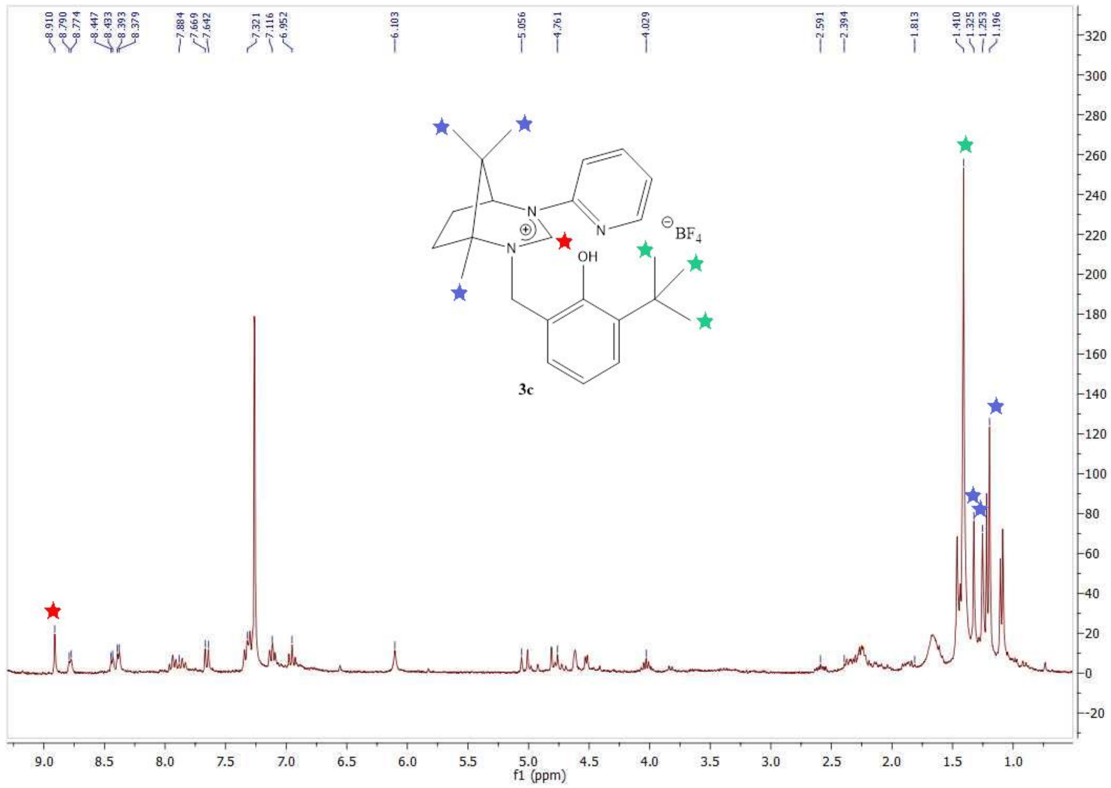


***Fig. 2.5**: ^{1}H-NMR of **3c**.*

Another evidence for **3c** is proven by ESI-TOF (fig. 2.6) where is showed a signal at 392 m/z that corresponds to $[M]^+$.

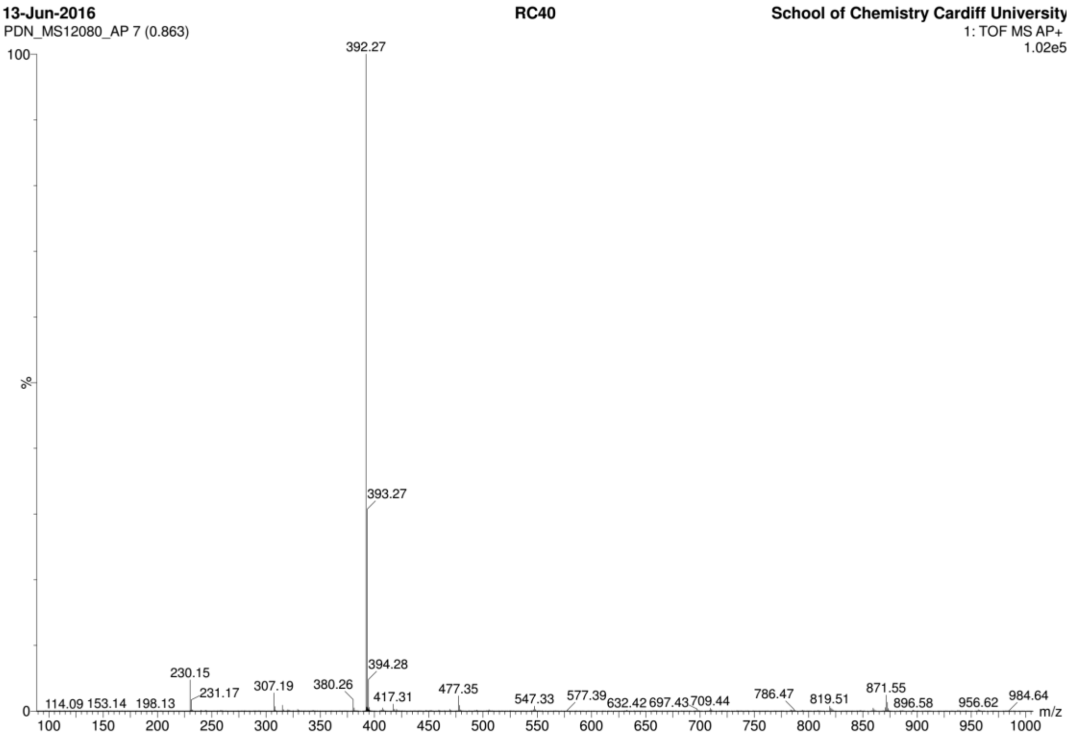
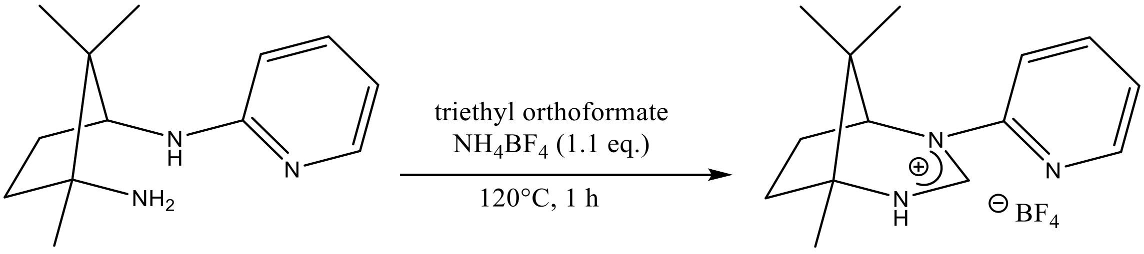


***Fig. 2.6**: ESI-TOF of **3c**.*

2.5. Synthesis of (1R-5S)-N^4-pyrid-2-yl-1,8,8-trimethyl-2,4-diazabicyclo[3.2.1]oct-2-en-2-ium tetrafluoroborate (4b)



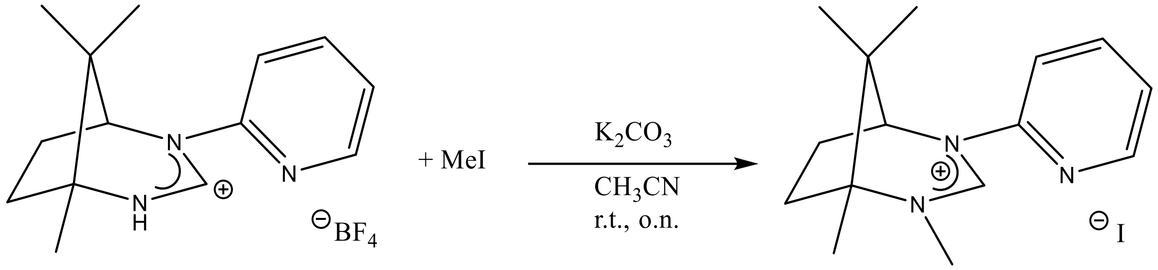
3a

4b

Scheme 2.9

This reaction is the first of second strategy followed. Mono-functionalized product **3a** is reacted in triethyl orthoformate with 1.1 equivalents of sodium borohydride at 120°C for one hour (scheme 2.9). A dark orange oil came out and triethyl orthoformate is removed under vacuum. After work-up the product is obtained in quantitative yield and characterized by NMR. In ^{1}H-NMR resonances for new proton between nitrogen resonates at 8.71 ppm, the pyridine signals are shifted and the diagnostic signals of methyls are found at 1.33, 1.18 and 1.02 ppm. In ^{13}C-NMR all resonances are found, of particular interest are signal at 150.09 ppm for carbon between nitrogen atoms and signals of methyl of camphor skeleton at 20.51, 16.50 and 15.30 ppm. In ^{19}F-NMR is found a resonance at -150.58 ppm ascribable to BF_4^- counterion.

2.6. Synthesis of (1R-5S)-N^2-methyl-N^4-pyrid-2-yl-1,8,8-trimethyl-2,4-diazabicyclo[3.2.1]oct-2-en-2-ium iodide (4c)



4b **4c**

Scheme 2.10

Ring closed product **4b** is alkylated by 1.2 equivalents of MeI in acetonitrile and 2 equivalents of potassium carbonate are added to remove acidic proton generated. After overnight reaction at room temperature a yellow oil is isolated in 87 % yield and the product is characterized by NMR and ESI-TOF. In ^{1}H-NMR (fig. 2.7) the signal of proton between nitrogen is downshifted at 9.51 ppm, also pyridine resonance are downshifted and new methyl signal is shown at 3.61 ppm.

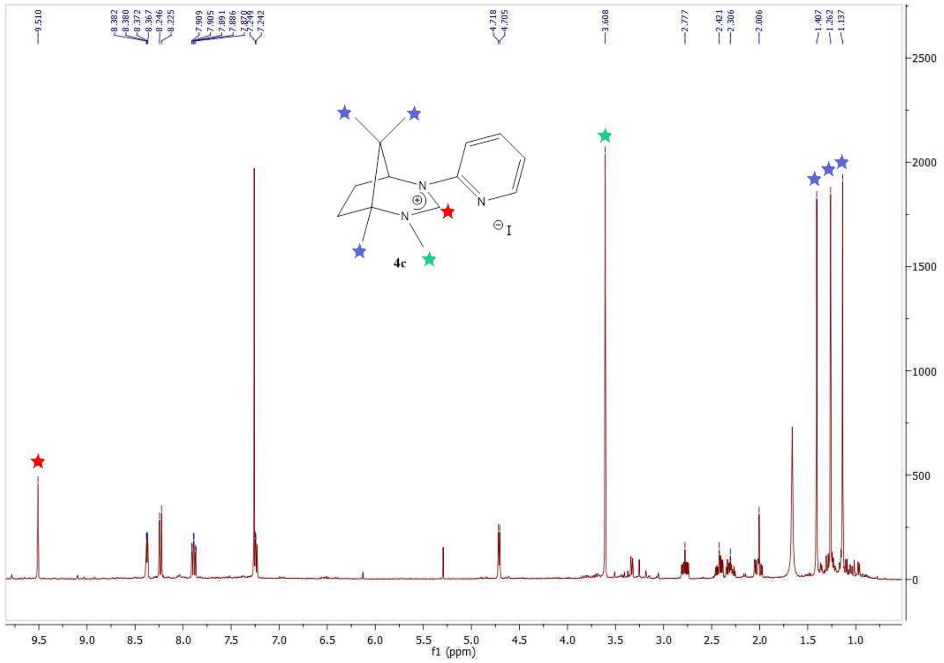


***Fig. 2.7**: ^{1}H-NMR of **4c**.*

In ^{13}C-NMR (fig 2.8) the signal of carbon between nitrogen atoms is shown at 151.61 ppm and the new methyl at 38.91 ppm, while methyl of camphor skeleton are at 21.87, 16.91 and 14.18 ppm.

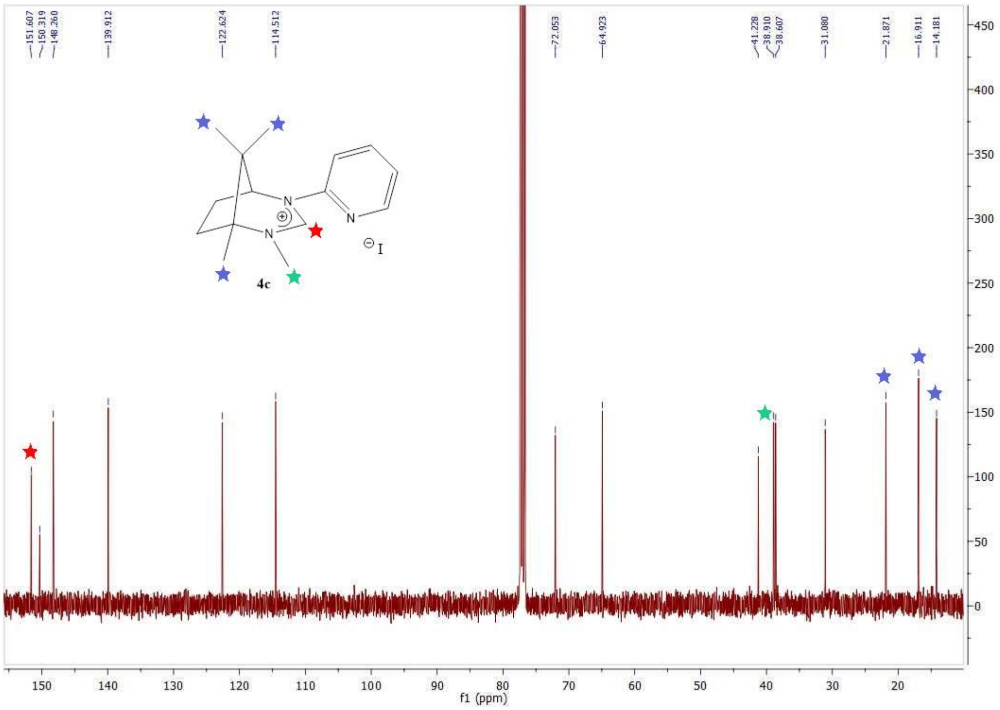


Fig. 2.8: *^{13}C-NMR of **4c**.*

From ESI-TOF (fig. 2.9) in positive ion the right signal for product is shown at 244 m/z, while in negative ion is shown that the counterion is changed and a signal at 126 m/z for iodide is found.

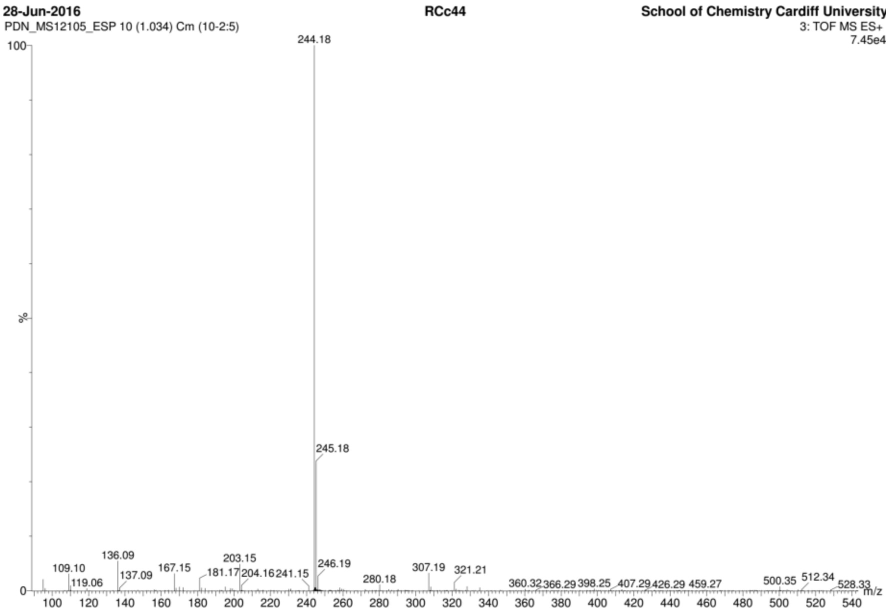
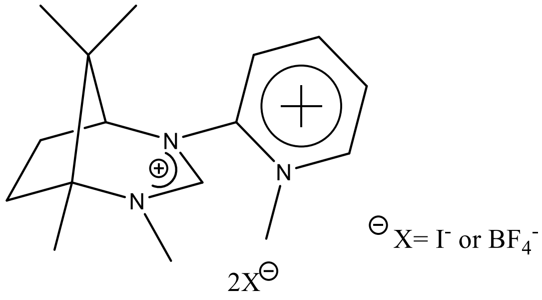


Fig. 2.9: *ESI-TOF of **4c**.*

2.7. Synthesis of (1R-5S)-N^2-methyl-N^4-(N-methylpyridinium-2-yl)-1,8,8-trimethyl-2,4-diazabicyclo[3.2.1]oct-2-en-2-ium 2[X$^-$] (4d)

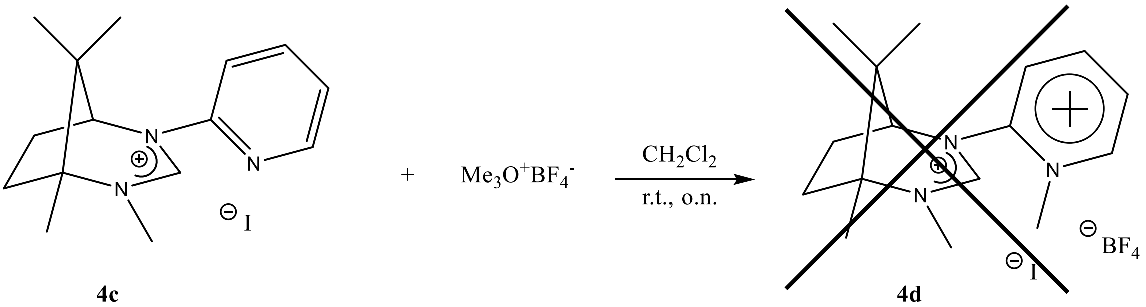


⊖ X= I$^-$ or BF$_4^-$

4d

Fig. 2.10

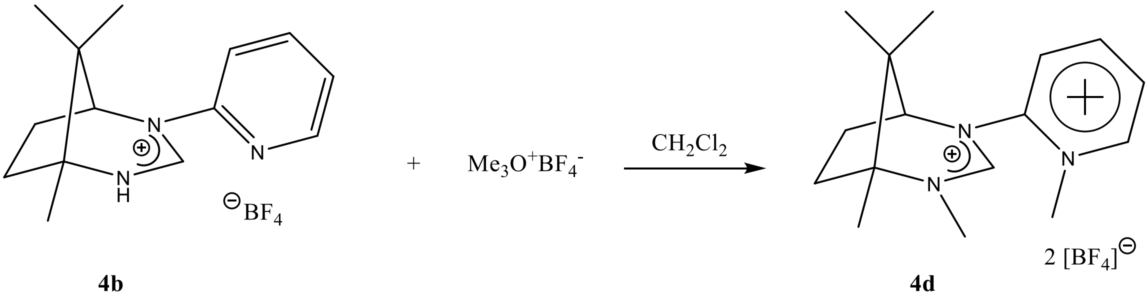
In order to obtain a very electron poor system like **4d** we have investigated the methylation of **4b** and **4c**.



4c **4d**

Scheme 2.11

The first synthesis has been tried performing a methylation of **4c** with one equivalent of trimethyloxonium tetrafluoroborate which is a strong methylating agent. It is carried out in dichloromethane overnight and at room temperature. The crude product is characterized by ^{1}H-NMR but no evidence for **4d** are found.



4b **4d**

Scheme 2.12

In order to reach our objective methylation of **4b** with trimethyloxonium tetrafluoroborate has been tried. The reaction occurs in dichloromethane using different equivalents of methylating agent and reaction temperature. Best condition has been found with two equivalents of methylating agent and one hour of reaction at reflux. The crude product is obtained in 24 % yield and characterized by NMR and ESI-TOF. From ^{1}H-NMR (fig. 2.11) we can observe the resonance of proton between nitrogen atoms at 9.77 ppm, the pyridyl signals shifted at 8.70, 8.85, 8.02 ppm and two de-shielded methyl at 3.00 and 2.98 which are methyls on pyridine and nitrogen. Moreover the methyl resonances of camphor skeleton can be observed at 1.42, 1.25 and 1.18 ppm.

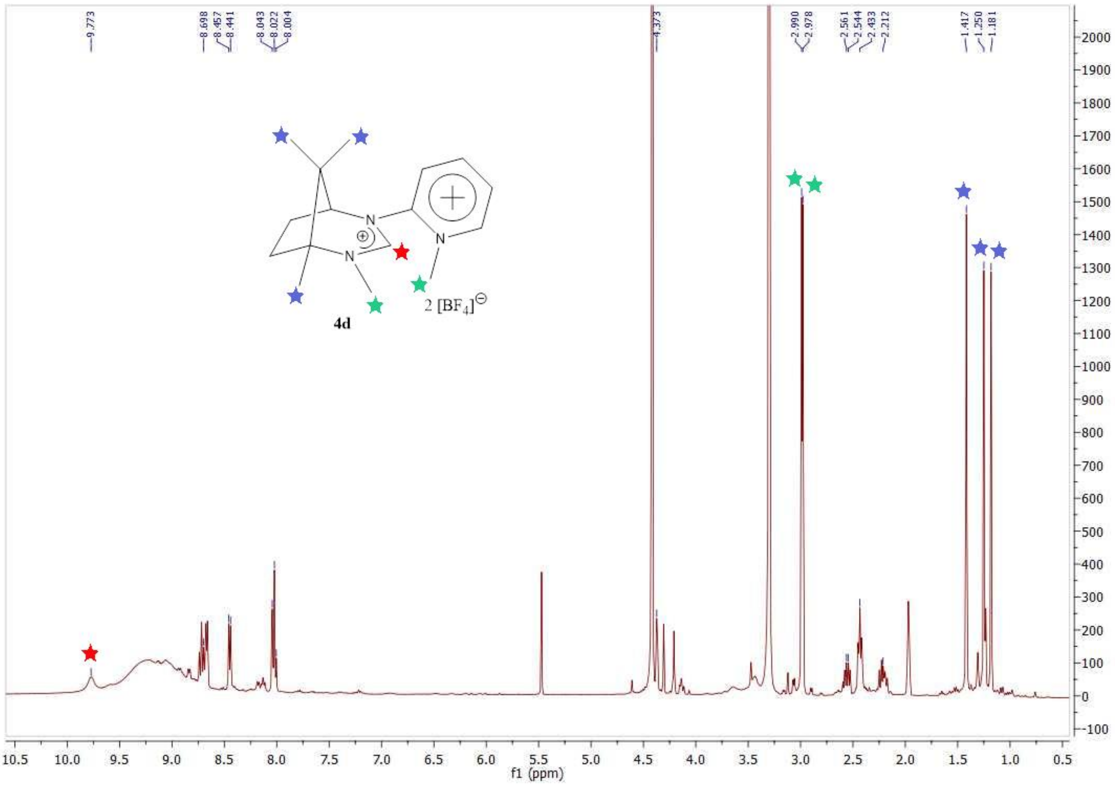


***Fig. 2.11**: ^{1}H-NMR of **4d**.*

From ^{13}C -NMR (fig. 2.12) we can observe signals of carbon between nitrogen atoms at 177.26 ppm, methyl on pyridine at 60.51, methyl on nitrogen at 41.41ppm and the resonances of methyl of camphor skeleton are at 20.33, 16.32 and 15.12 ppm.

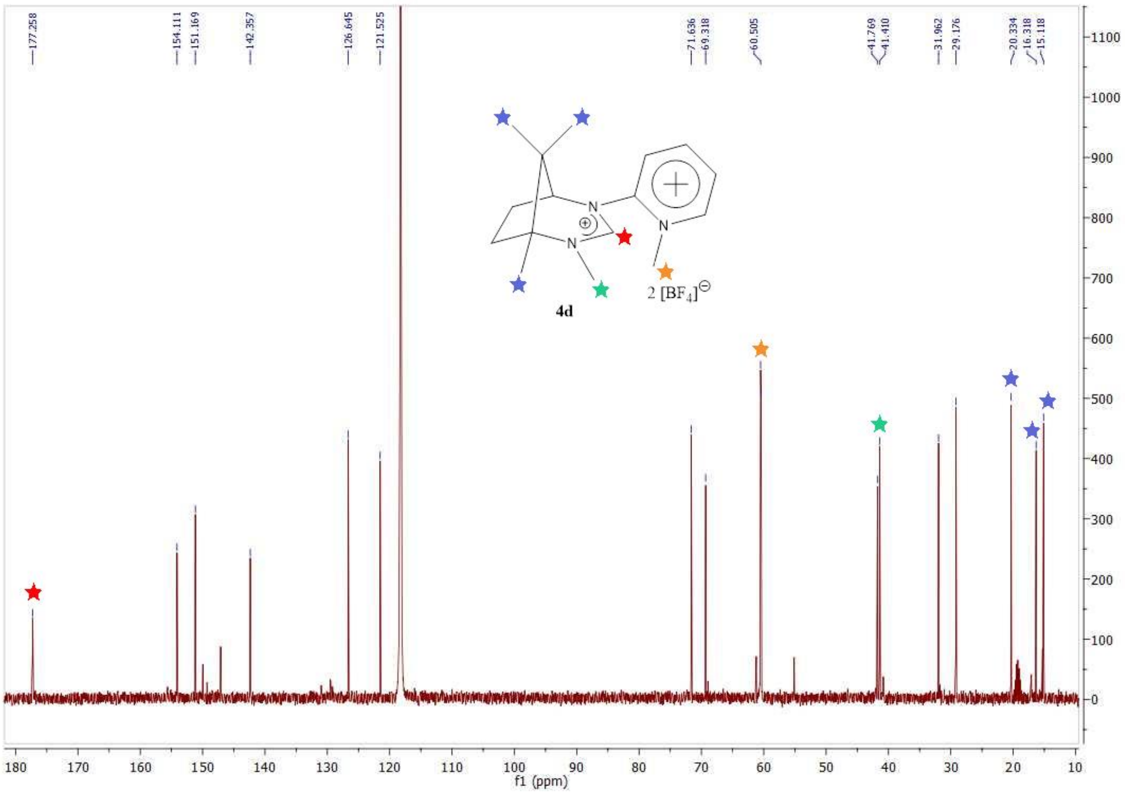


***Fig. 2.12**: ^{13}C-NMR of **4d**.*

In ^{19}F-NMR signal of counterion is observed at -150.87 ppm which corresponds to BF_4^- counterion. Also a ESI-TOF spectra is acquired but it shows a signal at 230 m/z that correspond at **4d** where both methyl on nitrogen are lost. It might depend on instability of **4d** in mass spectrometer conditions.

2.8. Reactivity of 2c toward Aluminium

The reactivity of **2c** toward aluminium has been investigated getting inspired by the idea developed in a work on gallium-NHCs chemistry.[50] In that work two strategies have been developed (fig. 2.13): first one is reaction with trimethyl gallium followed by activation of NHC by KH; second one is formation of a cyclic acetal by reacting of ligand with KH followed by reaction of cyclic acetal with trimethyl gallium.

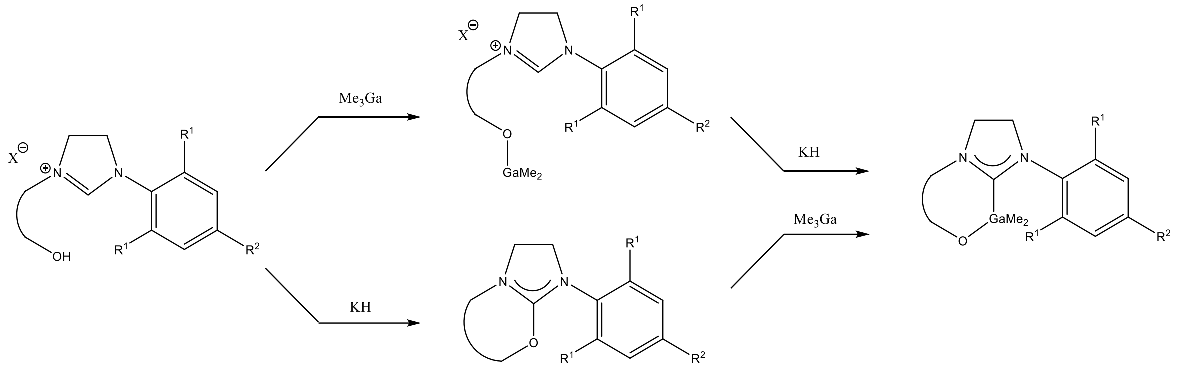
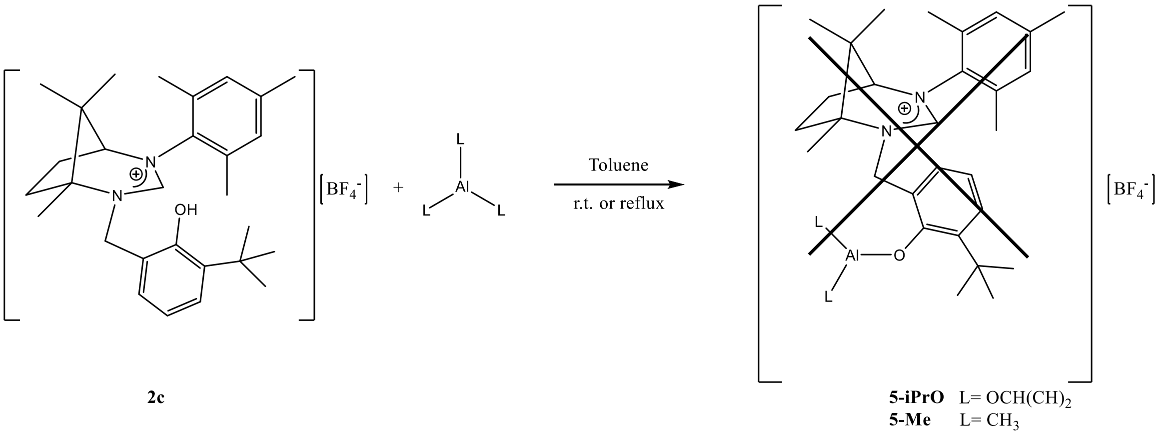


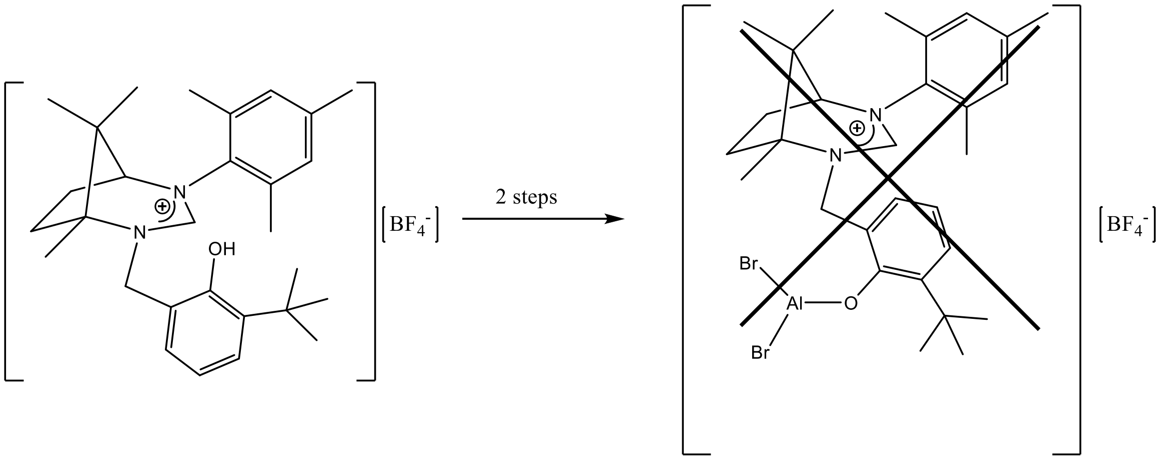
***Fig. 2.13**: pathways used to coordinate NHCs to gallium.*

We used first strategies toward different aluminium precursors and reaction condition with the aim to find the right way of synthesis. The crude products have been characterized by ^{1}H-NMR, ^{13}C-NMR, ^{19}F-NMR and ^{27}Al-NMR.



Scheme 2.13

At first aluminium iso-propoxyde and trimethyl aluminium are used as precursors (scheme 2.13). Reactions have been carried out both at room temperature and at reflux in toluene but neither **5-iPrO** nor **5-Me** have been found by NMR. In most cases NMR shown very broad peaks and very complex patterns where only some resonances ascribable to **2c** were found, but no confident attribution was possible.



2c **5-Br**

Scheme 2.14

Since no product has been obtained by first strategy we moved on a different one with two steps. For the activation of ligand **2c** by removing hydroxy proton one equivalent of a strong and bulky base like KHMDS is used in the first step, then one equivalent of aluminium bromide is used as aluminium precursor. Different reaction conditions (table 2.1) have been used for both steps with the aims to help selectivity of very reactive reagents employed especially for second step. Unfortunately product **5-Br** has not been isolated and NMR acquired showed very complex pattern with some similarity to pattern of **2c** but not confident characterization was possible.

Entry	Step 1	Step 2
A	Room temperature, 30 min	Room temperature, 30 min
B	-78°C, 1 h	-78°C, 1 h
C	Room temperature, 1 h	Room temperature, overnight
D	Room temperature, 30 min	-78°C→room temperature, 1 h

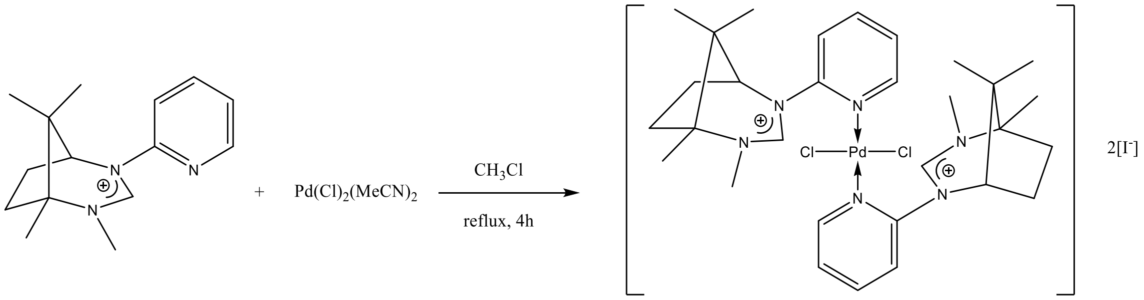
***Table 2.1**: reaction conditions for first and second steps.*

Due to the poor results and complex reactivity no further investigations have been performed with aluminium.

2.9. *Reactivity of 4c toward Palladium*

Ligand **4c** is investigated as C-N chelating ligand for palladium via pyridyl function and carbene. Synthetic strategy passes through coordinating the azonium salt via pyridyl substituent followed by activation of carbene precursor via strong base.

In the first reaction ligand **4c** reacts with $Pd(Cl)_2(MeCN)_2$ in dried toluene for four hours at reflux. This is a standard procedure to coordinate a pyridine to palladium and complex **5-N** is isolated in 74% yield.



4c **5-N**

Scheme 2.15

5-N is characterized by NMR. In ^{1}H-NMR (fig. 2.14) resonances are downshifted, in particular signal of proton between nitrogen atoms is shifted at 9.83 and protons of pyridine at 8.39, 8.28, 8.01 and 7.28 ppm. Methyl resonances of camphor structure are at 1.42, 1.26 and 1.13 ppm.

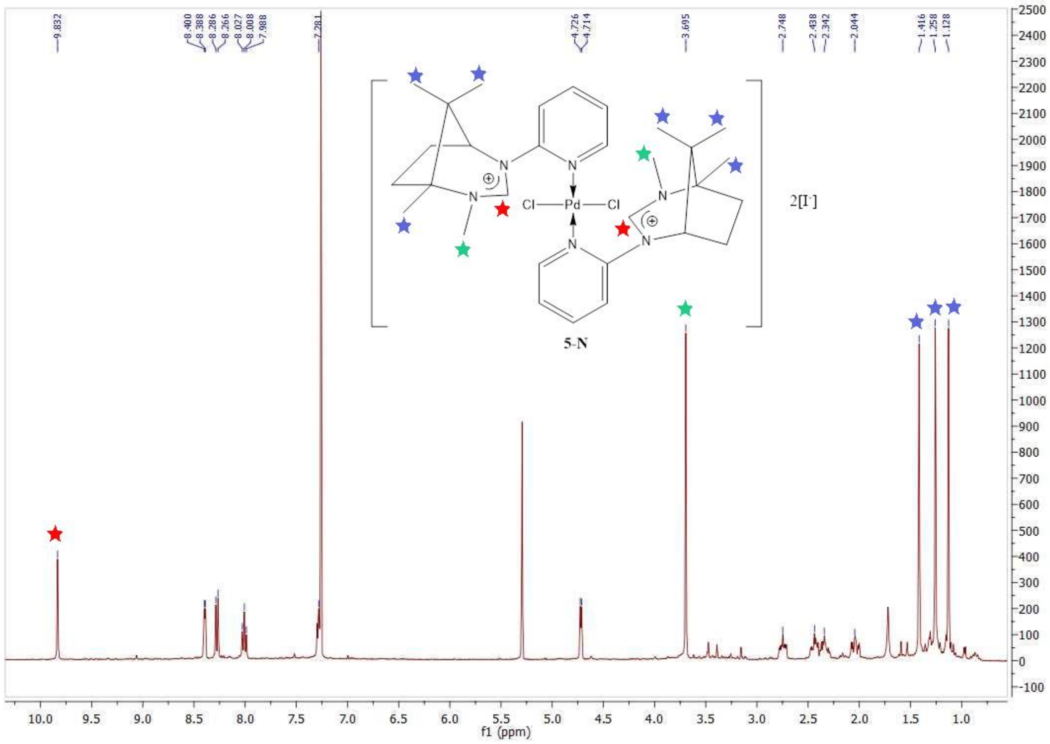


Fig. 2.14: *^{1}H-NMR of complex **5-N**.*

In ^{13}C -NMR (fig. 2.15) the carbon between nitrogen atoms resonates at 152.68 ppm and pyridine pattern is 150.34 (quaternary), 148.28, 140.46, 122.74 and 114.44 ppm. The signals of methyl on camphor skeleton resonate at 21.91, 17.00 and 14.20 ppm.

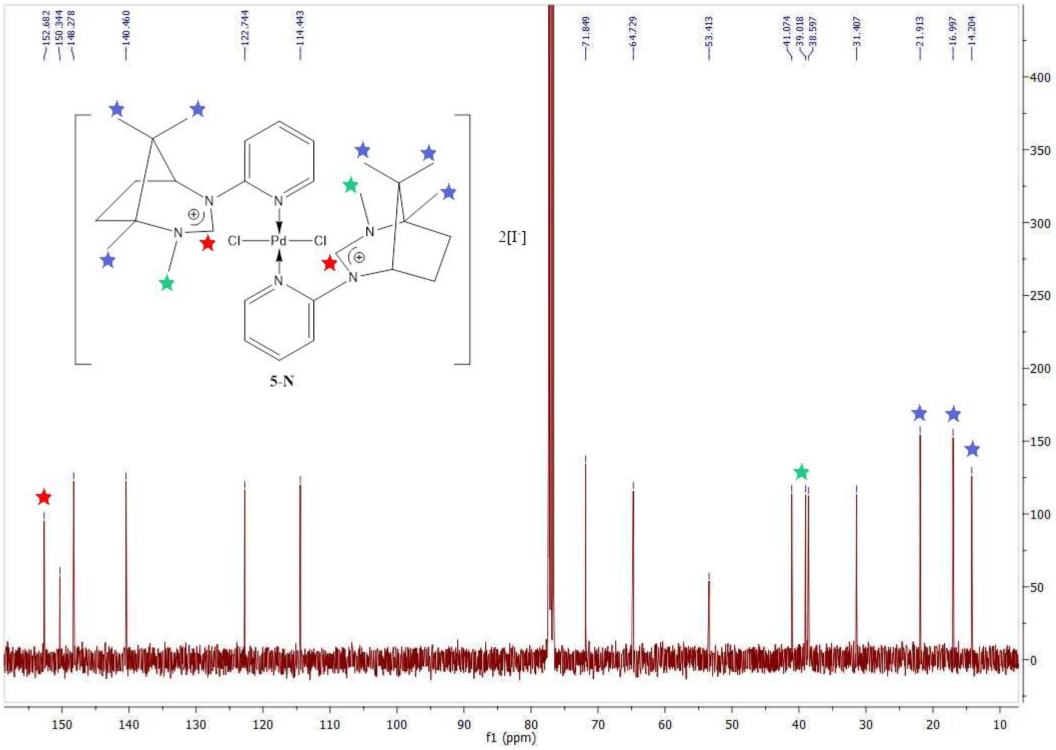
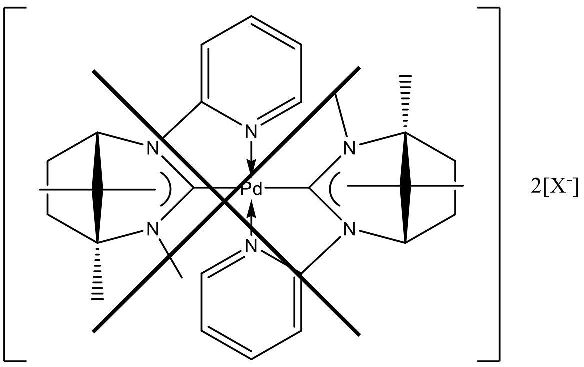


Fig. 2.15: *^{13}C-NMR of complex **5-N**.*

The crude product of first step is employed in the second reaction by changing solvent in THF. With the aim to activate carbene precursor a strong base as KHMDS is used after the mix is cooled down to -78°C. The crude product is characterized by NMR but no evidences for product **5-CN** (fig. 2.16) have been found, in particular in ^{13}C -NMR no carbene resonance is shown which would be the most important evidence for Pd-carbene bond formation. The latter behaviour is probably due to steric encumbrance that not allows NHC coordination.



5-CN

***Fig. 2.16**: expected complex **5-CN**.*

2.10. Ruthenium-NHC complexes employed as hydrogen transfer catalysts

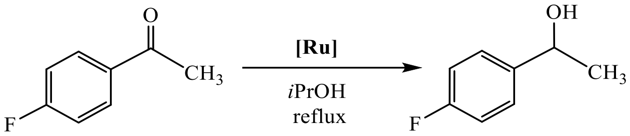
As mentioned in introduction the research group where I have worked in Bologna works on novel Ruthenium-NHC complexes for transfer hydrogenation of polar double bonds.[34] Complexes developed which are studied as catalyst are reported in fig. 2.17.

Ru-1 $R_1 = R_2 = CH_3$;
Ru-2 $R_1 = CH_3$, $R_2 = CH_2CH_2CH_2CH_3$;
Ru-3 $R_1 = CH_3$, $R_2 = CH_2CH_2OH$;
Ru-4 $R_1 = CH_2CH_2CH_2CH_3$, R_2 = 2-pyridine.

Ru-1[X] $R_1 = R_2 = CH_3$; $X = CF_3SO_3^-, Cl^-, BF_4^-$;
Ru-2[X] $R_1 = CH_3$, $R_2 = CH_2CH_2CH_2CH_3$; $X = CF_3SO_3^-$;
Ru-3[X] $R_1 = CH_3$, $R_2 = CH_2CH_2OH$; $X = CF_3SO_3^-$;
Ru-4[X] $R_1 = CH_2CH_2CH_2CH_3$, R_2 = 2-pyridine. $X = CF_3SO_3^-, Cl^-, BF_4^-$.

***Fig. 2.17**: complexes developed for transfer hydrogenation.*

Both **Ru-n** and **Ru-n[CF_3SO_3]** have been employed in transfer hydrogenation of 4-fluoroacetophenone in isopropanol. The isopropanol acts both as the solvent and as the hydrogen donor. Below are reported significant results obtained by research group.[34]



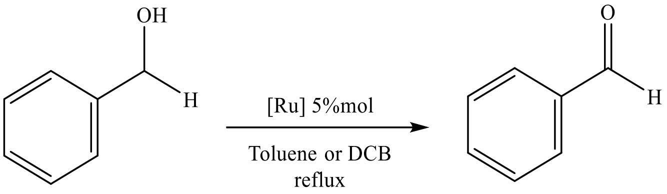
entry	[Ru]	additive	conversion (%) 8 h	conversion (%) 24 h
1	**Ru-1**	---	0	0
2	**Ru-2**	---	0	0
3	**Ru-3**	---	0	0
4	**Ru-4**	---	0	0
5	**Ru-1**	CAN[a]	25	61
6	**Ru-2**	CAN[a]	10	87
7	**Ru-3**	CAN[a]	10	25
8	**Ru-4**	CAN[a]	0	9
9	**Ru-1[CF_3SO_3]**	---	58	93
10	**Ru-2[CF_3SO_3]**	---	9	60
11	**Ru-3[CF_3SO_3]**	---	35	46[g]
12	**Ru-4[CF_3SO_3]**	---	84	>99

***Table 2.2**: Catalytic transfer hydrogenation of 4-fluoroacetophenone. General conditions: Ruthenium complex (5 mol% Ru), iPrOH (3 mL), reflux; conversions determined by ^{19}F NMR spectroscopy; [a]CAN 1 mol equiv. per ruthenium center.*

As showed in table 2.2 the neutral species **Ru-n** do not show any catalytic activity when additive is not used (entries 1 to 4), while adding CAN (entries 5 to 8) they are activated and perform reactions. The best result is achieved by **Ru-2** (entry 6) with a conversion of 87%. Also cationic species **Ru-n[CF_3SO_3]** have been employed in transfer hydrogenation (entries 9 to 12) and best result is achieved by **Ru-4[CF_3SO_3]** which contain a pyridine functionality on NHC. As showed in table 2.2 cationic species are active without using

CAN. Oxidation of catalyst seems to be relevant in catalyst activation and in general better conversions are reached by protonated species than which obtained employing neutral complex with CAN additive (entries 9 to 12 vs. entries 5 to 8).

Catalysts **Ru-1** and **Ru-1[CF$_3$SO$_3$]** have been also investigated in transfer dehydrogenation of benzyl alcohol in toluene or dichlorobenzene and results obtained by research group are reported in table 2.3.



entry	[Ru]	additive	conversion (%) 8 h	conversion (%) 24 h
1	**Ru-1**[a]	CAN[b]	21	34
2	**Ru-1**[a]	---	71	75
3	**Ru-1**[c]	---	16	67
4	**Ru-1**[c]	CAN[b]	0	18
5	**Ru-1[CF$_3$SO$_3$]**[a]	---	60	66
6	**Ru-1[CF$_3$SO$_3$]**[c]	---	72	80
7	**Ru-1[CF$_3$SO$_3$]**[c]	Benzoquinone[d]	>99[e]	

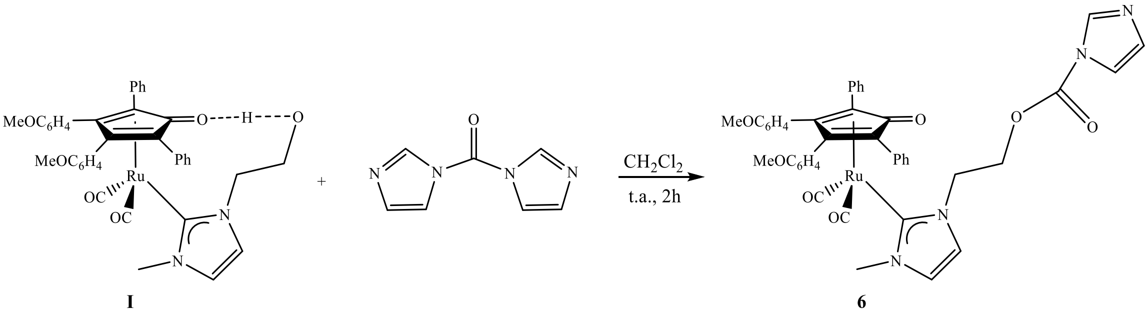
Table 2.3: *Catalytic oxidation of benzyl alcohol to benzaldehyde. General conditions: Ruthenium complex (5 mol% Ru), solvent (3 mL), reflux; conversions determined by GC; [a]solvent: DCB; [b]CAN 1 mol equiv. (dissolved in 1mL of CH$_3$CN) per ruthenium center; [c]solvent: toluene; [d]2 equivalents of benzoquinone per ruthenium center; [e]conversion is complete already after 1h.*

As showed **Ru-1** is active without additive (entry 2 and 3) and better results are achieved in dichlorobenzene at reflux due to higher temperature reached by using this very high boiling point solvent. Lower activity is observed by adding CAN additive (entry 1 and 4), observing a very poor conversion of 18% in toluene (entry 4). Using cationic species **Ru-1[CF$_3$SO$_3$]** higher conversion is surprisingly obtained in toluene (entry 6) than in dichlorobenzene (entry 5). In entry 7 complete conversion is observed after one hour using **Ru-1[CF$_3$SO$_3$]** in toluene adding benzoquinone which acts as hydrogen acceptor.

After those catalytic studies the research group has decided to explore the use of NHC ligand as linker to dendrimer support with the aim to obtain a new heterogenized catalytic system. Functionalized dendrimers are then synthetized and employed in transfer hydrogenation and dehydrogenation reactions and compared with mononuclear species.

2.11. *Synthesis and characterization of the ruthenium tetraarylcyclopentadienone NHC-decorate dendrimers*

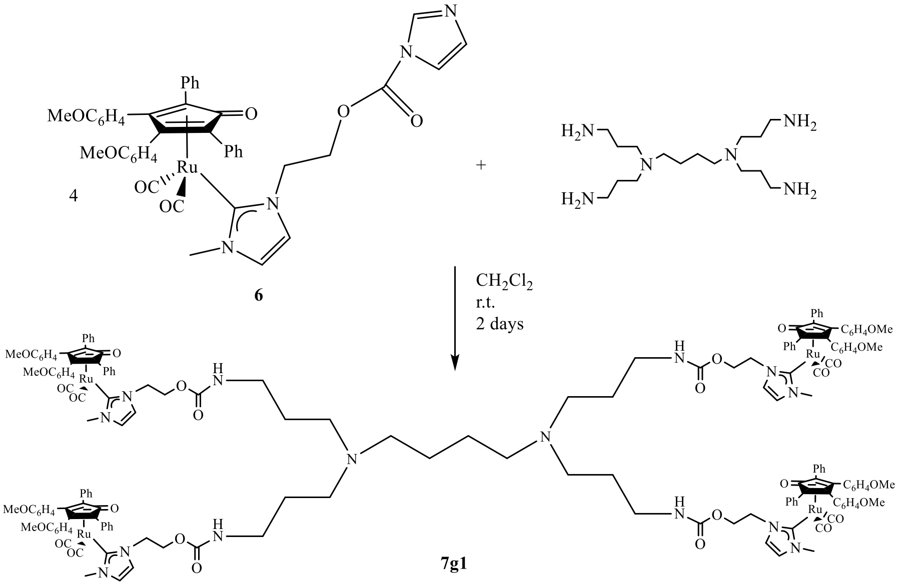
The straightforward preparation of the new CO_2-imidazole functionalized cyclopentadienone NHC ruthenium(0) complex **6** in 84% yield was achieved by reacting **I** with a slight excess of CDI (CDI : **I** = 1.1) in CH_2Cl_2 at room temperature for 2 h as described in Scheme 2.16. Precursor **I** is prepared as previously reported by the group where I have worked in Bologna through a silver trasmetalletion to insert NHC.[51] The product **6** is easily purified by extracting the imidazolium co-product in water (see experimental section).



Scheme 2.16: *Synthesis of CO_2Im functionalized cyclopentadienone NHC ruthenium complex (**6**).*

The air-stable white-brown solid **6** has been fully characterized by analytical and spectroscopic measurements. The NMR spectra in $CDCl_3$ show a pattern similar to that of complex **I**. In particular, the ^{13}C-NMR spectrum shows the downfield shifted resonance of the carbene ($\delta = 174.80$ ppm). Moreover, the imidazole moiety (^1H-NMR $\delta = 8.03$, 7.33, 7.08 ppm, ^{13}C-NMR $\delta = 136.95$, 130.88, 116.97 ppm) displays, as expected, chemical shifts comparable to those of the starting material **CDI**, whereas at 147.89 ppm resonate the C=O group typical of the carbamate (-OC(O)N-). The IR spectrum shows CO stretching bands ($\nu_{CO} = 2007 cm^{-1}$, $1948 cm^{-1}$) consistent with those of **I**, and an absorption, ν(C=O,-O_2CIm): $1768 cm^{-1}$, ascribable to the carbamate group. Further evidences were produced by ESI-MS (see experimental section).

The reaction of a 4.8 fold excess of the complex **6** in CH_2Cl_2 at room temperature with the commercially available poly(propylenimine) dendrimer DAB-dendr-$(NH_2)_4$ leads, after 2 h, to the quantitative formation of DAB-dendr-$[NH(O)CO(NHC)Cp{=}ORu(CO)_2]_4$ (**7g1**) (scheme 2.17).



***Scheme 2.17**: Synthesis of DAB-dendr-$[NH(O)CO(NHC)Cp{=}ORu(CO)_2]_4$ (**7g1**)*

Under the same experimental conditions the CO_2-imidazole group of the ruthenium derivative **6** reacts with the DAB-*dendr*- $(NH_2)_n$ {n = 8, 16, 32, 64}, up to the fifth generation, to form the completely functionalized new dendritic organometallic macromolecules DAB-dendr-$[NH(O)CO(NHC)Cp{=}ORu(CO)_2]_n$ (**7gn**) in quantitative yields (figure 2.18).

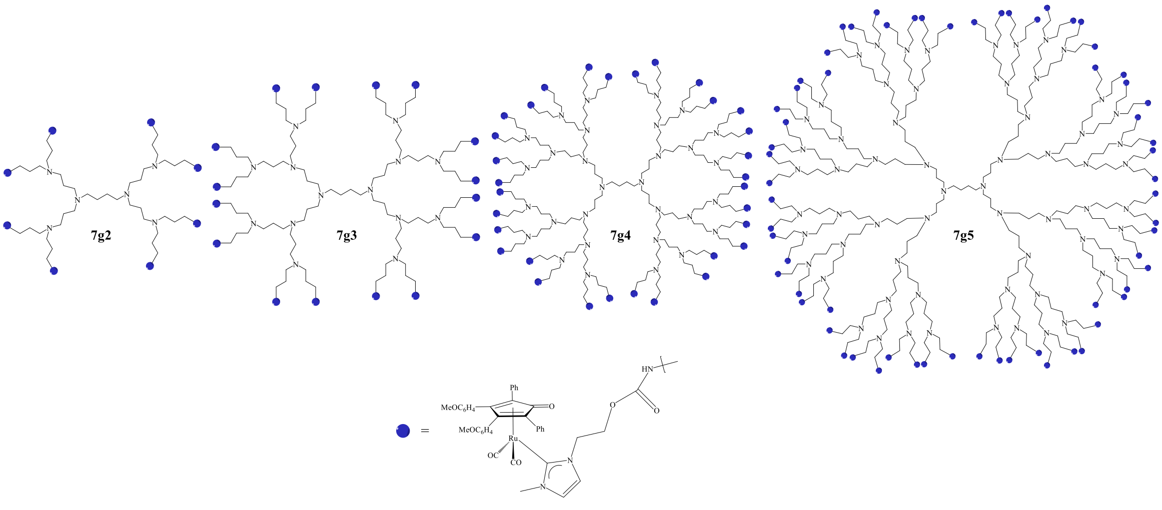


***Fig. 2.18:** Structure of functionalized dendrimers from second to fifth generation: DAB-dendr-$[NH(O)CO(NHC)Cp{=}ORu(CO)_2]_n$ n=8 (**7g2**), n=16 (**7g3**), n=32 (**7g4**) n=64 (**7g5**).*

The excess of **6** and the side products can be removed easily from the crude reaction mixture by water extraction, followed by washing with Et_2O. All five organometallic dendrimers **7gn** were isolated as yellow-brown solids and are air and moisture stable. They are soluble in dichloromethane and THF, slightly soluble in Et_2O, insoluble in hexane and toluene and aqueous solvents.

The dendritic compounds were characterized by ^{1}H-NMR, ^{13}C-NMR and IR spectroscopy and mass spectrometry when possible. The NMR spectra in $CDCl_3$ combine the signals due to the diaminobutane-based poly(propylenimine) framework (^{1}H: four broad multiplets in the range of 3.8–1.3 ppm; ^{13}C: four broad resonances in the range of 63–25 ppm) with those derived from the newly introduced peripheral NHC ruthenium moieties (see figures 2.19, 2.20 and Experimental section).

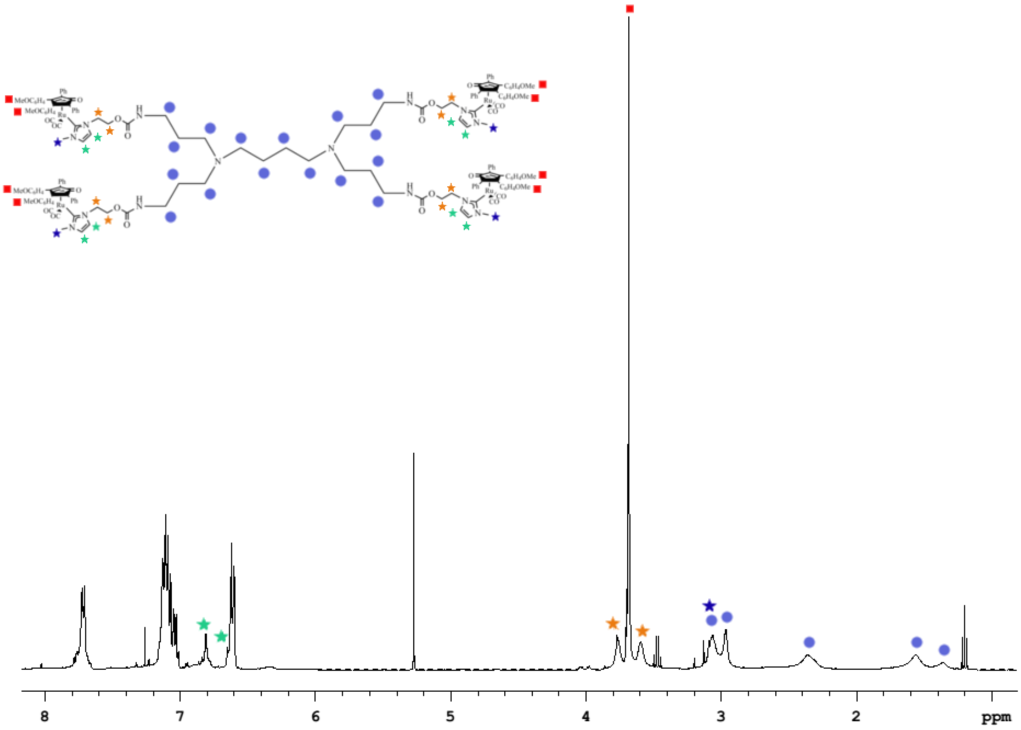


Fig. 2.19: *^{1}H-NMR spectrum($CDCl_3$) of **7g1**.*

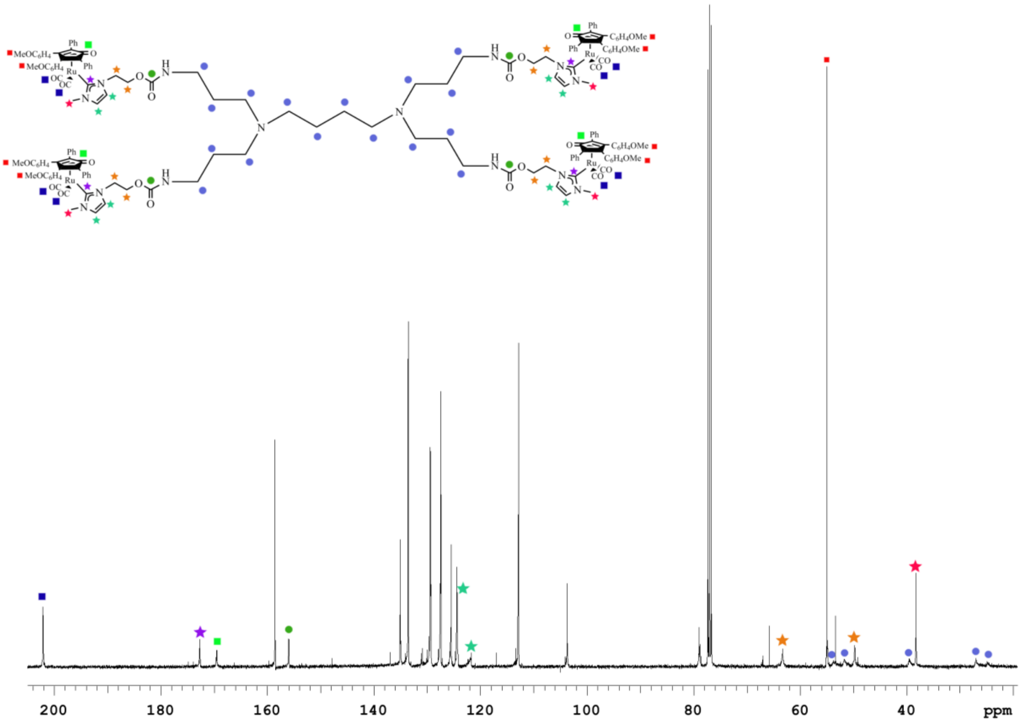


__Fig. 2.20__: ^{13}C-NMR spectrum(CDCl$_3$) of __7g1__.

In addition, evaluation of the signal intensities also provided evidence of the complete polyamines functionalization. Even though all the signals of the proton spectra presented the typical peak broadness of a polymer-like structure, they clearly show that the proton resonances of the two methylene groups in the linker unit (–NHCCH_2CH_2O$_2$CNH–) of the organometallic moieties (at 3.77 and 3.59 ppm) are more shielded than those of complex **6** (4.05 and 3.99 ppm –NHCCH_2CH_2O$_2$CIm).

In the ^{1}H-NMR, the signal of the –NH– belonging to the carbamate linkers residing on the surface of the poly(propylenimine) dendrimer is not easily recognizable due the fact the resonance is expected in the same region of aromatic signals and that hydrogen bonds –NH•••(O)CO– or –NH•••cyclopentadienone become more relevant when the interacting groups get in closer contact, namely with increasing generation. The IR spectra in CH$_2$Cl$_2$ of all five dendritic species show a strong absorption at 1718 cm^{-1} due to stretching bands of carbonyl of carbamate group.

The structures of the first- (n = 4) (**7g1**) generation dendrimers (Scheme 2.17) was confirmed by ESI mass spectroscopy, which showed molecular ions at m/z 3355 [M + Na]$^+$. The higher molecular weight of the upper generations **7g2-5** prevented their mass detection.

The straightforward and quantitative reaction between complex **6** and DAB-*dendr*-$(NH_2)_n$ $\{n = 4, 8, 16, 32, 64\}$ here described (scheme 2.17) provides a valuable route towards the immobilization of –OH functionalized NHC complexes on organic and inorganic amino functionalized supports.

The reaction of **7g1** with a strong acid such as HCF_3SO_3, leads to the quantitative formation of the hydroxycyclopentadienyl tetra-cationic dendrimer **7g1-H** (fig. 2.21), in which Ru(0) is formally oxidized to Ru(II).

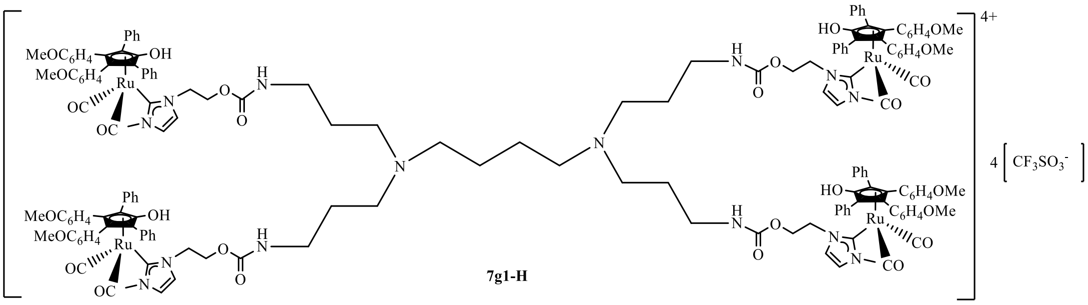


Fig. 2.21. *Structure of the tetra-cationic DAB-dendr-[NH(O)CO(NHC)Cp-OHRu(CO)$_2$]$_4$ (**7g1-H**).*

Infrared spectroscopy provides a convenient technique for monitoring the progress of the protonation in that, in agreement with the reduced back-donation from the metal centre to the carbonyl ligands, ν-C≡O stretch vibrations undergo a significant high-energy shift upon formation of the cationic complex [*e.g.* ν_{CO} = 2006 cm^{-1}, 1947 cm^{-1} (**7g1**), and 2039 cm^{-1}, 1988 cm^{-1} (**7g1-H**)]. It is important to underline that during the protonation stretching bands with intermediate frequency between the neutral and the tetra-cation form (ν_{CO} = 2017 cm^{-1}, 1958 cm^{-1}) appear in the CO region of the IR spectrum. These latter bands are probably associated to the formation of hydrogen bonds between the cationic and the adjacent neutral forms of the ruthenium complex. The change in the coordination from η^4-(cyclopentadienone ligand) to η^5-(hydroxycyclopentadienyl ligand) due to protonation, is further evidenced by ^{13}C-NMR shift of the resonance attributable to the endocyclic carbon involved in the ketone-alcohol transformation [δ 169.56 ppm (C=O, Cp, in **7g1**) vs δ 141.63 ppm (C-OH, Cp, in **7g1-H**)]. Ru-carbene signals are also shifted to higher fields; from δ 172.67 ppm (**7g1**) to δ 160.81 ppm (**7g1-H**) (see Experimental section for more details).

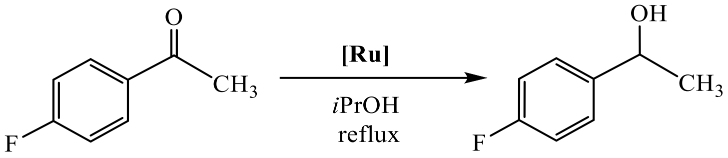
2.12. Catalytic transfer hydrogenation

The Ru-NHC peripherally functionalized dendrimers **7g1** and **7g1-H** were evaluated as catalyst precursors under transfer hydrogenation conditions *i.e.* refluxing *i*-PrOH as hydrogen source employing 4-fluoroacetophenone as model substrate. Catalytic runs were performed to investigate the stability of complexes on the polypropyleneimine dendrimers and eventual dendrimer effect due to close proximity of complexes in connection with the mononuclear species already studied by research group.[34] The role of CAN in the activation of the **7g1** has been investigated, and the catalytic activity of the ruthenium(0) dendrimer **7g1** compared with the corresponding ruthenium(II) cationic complexes **7g1-H**. Results are reported in Table 2.4: in all cases selectivity is complete and conversion corresponds to yield unless otherwise stated.

The neutral dendrimer **7g1** did not present any catalytic activity in the absence of additives (entry 1). In the monomeric neutral form studied by research group the addition of one equivalent of an oxidizing agent such as CAN promote the CO release giving rise to active intermediates as mentioned above in paragraph 2.10.[34] Under the same conditions a detrimental effect of the dendritic form is observed since only 17% conversion is reached after 24 hours. The oxidation state of the metal centre in **7g1** remains the key point in order to activate the catalyst (entry 1 vs. entry 2) as observed previously for mononuclear catalysts (paragraph 2.10).

Further investigation on activation has been carried so neutral **7g1** has been refluxed in isopropanol with 10 eq. per ruthenium center of pyridine as additive (entry 3). After 8 hours of reaction no conversion was found, but after 24 hours an approximate conversion of 20% has been reached. It is supposed that pyridine might have a role in activation of catalyst and help to lose a carbonyl to form an activated species. A similar species to **7g1-H** can be observed by IR analysis of catalyst residues and further investigation are needed to understand the role of a base as additive.

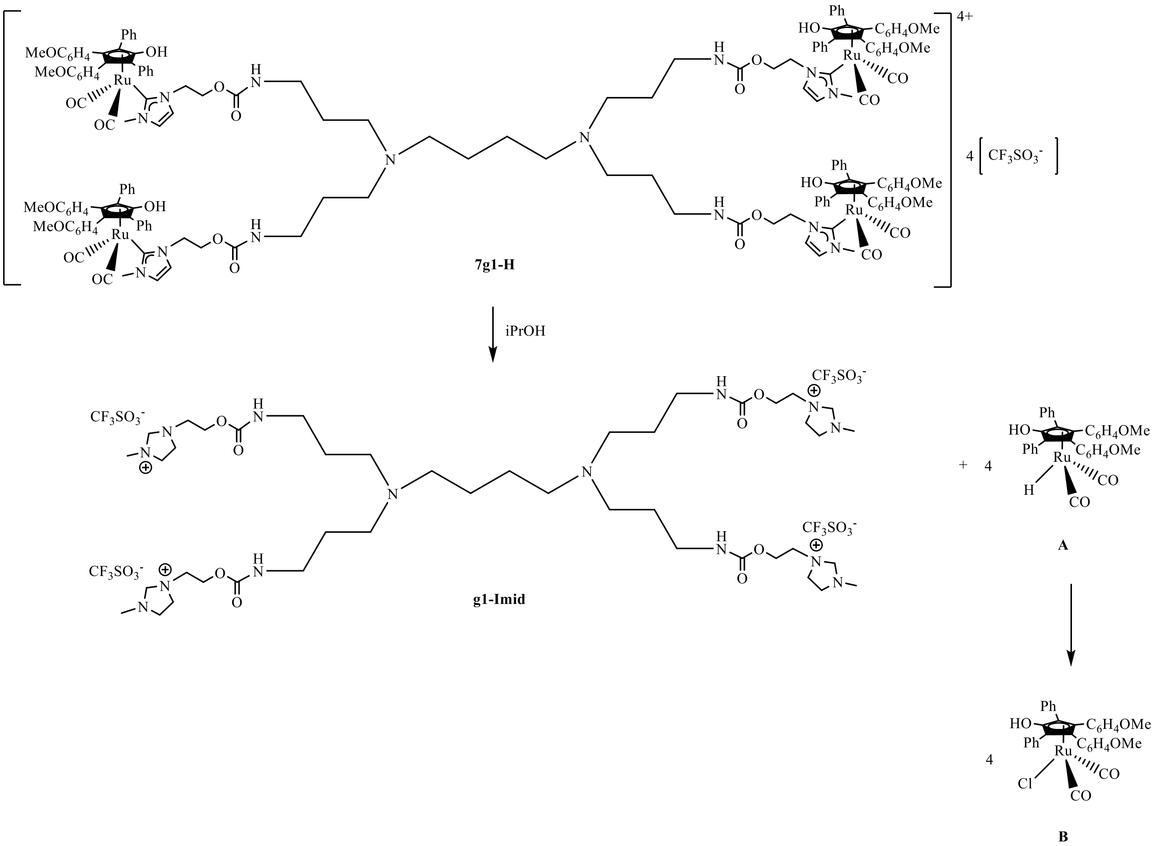
Moving to tetra-cationic **7g1-H** better conversion has been found (entry 4 vs. entries 1 and 2). Looking forward a dendrimer effect the crude of catalytic reaction has been dried under vacuum and washed with hexane in order to remove the organic product. Then it was deeply analyzed by NMR and IR spectroscopy. Form the fraction soluble in organic solvents such as CH_2Cl_2 and $CDCl_3$ a ruthenium complex corresponding to the Shvo catalyst was identified.[52] While the NMR signals arising from dendrimer skeleton and imidazolium salt are found in a water soluble fraction analyzed in D_2O. This means that the better behavior of **7g1-H** as transfer hydrogenation catalyst precursor is not ascribable to dendritic effect since it is explained by the decomposition of the cationic dendrimer under the reaction conditions, which led to the release of a peripheral ruthenium based monomeric active species without the NHC moiety. This behavior, not observed in the case of monomeric complexes studied by the research group, should arise from the structure of the dendrimer itself which contain non innocent nitrogen atoms adjacent to methylenic group susceptible of both acid-base chemistry and dehydrogenation, on the other hand a role of the crowding with put the mononuclear complexes more in contact one to each other can also be taken into consideration. In order to understand the real mechanism which cause the detachment of the complex the reactivity of **7g1-H** is still under investigation.



entry	[Ru]	additive	conversion (%) 8 h	conversion (%) 24 h
1	**7g1**	---	0	0
2	**7g1**	CAN[a]	9	17
3	**7g1**	Pyridine[b]	0	20
4	**7g1-H**	---	>99[c]	>99

Table 2.4: *Catalytic transfer hydrogenation of 4-fluoroacetophenone. General conditions: Ruthenium complex (5 mol% Ru), i-PrOH (3 mL), reflux; conversions determined by ^{19}F NMR spectroscopy; [a]CAN 1 mol equiv. per ruthenium center; [b]10 eq. of pyridine per ruthenium center; [c]conversion is complete already after 6h.*

With the aim to understand the role of the solvent **7g1-H** has been refluxed in *i*-PrOH for 5 hours. The reaction mixture has been cooled under inert atmosphere of argon and the solvent removed under vacuum. ^1H-NMR performed in a J-Young valve NMR tube under inert conditions allow to identify the formation of the hydride derivative [$Ru(CO)_2HCpOH$] (**A**) which, in $CDCl_3$ solution, evolve to the formation of [$Ru(CO)_2ClCpOH$] (**B**) in 24 hours also identified by means of IR spectroscopy.[53] Trace of the Shvo complex[52] (in ^{1}H-NMR the bridging hydride is revealed at -18.46 ppm) were also detected while no signals ascribable to the methylene groups of the dendrimer are observed in this fraction of the crude reaction (soluble in $CDCl_3$). By dissolving the residual in D_2O typical signals of both the dendrimer skeleton and imidazolium salt have been identified as (**g1-Imid**). The decomposition pathway proposed on the light of these results is reported in Scheme 2.18.

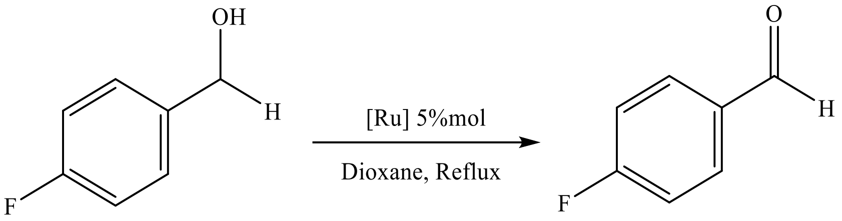


Scheme 2.18: *Detachment of ruthenium hydride complex from the first generation* ***7g1-H.***

Since the solvent *i*-PrOH is supposed to have a crucial role as hydrogen donor in the detachment of the hydroxycyclopentadienyl complex reported in scheme 2.18 we performed the same decomposition test under reflux in toluene for 16 hours. It is important to underline that along all the reaction time an insoluble wax was rising and falling in the solution so we are not able to state the eventual partial solubility of **7g1-H** in toluene at 110°C. Anyway once removed the solvent under vacuum only trace of the crude were soluble in toluene at room temperature. Indeed the ^{1}H-NMR spectrum in Tol-d_8 showed the presence of a small quantity of cyclopentadienone ligand, while no trace of ruthenium complexes or dendrimer signals were detected in this solution. The residual of the crude was completely insoluble in D_2O. On the other hand the great majority of the crude was soluble in $CDCl_3$. ^1H-NMR of this latter solution showed the pattern ascribable both to dendrimer skeleton and to ruthenium complexes. IR spectrum ν(CO) = 2009, 1951 cm^{-1}; ν(C=O) = 1720 cm^{-1} revealed the formation of a neutral species in which both the ruthenium terminal carbonyl and carbamate linker are present. The IR frequencies are slightly higher than those found for **7g1**. This behaviour could be ascribed to the formation of an hydrogen bond between C=O of cyclopentadienyl and a protonated species.[51] From research group's previous experience we could speculate that during the reaction the protons move from the hydroxycyclopentadienyl moiety to the nitrogen atoms available in the dendrimer skeleton. The latter hydrogen maintaining an hydrogen bond with the C=O group of cyclopentadienone. Otherwise in the hypothesis that hydrogen could leave the reaction mixture due to the high temperature as triflic acid leaving the neutral specie **7g1** within the flask the slightly different frequency could be ascribed to an heating-favored rearranged scheme of hydrogen bonds. Both the previously described hypothesis are in agreement with the small shift of the signals due to $-CH_2-$ (broad signals around 3 ppm and 1.6 ppm) from dendrimer if compared with 7**g1**.

2.13. Catalytic oxidation of alcohols

Since the ruthenium complexes look to remain linked to the dendrimer in refluxing toluene we moved to check the behavior of functionalized dendrimers versus mononuclear complexes (described in paragraph 2.10) under oxidative conditions in the transfer dehydrogenation of 4-fluorobenzylalcohol to 4-fluorobenzaldehyde employing aprotic solvents.



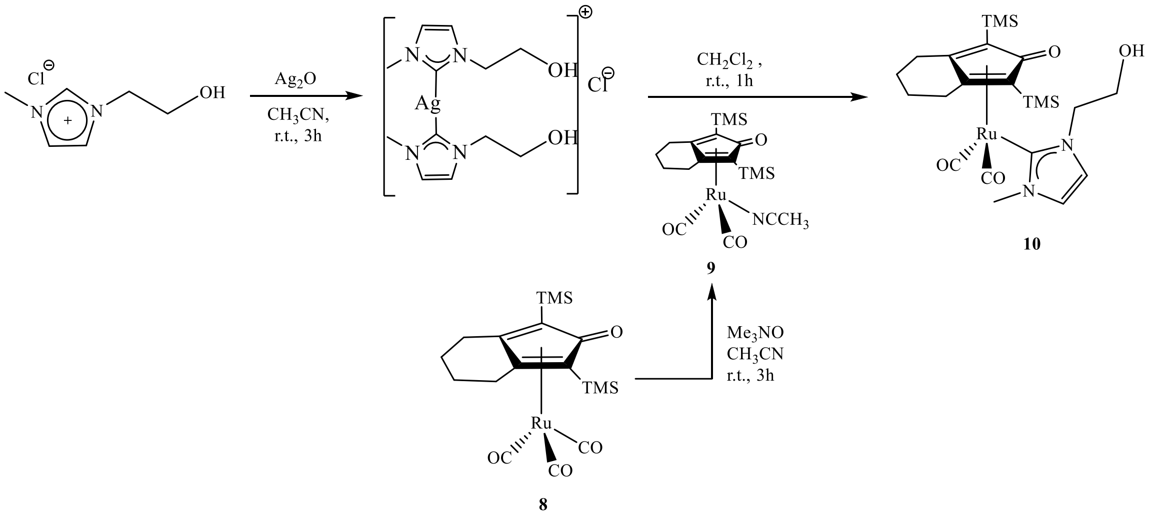
entry	**[Ru]**	additive	conversion (%) 8 h	conversion (%) 24 h
1	**7g1**	---	0	---[a]
2	**7g1**	p-benzoquinone	0	0
3	**7g1-H**	---	11	25
4	**7g1-H**	p-benzoquinone	---[b]	---[b]

***Table 2.5**: Catalytic oxidation of 4-fluorobenzylalcohol to 4-fluorobenzaldehyde. General conditions: Ruthenium complex (5 mol% Ru), dioxane (3 mL), reflux; conversions determined by ^{19}F NMR spectroscopy;[a] stopped after eight hours; [b] fluorotoluene isomers are obtained instead 4-fluoroacetophenone.*

In order to improve catalyst solubility oxidation reactions were performed at reflux in dioxane. Both **7g1** and **7g1-H** have been tested without additive and with benzoquinone as additive. Benzoquinone is a common additive for those class of reaction as hydrogen acceptors and might help the regeneration of active catalyst from reduced form. The neutral species **7g1** has showed no catalytic abilities in both conditions tested (entry 1 and 2) and it is no activated as showed by IR spectra where signals of neutral **7g1** have been found during analysis of catalyst residues. Further investigation on activation of **7g1** are needed to understand how activate that precursor in oxidation reactions. We moved our interest in **7g1-H** and we tried same reactions used for neutral dendrimers (entry 3 and 4). In entry 3 where **7g1-H** without additive is employed we obtained a poor yield of 25 % after 24 hours and from IR and NMR characterization of catalyst residues interestingly no evidences of Shvo catalyst are found. By the entry 4 where benzoquinone is added we expected good results for **7g1-H** as found for mononuclear catalysts in paragraph 2.10 but the reaction give unexpected products which are identified by GC-MS as a mixture of fluorotoluene isomers.

2.14. Synthesis of bis-trimethylsilyl-cyclopentadienone Ru(NHC) complexes and new type of Dendrimer

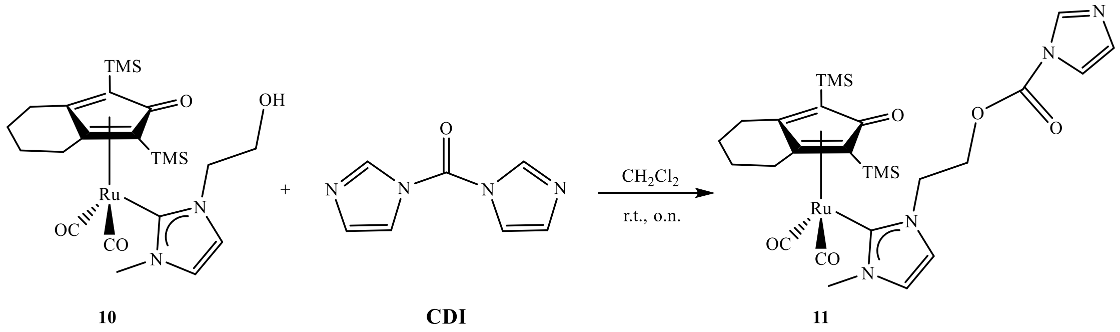
In order to further extend the ligand scope, with the principal aim to change the solubility of the complex in polar solvents such as water the ruthenium triscarbonyl bis(TMS)-substituted cyclopentadienone complex **8**, has been prepared with a novel method that exploit microwave irradiation (see Experimental section); our way of synthesis is indeed by far faster than that reported in the literature.[54] By treating **8** with Me_3NO in CH_3CN, intermediate **9** has been obtained and employed as a precursor for the synthesis of NHC complexes **10** by transmetallation with silver carbene complexes prepared *in situ* (Scheme 2.19).



Scheme 2.19. *Synthesis of dicarbonyl-bis(TMS)-substituted cyclopentadienone Ru(NHC) complexes (**10**).*

Complexes **10** has been completely characterized by IR, ^{1}H and ^{13}C-NMR and ESI-MS (see Experimental section).

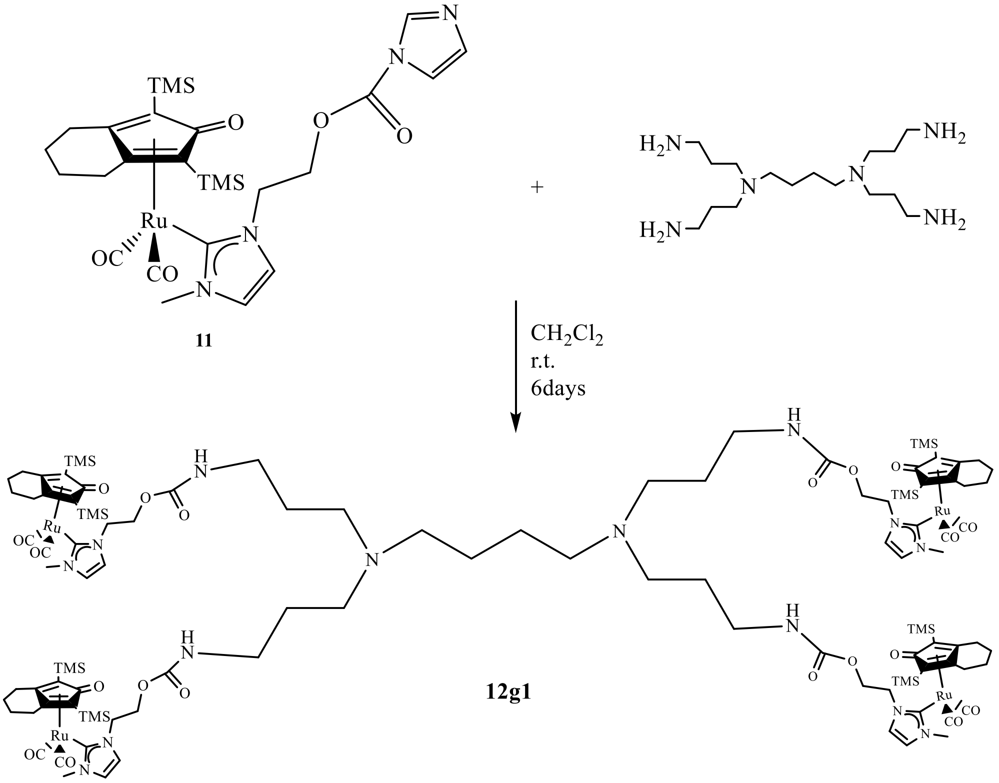
By using **CDI** hydroxy group of **10** is functionalised in the same way used to obtain complex **6** and the same purification previously developed to remove imidazole by-product is employed (scheme 2.20).



Scheme 2.20: *functionalyzation of compex* ***10****.*

The air-stable yellow solid **11** has been fully characterized by IR, ^{1}H-NMR, ^{13}C-NMR and ESI-MS. The NMR spectra in $CDCl_3$ show a pattern similar to that of complex **10**. In particular, the ^{13}C-NMR spectrum shows the downfield shifted resonance of the carbene (δ = 181.03 ppm). Moreover, the imidazole moiety (^{1}H-NMR δ = 8.12, 7.41, 7.09 ppm, ^{13}C-NMR δ = 137.00, 131.04, 117.02 ppm) displays, as expected, chemical shifts comparable to those of the starting material **CDI**, whereas at 148.15 ppm resonate the C=O group typical of the carbamate (-OC(O)N-). The IR spectrum shows CO stretching bands (ν_{CO} = 1998 cm^{-1}, 1935 cm^{-1}) consistent with those of **10**, and an absorption, ν(C=O,-O_2CIm): 1768cm^{-1}, ascribable to the carbamate group. Further evidences were produced by ESI-MS where are shown two signals with m/z of 657 ([M+H]$^+$) and 679 ([M + Na]$^+$).

11 is used to obtain the new functionalised dendrimer **12g1** performing a reaction employing similar condition used for other dendrimers in dichloromethane and using the first generation of poly(propylenimine) dendrimer (scheme 2.21). The new **12g1** is purified with same procedure already used for other dendrimers.



11

12g1

*Scheme. 2.21: synthesis of **12g1**.*

The dendritic compounds were characterized by ^{1}H, ^{13}C NMR and mass spectrometry. The NMR spectra in $CDCl_3$ combine the signals due to the diaminobutane-based poly(propylenimine) framework (^{1}H: four broad multiplets in the range of 3.19–1.41 ppm) with those derived from the newly introduced peripheral NHC ruthenium moieties (see Experimental section).

In addition, evaluation of the signal intensities also provided evidence of the complete polyamines functionalization. Even though all the signals of the proton spectra presented the typical peak broadness of a polymer-like structure, they clearly show that the proton resonances of the two methylene groups in the linker unit ($-NHCC\mathit{H}_2C\mathit{H}_2O_2CNH-$) of the organometallic moieties (at 4.52 and 4.33 ppm) are more shielded than those of complex **11** (4.75 ppm). The IR spectra in CH_2Cl_2 of **12g1** show a strong absorption at 1760 cm^{-1} (s) due to stretching bands of carbonyl of carbamate group.

Unfortunately the new dendrimer **12g1** has shown a solubility close to **7g1**.

3. CONCLUSIONS

This work of thesis has focused on synthesis and applications of NHCs. Concerning my training period at Cardiff University under the supervision of Professor Paul Newman different chiral bicyclic NHCs have been synthetized and preliminary studies on their reactivity have been performed.

Different functionalised NHCs have been obtained starting from camphoric diacid:

- (1R-5S)-N^2-(3-(*tert*-butyl)-2-hydroxybenzyl)-N^4-mesityl-1,8,8-trimethyl-2,4-diazabicyclo[3.2.1]oct-2-en-2-ium tetrafluoroborate (**2c**)
- (1R-5S)-N^2(3-(*tert*-butyl)-2-hydroxybenzyl)-N^4-pyrid-2-yl-1,8,8-trimethyl-2,4-diazabicyclo[3.2.1]oct-2-en-2-ium tetrafluoroborate (**3c**)
- (1R-5S)-N^4-pyrid-2-yl-1,8,8-trimethyl-2,4-diazabicyclo[3.2.1]oct-2-en-2-ium tetrafluoroborate (**4b**)
- (1R-5S)-N^2-methyl-N^4-pyrid-2-yl-1,8,8-trimethyl-2,4-diazabicyclo[3.2.1]oct-2-en-2-ium iodide (**4c**)
- (1R-5S)-N^2-methyl-N^4-(N-methylpyridinium-2-yl)-1,8,8-trimethyl-2,4-diazabicyclo[3.2.1]oct-2-en-2-ium 2[X^-] **(4d**) has been obtained by methylation of **4b** employing trimethyloxonium tetrafluoroborate after a first attempt starting from **4c**.

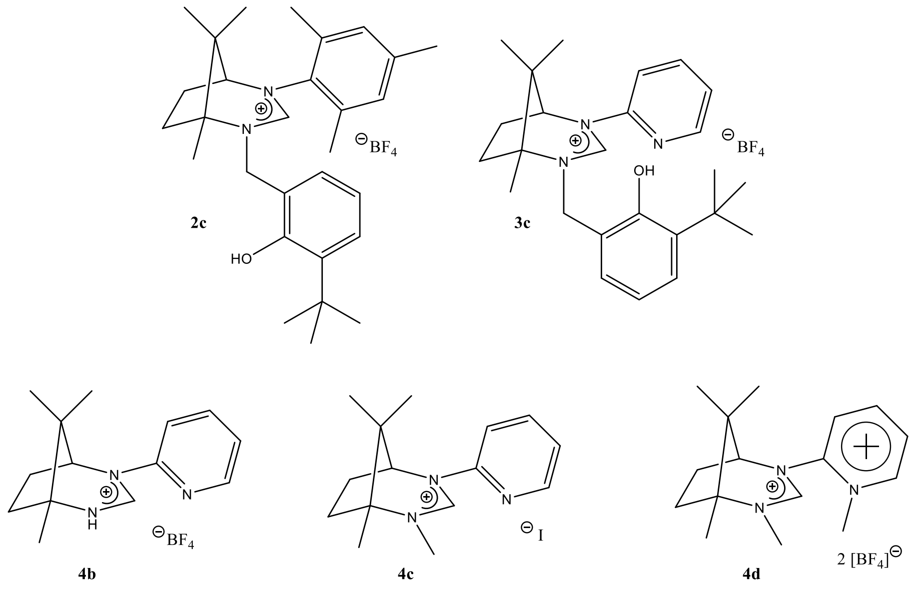
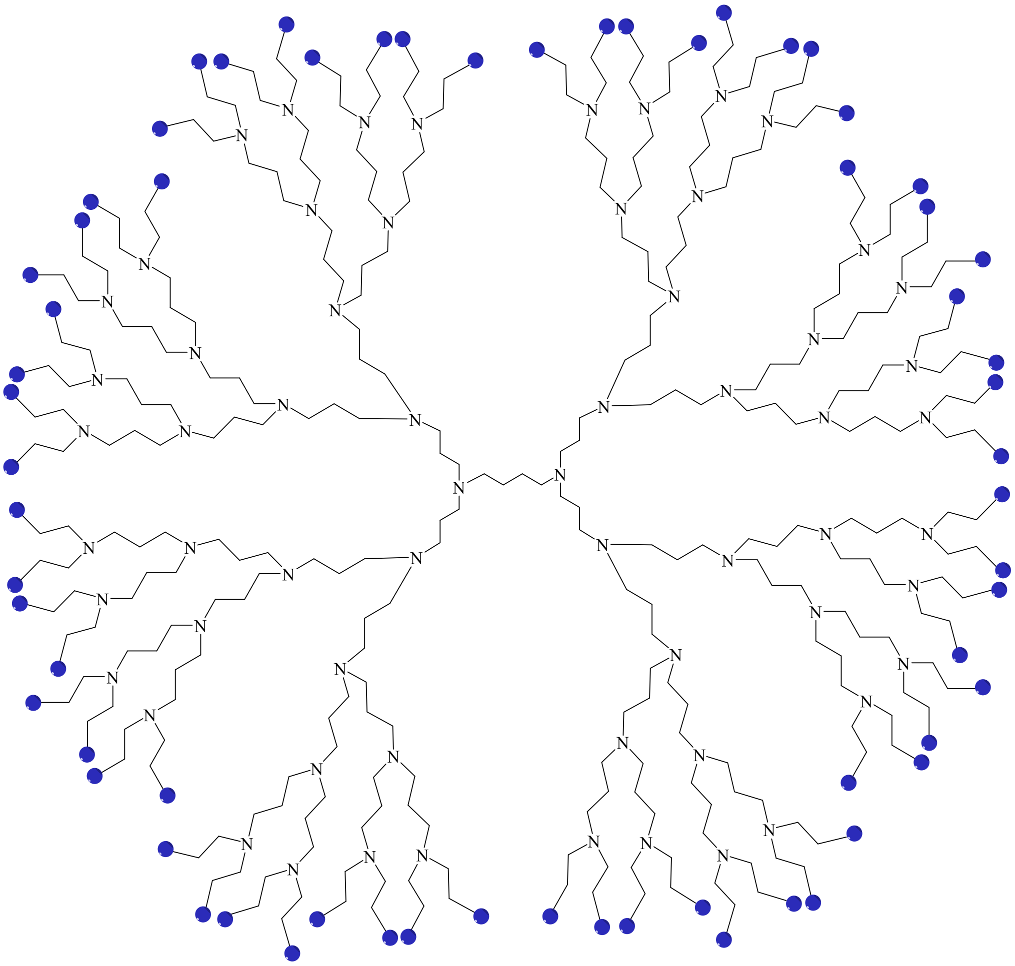


***Fig. 3.1**: precursor of NHCs obtained during my training period at Cardiff University.*

Preliminary studies on reactivity of **2c** with aluminium have been carried but no expected aluminium complex was obtained due to complex reactivity of aluminium. Ligand **3c** was employed with palladium and the pyridine-coordinated complex **5-N** has been obtained, but activation of carbene using a strong base to obtain **5-CN** did not give the Pd-carbene complex needed.

During training period developed in Bologna in the research group of Professor Rita Mazzoni NHCs ruthenium complexes have been immobilized on DAB-*dendr*- $(NH_2)_n$ {*n* = 4, 8, 16, 32, 64}. Functionalised dendrimer **7g1-5** have been obtained exploiting the reactivity between complex **6** and –NH2 periphery groups on dendrimers. The first generation **7g1** has been protonated to obtain **7g1-H**. Both **7g1** and **7g1-H** showed to be active in transfer hydrogenation and dehydrogenation although presenting a detrimental dendrimer effect if compared with the mononuclear complexes.



7g5

● = $[NH(O)CO(NHC)Cp{=}ORu(CO)_2]$

{NHC=[-CH_2CH_2-3-CH_3-imidazol-ilidene]; Cp=O =[3,4-$(CH_3O\text{-}C_6H_4)_2$-2,5-$Ph_2(\eta^4\text{-}C_4CO)$]}

***Fig. 3.2**: fifth generation of functionalised dednrimers **7g5**.*

Furthermore a new class of dendrimers **12g1** has been obtained employing the complex **11** which contain a bis(TMS)-substituted cyclopentadienone ligand. The novel functionalized dendrimers did not show any significant difference in solubility when compared with the congeners **7gn**.

4. EXPERIMENTAL SECTION

4.1. General Procedure

All reactions were performed under inert atmosphere (argon or nitrogen) with exclusion of moisture from reagents and glassware using standard techniques for manipulating airsensitive compounds. All Schlenk flasks were flame dried with heat gun and argon or nitrogen flushed.

4.1.1. Cardiff University

Solvents: chloroform ($CHCl_3$), Toluene and tetrahydrofurane (THF) were dried and distilled prior to use. Other solvents such as dichloromethane, 2-propanol (*i*PrOH), methanol, ethanol, diethyl ether, hexane, heptane, acetonitrile, $CDCl_3$, D_2O have been employed without further purification. Deuterated benzene (C_6D_6) is degassed and dried prior to use. Reagents: camphoric diacid, sulfuric acid, sodium azide, magnesium sulfate, sodium sulfate, sodium hydroxide, $PdCl_2$, $PdCl_2(MeCN)_2$, sodium acetate, KHDMS, 2-bromo-1,2,3-trimethylbenzol, sodium tert-butanoate, (±)-BINAP, 2-bromopyridine, 3-tert-buthylsalicylaldehyde, sodium borohydride, hydrochloric acid, triethyl orthoformate, NH_4BF_4, Al(*i*PrO)$_3$, $Al(Me)_3$ and $AlBr_3$ have been employed as purchased. $Pd_2(dba)_3$ has been prepared following a procedure reported in literature.[55] The prepared derivatives were characterized by spectroscopic methods. The ^{1}H and ^{13}C NMR spectra were recorded on a Jeol Eclipse 300 MHz or Bruker 400, 500 or 600 MHz spectrometers and referenced to tetramethylsilane ($\delta = 0$ ppm). Mass spectra were acquired by Cardiff University Mass Service.

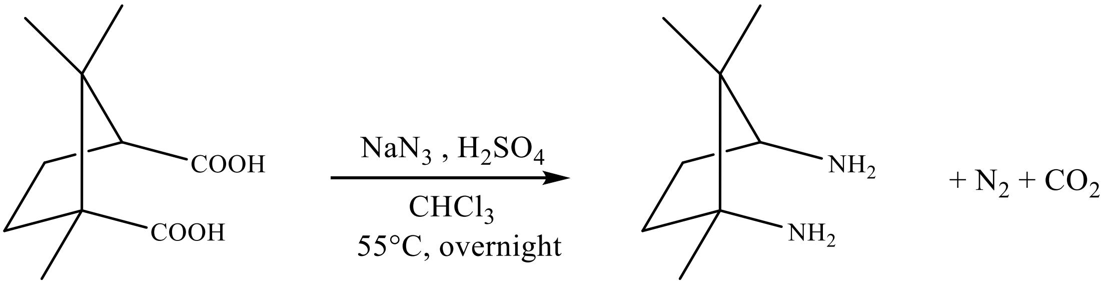
4.1.2. Bologna

Solvents: dichloromethane (CH_2Cl_2), diethyl ether (Et_2O), acetonitrile (CH_3CN), Toluene were dried and distilled prior to use. Acetone has been degassed and stored under inert atmosphere on molecular sieves. Other solvents such as 2-propanol (*i*PrOH), heptane, hexane, $CDCl_3$, D_2O, Toluene-d$_8$ (Sigma Aldrich) have been employed without further purification. Reagents: triruthenium-dodecacarbonil ($Ru_3(CO)_{12}$) (Strem), silver oxide, 1-methylimidazole, 1-chloroethanol, 1,3 diphenylacetone, 4,4'dimethoxybenzil (Alfa Aesar), 4-fluoroacetophenone, trifluoromethanesulfonic acid, 1,1'-carbonyldiimidazole (CDI) and DAB-dendr-(NH_2)$_n$ {n = 4, 8, 16, 32, 64}, cerium ammonium nitrate (CAN) (Sigma Aldrich) have been employed as purchased. 1-methyl-3-(2-

hydroxyethyl)imidazolium chloride, 3,4-Bis(4-methoxyphenyl)-2,5-diphenylcyclopenta-2,4-dienone, dicarbonyl(η^4-3,4-bis(4-methoxyphenyl)-2,5-diphenylcyclopenta-2,4-dienone) ruthenium dimer, dicarbonyl-η^4-3,4-bis(4-methoxyphenyl)-2,5-diphenylcyclopenta-2,4-dienone)-1-methyl-3-(2-hydroxyethyl-imidazol-2-ylidene)ruthenium, have been prepared as previously reported.[56] The prepared derivatives were characterized by spectroscopic methods. The NMR spectra were recorded using Varian Inova 300 (^{1}H, 300.1; ^{13}C, 75.5 MHz), Varian Mercury Plus VX 400 (^{1}H, 399.9; ^{13}C, 100.6 MHz), Varian Inova 600 (^{1}H, 599.7; ^{13}C, 150.8 MHz) spectrometers at 298 K; chemical shifts were referenced internally to residual solvent peaks. Full ^{1}H- and ^{13}C-NMR assignments were done, when necessary, by gHSQC and gHMBC NMR experiments using standard Varian pulse sequences. Infrared spectra were recorded at 298 K on a Perkin-Elmer Spectrum Two FT-IR spectrophotometer. ESI-MS spectra were recorded on Waters Micromass ZQ 4000 with samples dissolved in MeOH or CH_3CN. GC analysis have been performed on an Agilent Technologies 7890A Gas Cromatograph provided with a capillary column Agilent 19091J-433 HP-5 (5%phenyl)-methylpolysiloxane, 30 m x 0.320 mm x 0.25 μm.

Elemental analyses were performed on a Thermo-Quest Flash 1112 Series EA instrument. The conversions were monitored by ^{1}H-NMR ^{19}F-NMR.

4.2. Synthesis of (1R,3S)-1,3-Diamino-1,2,2-trimethylcyclopentane (1)



1

Scheme 4.1

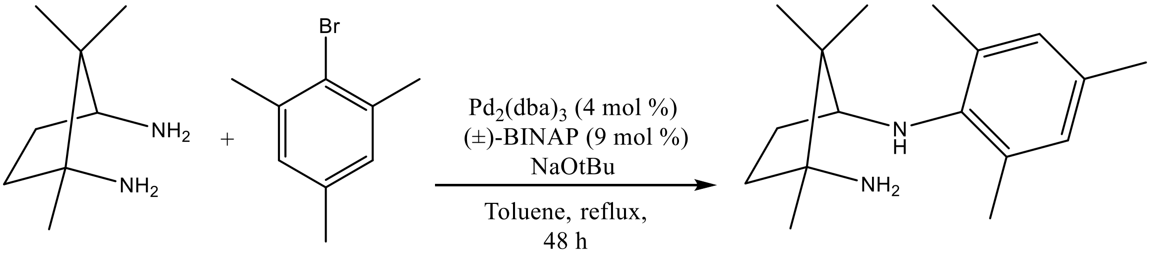
(1R, 3S)-camphoric acid (20.0 g, 99.88 mmol) is dissolved in 500 mL of $CHCl_3$ and 50 ml of H_2SO_4 in a dried three necked three litres flask. The mix is warmed to 55°C then NaN_3 (19.5 g, 300 mmol) is added portion-wise over four hours. Reaction runs overnight. Water (1 l) is added and aqueous phase is made strongly basic by NaOH and then extracted with

CH_2Cl_2 three times. Trace of water is removed from organic phase using anhydrous Na_2SO_4 then solvent is evaporated. A yellow oil is obtained and dissolved in Et_2O that is evaporated. A yellow pale solid is obtained in 63% yield and is identified as (1R,3S)-1,3-Diamino-1,2,2-trimethylcyclopentane (**1**) by ^{1}H-NMR.

^{1}H-NMR (400.1 MHz, $CDCl_3$):

δ (ppm): 2.99 (dd, J= 6.9 Hz, 8.5 Hz, 1H, CH), 2.03 (m, 1H, CH_2), 1.63 (m, 2H, CH_2), 1.44 (br, 4H, NH_2), 1.30 (m, 1H, CH_2), 1.02 (s, 3H, CH_3), 0.81 (s, 3H, CH_3), 0.79 (s, 3H, CH_3).

4.3. Synthesis of (1S, 3R)-N^1-mesityl-2,2,3-trimethylcyclopentan-1,3-diamine (2a)



1

2a

Scheme 4.2

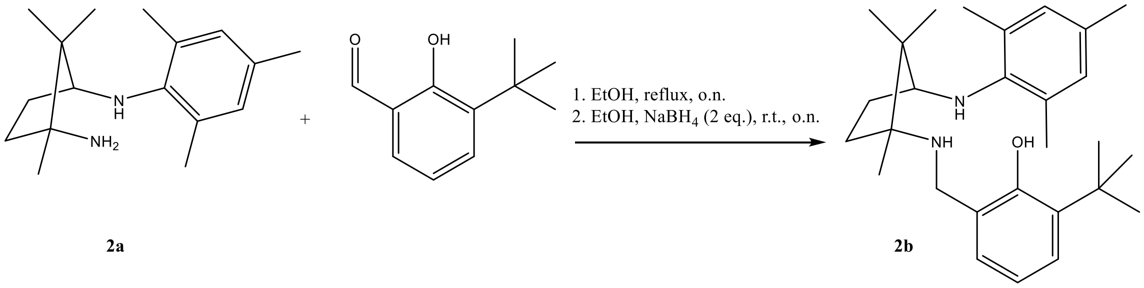
$Pd_2(dba)_3$•CH_3Cl (0.30 g, 0.29 mmol, 4 mol %), (±)-BINAP (0.4 g, 0.64 mmol, 9 mol %) and NaOtBu (2.06 g, 21.46 mmol) are dissolved in 350 ml of dried toluene under inert atmosphere and stirred for 20 minutes at room temperature in a 500 ml round bottomed flask fitted with a condenser. (1R,3S)-1,3-Diamino-1,2,2-trimethylcyclopentane (**1**) (1.00g, 7.03 mmol) and 2-bromo-1,3,5-trimetylbenzol (1.07 ml, d = 1.301 g/ml, 6.99 mmol) are added, then the solution is warmed to 110°C for 48h.

Crude product is filtered through a silica plug, that is eluted using toluene and then a mix dichloromethane : methanol of 9:1 until all product is recovered. Solvents are evaporated and the solid obtained is dissolved in dichloromethane. Organic phase is extracted with a solution of HCl 37 % V/V in water. A solution of NaOH 12 M in water is added carefully to water phase cooled to 0˚C until pH is 14. Water phase is extracted five times with dichloromethane and organic phase is dried using anhydrous Na_2CO_3, then solvent is evaporated. Solid is dissolved in n-eptane and mix is filtered to remove solid impurities, n-eptane is evaporated and a yellow oil is obtained in 70% yield. It is characterized as **2a** by ^{1}H-NMR.

^{1}H-NMR (400.1 MHz, $CDCl_3$):

δ (ppm): 6.78 (s, 2H, CH_{mes}), 4.24 (br, 1H, H-N^1), 3.42 (dd, J= 4.9 Hz, 7.7 Hz, 1H, CH), 2.25 (s, 6H, m-$CH_{3\ mes}$), 2.21 (s, 3H, p-$CH_{3\ mes}$), 1.86 (m, 1H, CH_2), 1.67 (m, 2H, CH_2), 1.48 (m, 1H, CH_2), 1.11 (s, 3H, CH_3), 1.08 (s, 3H, CH_3), 0.94 (s, 3H, CH_3).

4.4. *(1R,3S)-N^1-(3-(tert-butyl)-2-hydroxybenzyl)-N^3-mesityl-1,2,2-trimethylcyclopentan-1,3-diamine (2b)*



Scheme 4.3

In a schlenk under inert atmosphere (1S, 3R)-N^1-mesityl-2,2,3-trimethylcyclpentan-1,3-diamine (**2a**) (0.777 g, 2.98 mmol) is dissolved in EtOH (20.0 ml) and 3-*tert*-butylsalicylaldehyde (0.531 g, 0.506 ml, 2.98 mmol) is added to the stirred mix, then reaction runs under reflux overnight.

Reaction mix is cooled down to room temperature, then $NaBH_4$ (0.225g, 5.96 mmol, 2 eq.) is added and reaction runs overnight at room temperature. Reaction is quenched with HCl, that is neutralized using $NaHCO_3$. Crude mix is filtered and solvent evaporated, the solid obtained is dissolved using both CH_2Cl_2 (10 ml) and water (10 ml), CH_2Cl_2 is collected then water phase is extracted using CH_2Cl_2 (3x15 ml). The organic phase containing the product (all CH_2Cl_2 fractions) is dried using Na_2CO_3 anhydrous, then the solvent is evaporated. Product **2b** is obtained in 90% yield and characterized by ^{1}H-NMR and ESI-TOF.

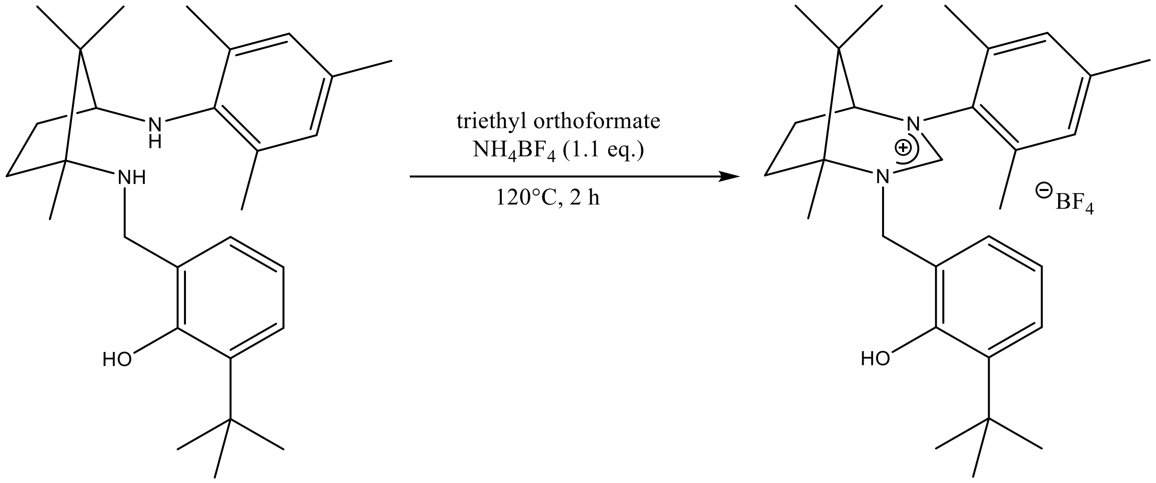
^{1}H-NMR (400.1 MHz, $CDCl_3$):

δ (ppm): 7.20 (m, 1H, CH_{aryl}), 6.89 (m, 1H, CH_{aryl}), 6.80 (s, 2H, CH_{mes}), 6.73 (m, 1H, CH_{aryl}), 3.94 (m, 2H, N-CH_2-), 3.48 (m, 16.47 Hz, 1H, CH), 2.27 (s, 6H, m-$CH_{3\ mes}$), 2.22

(s, 3H, p-$CH_{3\,mes}$), 1.95 (m, 2H, CH_2), 1.65 (m, 1H, CH_2), 1.49 (m, 1H, CH_2), 1.43 (s, 9H, *t*-Butyl), 1.20 (s, 3H, CH_3), 1.09 (s, 3H, CH_3), 1.08 (s, 3H, CH_3).

ESI-TOF (m/z) (+): 423 $[M+H]^+$.

4.5. Synthesis of (1R-5S)-N^2-(3-(tert-butyl)-2-hydroxybenzyl)-N^4-mesityl-1,8,8-trimethyl-2,4-diazabicyclo[3.2.1]oct-2-en-2-ium tetrafluoroborate (2c)



2b **2c**

Scheme 4.4

In a schlenk under inert atmosphere **2b** (1.129 g, 2.67 mmol) is dissolved in triethyl orthoformate (10 ml) and NH_4BF_4 (0.308 g, 2.94 mmol, 1.1 eq.) is added to reaction mixture under stirring. The reaction mixture is warmed to 120°C for two hours. An orange oil precipitates then triethyl orthoformate is evaporated under vacuum. Diethyl ether is added to wash the product with help by sonication, so solvent is evaporated and product turns solid. Product **2c** is obtained in 61% yield and characterized by ^{1}H-NMR, ^{19}F-NMR and ESI-TOF.

^{1}H-NMR (400.1 MHz, $CDCl_3$):

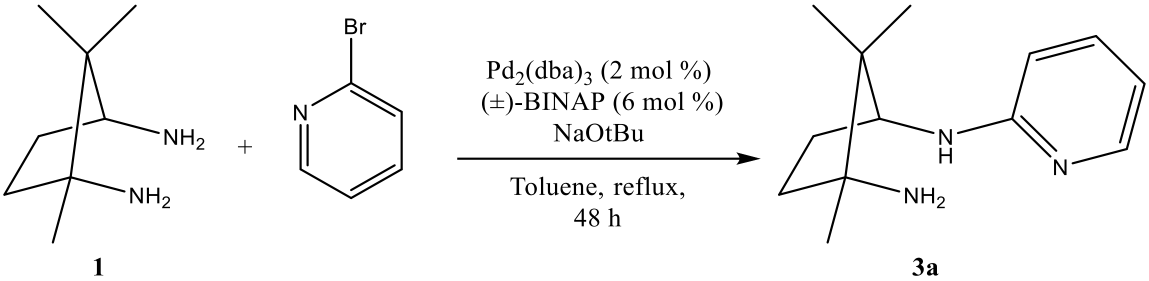
δ (ppm): 7.69 (s, 1H, N-CH-N) 7.30 (m, 1H, CH_{aryl}), 7.09 (m, 1H, CH_{aryl}), 6.95 (s, 2H, CH_{mes}), 6.90 (m, 1H, CH_{aryl}), 4.96 (m, 1H, N-CH_2-) 4.73 (m, 1H, N-CH_2), 6.23 (s, 1H, OH) 3.44 (m, 1H, CH), 2.74 (m, 1H, CH_2), 2.29 (s, 3H, p-$CH_{3\,mes}$), 2.27 (s, 6H, m-$CH_{3\,mes}$), 2.17-2.02 (m, 3H, CH_2), 1.39 (s, 9H, *t*-Butyl), 1.32 (s, 3H, CH_3), 1.31 (s, 3H, CH_3), 1.16 (s, 3H, CH_3).

^{19}F-NMR (376.50 MHz, D_2O):

δ (ppm): -148.19

ESI-TOF (m/z) (+): 433 $[M]^+$.

4.6. Synthesis of (1S, 3R)-N^1-pyrid-2-yl-2,2,3-trimethylcyclopentan-1,3-diamine (3a)



Scheme 4.5

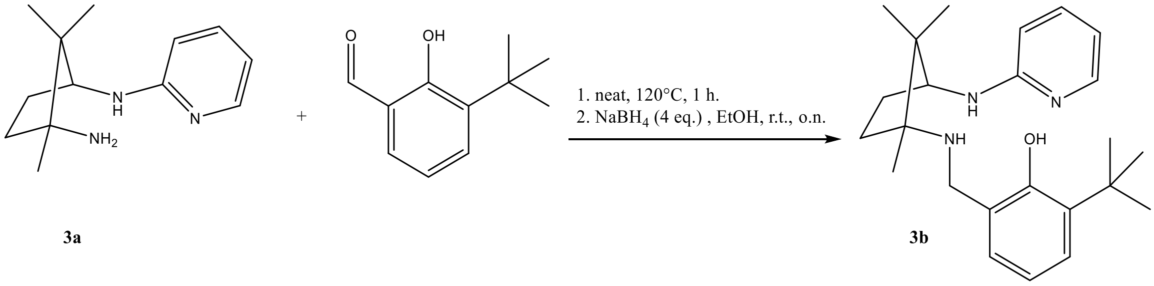
$Pd_2(dba)_3 \cdot CH_3Cl$ (0.11 g, 0.11 mmol, 2 mol %), (±)-BINAP (0.3 g, 0.48 mmol, 6 mol %) and NaOtBu (2.00 g, 21.46 mmol) are dissolved in 125 ml of dried toluene under inert atmosphere and stirred for 20 minutes at room temperature in a 250 ml round bottomed flask fitted with a condenser. (1R,3S)-1,3-Diamino-1,2,2-trimethylcyclopentane (**1**) (1.00g, 7.03 mmol) and 2-bromopyridine (0.7 ml, d = 1.657 g/ml, 7.34 mmol) are added, then the solution is warmed to 110°C for 48h.

Crude product is filtered through a silica plug, that is eluted using toluene and then a mix dichloromethane : methanol of 9:1 until all product is recovered. Solvents are evaporated and the solid obtained is dissolved in dichloromethane. Organic phase is extracted with a solution of HCl 37 % V/V in water. A solution of NaOH 12 M in water is added carefully to water phase cooled to 0˚C until pH is 14. Water phase is extracted five times with dichloromethane and organic phase is dried using anhydrous Na_2CO_3, then solvent is evaporated. Solid is dissolved in n-eptane and mix is filtered to remove solid impurities, n-eptane is evaporated and a yellow oil is obtained in 90% yield. It is characterized as **3a** by ^{1}H-NMR.

^{1}H-NMR (400.1 MHz, CDCl$_3$):

δ (ppm): 8.01 (m, 5.03 Hz, 1H, CH$_{pyr}$), 7.30 (m, 1H, CH$_{pyr}$), 6.43 (m, 7.04 Hz, 1H, CH$_{pyr}$), 6.31 (m, 1H, CH$_{pyr}$), 6,04 (m, 1H, H-N^1), 4.00 (m, 1H, CH), 2.22 (m, 1H, CH$_2$), 1.75 (m, 1H, CH$_2$), 1.55 (m, 2H, CH$_2$), 1.11 (s, 3H, CH$_3$), 0.91 (s, 6H, gem-CH$_3$).

4.7. Synthesis of (1R,3S)-N^1-(3-(tert-butyl)-2-hydroxybenzyl)-N^3-pyrid-2-yl-1,2,2-trimethylcyclopentan-1,3-diamine (3b)



Scheme 4.6

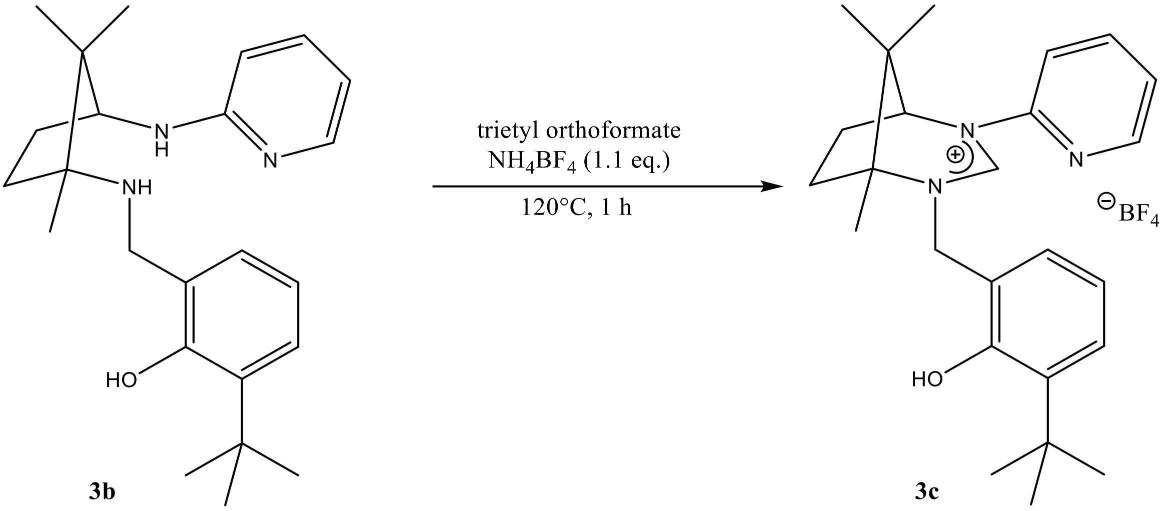
In a 100 ml round bottomed flask set with a drying trap and under inert atmosphere (1S, 3R)-N^1-pyrid-2-yl-2,2,3-trimethylcyclopentan-1,3-diamine (**3a**) (0.500 g, 2.28 mmol) is warmed at 70°C for 30’, when the viscous oil is melted 3-*tert*-butylsalicylaldehyde (0.406 g, 0.386 ml, 2.28 mmol) is added, then it is warmed to 120°C for one hour. Crude product is cooled down to room temperature and it is dissolved in 10 ml of ethanol, then NaBH$_4$ (0.346 g, 9.12 mmol, 4 eq.) is added and reaction runs overnight at room temperature. Reaction is quenched with HCl, that is neutralized using NaHCO$_3$. Crude mix is filtered and solvent evaporated, the solid obtained is dissolved using both DCM and water, then water phase is extracted using DCM (3x15 ml). The organic phase is dried using Na$_2$CO$_3$ anhydrous, then the solvent is evaporated. Product is obtained in 70% yield and characterized as **3b** by ^{1}H-NMR and ESI-TOF.

^{1}H-NMR (400.1 MHz, CDCl$_3$):

δ (ppm): 8.07 (m, 1H, CH$_{pyr}$), 7.40 (m, 1H, CH$_{pyr}$), 7.24 (m, 1H, CH$_{aryl}$), 6.93 (m, 1H, CH$_{aryl}$), 6.77 (m, 1H, Ch$_{aryl}$) 6.55 (m, 1H, CH$_{pyr}$), 6.44 (m, 1H, CH$_{pyr}$), 4.61 (m, 1H, H-N), 4.26 (m, 1H, CH), 3.98 (m, 2H, N-CH$_2$-), 2.28 (m, 1H, CH$_2$), 1.96 (m, 1H, CH$_2$), 1.76 (m, 2H, CH$_2$), 1.48 (s, 9H, t-Butyl), 1.31 (s, 3H, CH$_3$), 1.04 (s, 3H, CH$_3$) 1.00 (s, 3H, CH$_3$).

ESI-TOF (m/z) (+): 381 $[M+H]^+$.

4.8. Synthesis of (1R-5S)-N^2(3-(tert-butyl)-2-hydroxybenzyl)-N^4-pyrid-2-yl-1,8,8-trimethyl-2,4-diazabicyclo[3.2.1]oct-2-en-2-ium tetrafluoroborate (3c)



Scheme 4.7

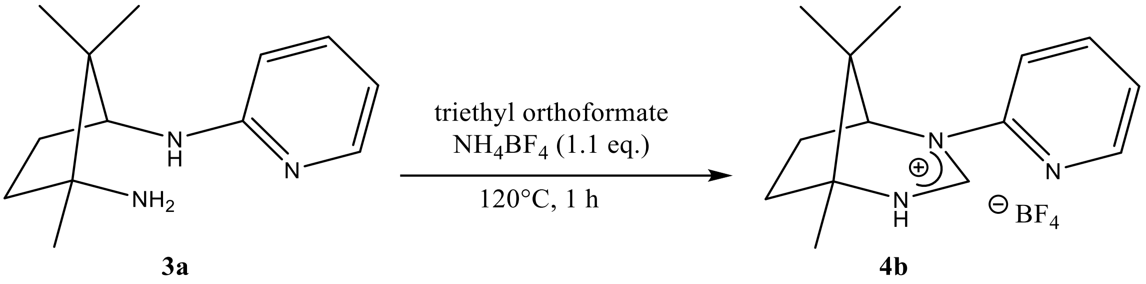
In a schlenk under inert atmosphere **3b** (0.599 g, 1.57 mmol) is dissolved in trietylorthoformate (10 ml) and NH_4BF_4 (0.181 g, 1.73 mmol, 1.1 eq.) is added to reaction mixture under stirring. The reaction mixture is warmed to 120°C for 1 hour. An orange oil precipitates then triethyl orthoformate is evaporated under vacuum. Diethyl ether is added to wash the product with help by sonication, so solvent is evaporated and product turns solid. It is dissolved in isopropanol at reflux for 30 minutes and cooled down to room temperature slowly then waste precipitate and product which remain in solution is recovered. Product **3c** is obtained in quantitative yield and characterized by ^{1}H-NMR and ESI-TOF.

^{1}H-NMR (400.1 MHz, $CDCl_3$):

δ (ppm): 8.91 (s, 1H, N-CH-N), 8.77 (m, 1H, CH_{aryl}), 8.40 (m, 1H, CH_{pyr}), 7.90 (m, 1H, CH_{pyr}), 7.66 (m, 1H, CH_{aryl}), 7.31 (m, 1H, CH_{aryl}), 7.11 (m, 1H, CH_{pyr}), 6.95 (m, 1H, CH_{pyr}), 5.06-4.76 (m, 2H, N-CH_2-), 4.03 (m, 1H, CH), 2.56 (m, 1H, CH_2), 2.39-1.81 (m, 3H, CH_2), 1.41 (s, 9H, t-butyl), 1.33 (s, 3H, CH_3), 1.25 (s, 3H, CH_3), 1.20 (s, 3H, CH_3).

ESI-TOF (m/z) (+): 392 $[M]^+$.

4.9. *Synthesis of (1R-5S)-N^4-pyrid-2-yl-1,8,8-trimethyl-2,4-diazabicyclo[3.2.1]oct-2-en-2-ium tetrafluoroborate (4b)*



Scheme 4.8

In a schlenk under inert atmosphere **3a** (1.247 g, 5.69 mmol) is dissolved in trietylorthoformate (20 ml) and NH_4BF_4 (0.656 g, 6.25 mmol, 1.1 eq.) is added to reaction mixture under stirring. The reaction mixture is warmed to 120°C for 1 hour. An orange oil precipitates then triethyl orthoformate is evaporated under vacuum. Diethyl ether is added to wash the product with help by sonication, so solvent is evaporated and product turns solid. Product **4b** is obtained in 94% yield and characterized by ^{1}H-NMR, ^{13}C-NMR, and ^{19}F-NMR.

^{1}H-NMR (400.1 MHz, $CDCl_3$):

δ (ppm): 9.08 (s, 1H, N-H), 8.71 (m, 1H, N-CH-N), 8.32 (m, 1H, CH_{pyr}), 7.81 (m, 1H, CH_{pyr}), 7.30 (m, 1H, CH_{pyr}), 7.22 (m, 1H, CH_{pyr}), 4.42 (d, J= 5.12 Hz, 1H, CH), 2.50 (m, 1H, CH_2), 2.34 (m, 1H, CH_2), 2.18 (m, 1H, CH_2), 2.07 (m, 1H, CH_2), 1.33 (s, 3H, CH_3), 1.18 (s, 3H, CH_3), 1.02 (s, 3H, CH_3).

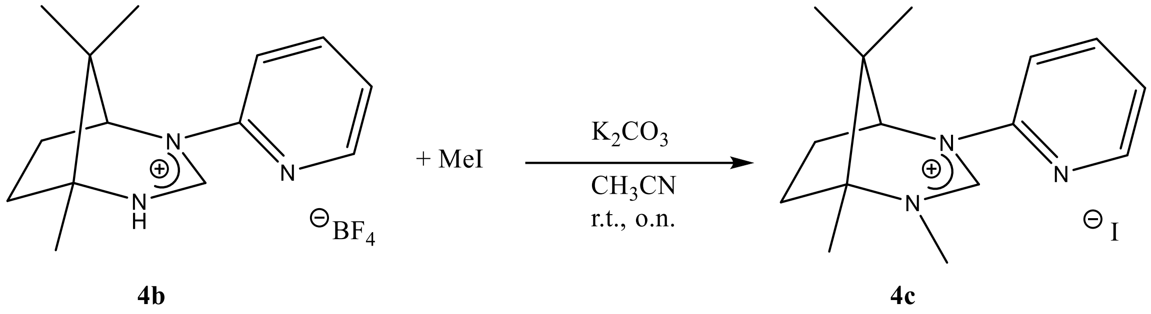
^{13}C-NMR (100.61 MHz, $CDCl_3$):

δ (ppm): 150.09 (N-CH-N), 150.03 ($C_{q\ pyr}$), 148.84 (CH_{pyr}), 140.00 (CH_{pyr}), 122.89 (CH_{pyr}), 112.18 (CH_{pyr}), 66.51 (CH), 66.36 (C_q), 40.97 (C_q), 39.90 (CH_2), 31.65 (CH_2), 20.51 (CH_3), 16.50 (CH_3), 15.30 (CH_3).

^{19}F-NMR (376.50 MHz, $CDCl_3$):

δ (ppm): -150.58

4.10. Synthesis of (1R-5S)-N²-methyl-N⁴-pyrid-2-yl-1,8,8-trimethyl-2,4-diazabicyclo[3.2.1]oct-2-en-2-ium iodide (4c)



Scheme 4.9

In a schlenk under inert atmosphere **4b** (0.891 g, 2.79 mmol) and K_2CO_3 (0.772 g, 5.58 mmol) are dissolved in 10 ml of dried acetonitrile and under stirring MeI (0.476 g, 0.21 ml, 3.35 mmol, 1.2 eq) is added. Reaction runs overnight at room temperature than crude mix is filtered and solvent evaporated under vacuum. Product **4c** is obtained in 87% yield and characterized by ^{1}H-NMR, ^{13}C-NMR and ESI-TOF.

^{1}H-NMR (400.1 MHz, $CDCl_3$):

δ (ppm): 9.51 (s, 1H, N-CH-N), 8.37 (m, 1H, CH_{pyr}), 8.24 (m, 1H, CH_{pyr}), 7.89 (m, 1H, CH_{pyr}), 7.24 (m, 1H, CH_{pyr}), 4.71 (m, 1H, CH), 3.61 (s, 3H, N-CH_3), 2.78 (m, 1H, CH_2), 2.42 (m, 1H, CH_2), 2.30 (m, 1H, CH_2), 2.01 (m, 1H, CH_2), 1.41 (s, 3H, CH_3), 1.26 (s, 3H, CH_3), 1.14 (s, 3H, CH_3).

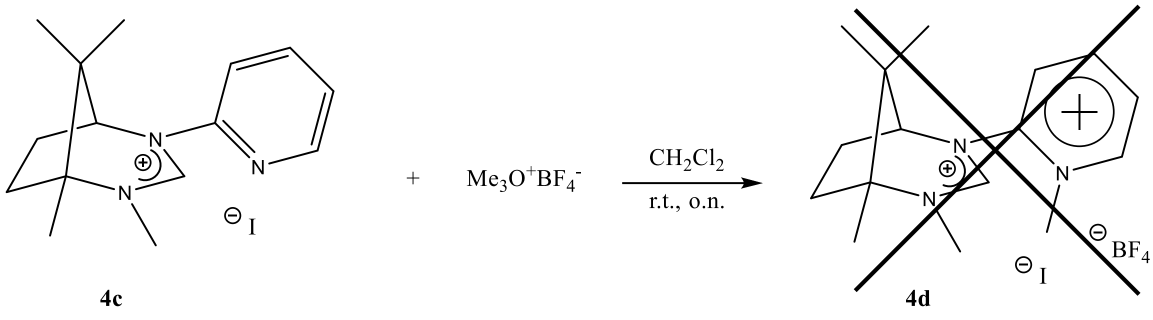
^{13}C{^{1}H}DEPT-NMR (100.61 MHz, $CDCl_3$):

δ (ppm): 151.61 (N-CH-N), 150.32 ($C_{q\ pyr}$), 148.26 (CH_{pyr}), 139.91 (CH_{pyr}), 122.62 (CH_{pyr}), 114.51 (CH_{pyr}), 72.05 (C_q), 64.92 (CH), 41.23 (C_q), 38.91 (N-CH_3), 38.61 (CH_2), 31.08 (CH_2), 21.87 (CH_3), 16.91 (CH_3), 14.18 (CH_3).

ESI-TOF (m/z) (+): 244 $[M]^+$.

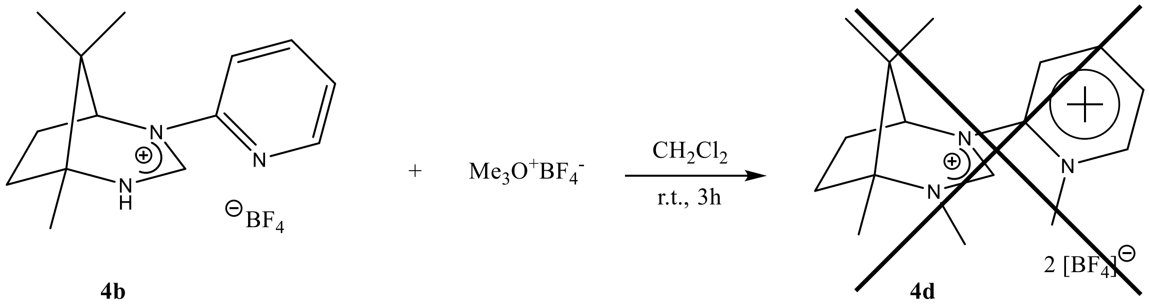
ESI-TOF (m/z) (-): 126 $[I]^-$.

4.11. Synthesis of (1R-5S)-N^2-methyl-N^4-(N-methylpyridinium-2-yl)-1,8,8-trimethyl-2,4-diazabicyclo[3.2.1]oct-2-en-2-ium 2[X$^-$] (4d)



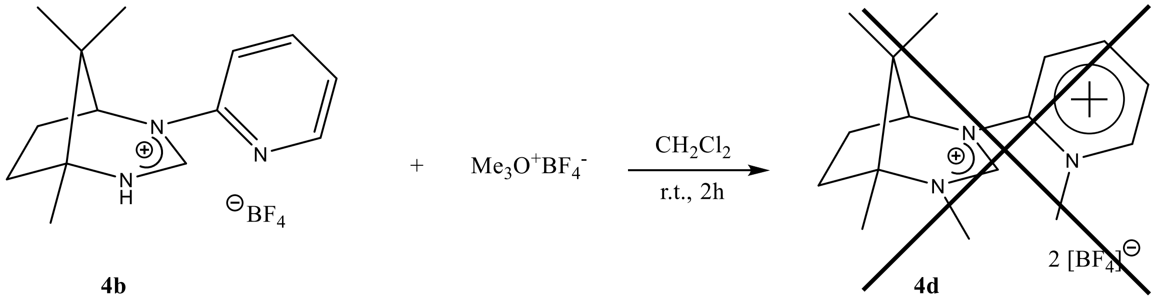
Scheme 4.10

In a schlenk under inert atmosphere **4c** (0.050 g, 0.135 mmol) is dissolved in 10 ml of dichloromethane than trimethyloxonium tetrafluoroborate (0.020 g, 0.135 mmol, 1 eq.) is added under stirring. Reaction runs at room temperature overnight. Solvent is removed under vacuum. The brown solid is characterized by NMR but no evidence for **4d** are found.



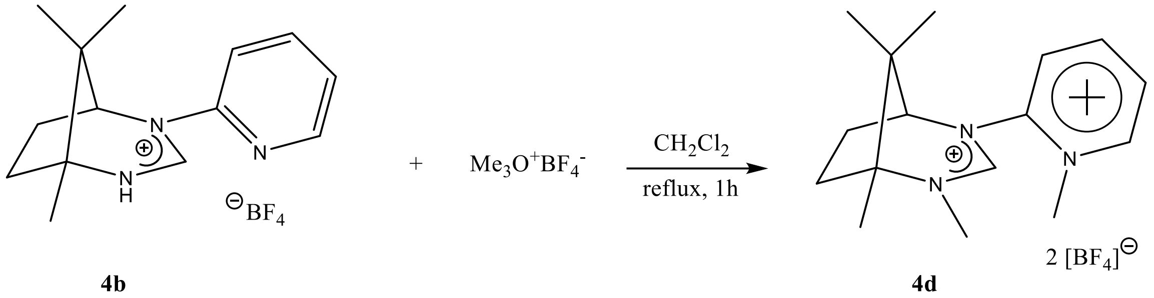
Scheme 4.11

In a schlenk under inert atmosphere **4b** (0.050 g, 0.158 mmol) is dissolved in 10 ml of dichloromethane than trimethyloxonium tetrafluoroborate (0.047 g, 0.315 mmol, 2 eq.) is added under stirring. Reaction runs at room temperature for 3 hours. Solvent is removed under vacuum. The yellow solid is characterized by NMR but no evidence for **4d** are found.



Scheme 4.12

In a schlenk under inert atmosphere **4b** (0.050 g, 0.158 mmol) is dissolved in 10 ml of dichloromethane than trimethyloxonium tetrafluoroborate (0.093 g, 0.632 mmol, 4 eq.) is added under stirring divided into two aliquots of 2 equivalent each. The second aliquots is added after one hour. Reaction runs at room temperature for 2 hours. Solvent is removed under vacuum. The yellow solid is characterized by NMR but no evidence for **4d** are found.



Scheme 4.13

In a schlenk under inert atmosphere **4b** (0.050 g, 0.158 mmol) is dissolved in 10 ml of dichloromethane than trimethyloxonium tetrafluoroborate (0.047 g, 0.315 mmol, 2 eq.) Reaction runs at room temperature for 2 hours. When yellow solid precipitates the solvent is removed by using a cannula with filter and solid is dried under vacuum. The yellow solid is obtained in 24 % yield and characterized as **4d** by ^{1}H-NMR, ^{13}C-NMR, ^{19}F-NMR and ESI-TOF.

^{1}H-NMR (400.1 MHz, $CDCl_3$):

δ (ppm): 9.77 (s, 1H, N-CH-N), 8.70 (m, 2H, CH_{pyr}), 8.45 (m, 1H, CH_{pyr}), 8.02 (m, 1H, CH_{pyr}), 4.37 (s, 1H, CH), 3.00 (s, 3H, CH_3), 2.98 (s, 3H, CH_3), 2.55 (m, 1H, CH_2), 2.43 (m, 2H, CH_2), 2.21 (m, 1H, CH_2), 1.42 (s, 3H, CH_3), 1.25 (s, 3H, CH_3), 1.18 (s, 3H, CH_3).

$^{13}C\{^1H\}$DEPT-NMR (100.61 MHz, $CDCl_3$):

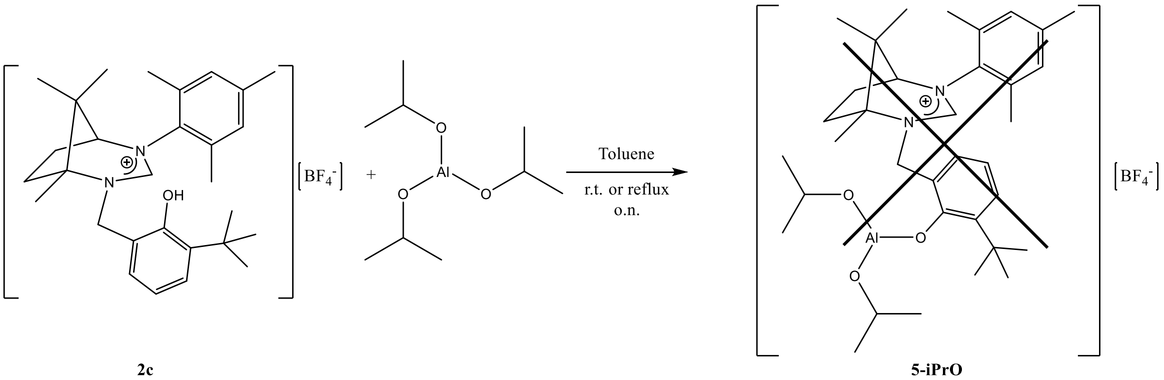
δ (ppm): 177.26 (N-CH-N), 154.11 ($C_{q\ pyr}$), 151.17 (CH_{pyr}), 142.36 (CH_{pyr}), 126.65 (CH_{pyr}), 121.53 (CH_{pyr}), 71.64 (C_q), 69.32 (CH), 60.51 (pyr-CH_3) 41.77 (C_q), 41.41 (N-CH_3), 31.96 (CH_2), 29.18 (CH_2), 20.33 (CH_3), 16.32 (CH_3), 15.12 (CH_3).

^{19}F-NMR (376.50 MHz, $CDCl_3$):

δ (ppm): -150.87

ESI-TOF (m/z) (+): 230 $[M-2Me]^+$.

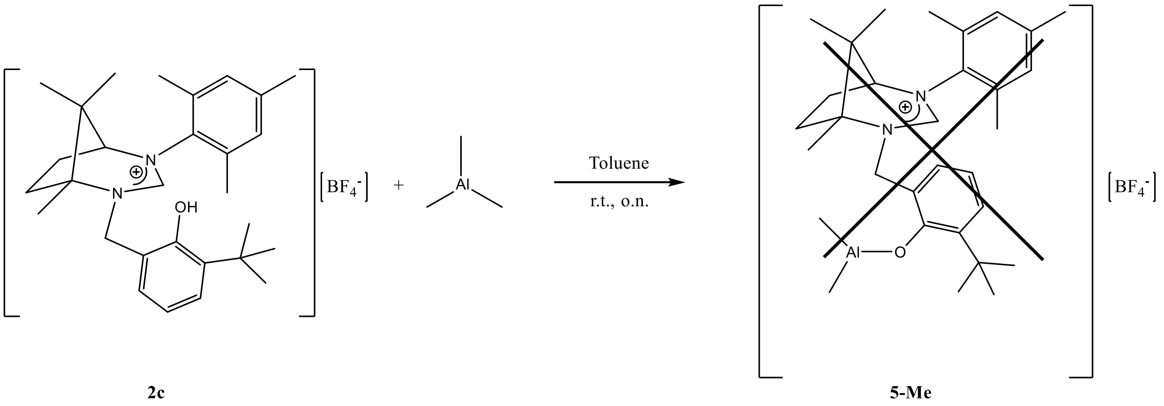
4.12. Preliminary studies on reactivity of 2c with aluminium



2c **5-iPrO**

Scheme 4.14

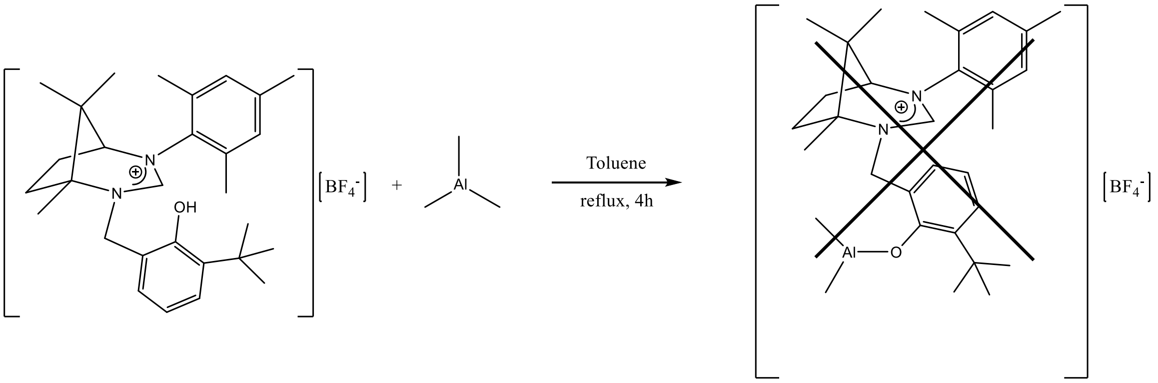
In a schlenk under inert athmosphere **2c** (0.050 g, 9.61 • 10^{-5} mol) is dissolved in 15 ml of dried toluene. When it is completely dissolved Al(*i*-PrO)$_3$ (0.020 g, 9.79 • 10^{-5} mol) is added to stirred mix. One reaction is carried at room temperature and one at reflux both overnight. At the end of reactions solvent is removed under vacuum and crude products are characterized by ^{1}H-NMR, ^{13}C-NMR, ^{19}F-NMR and ^{27}Al-NMR but no evidence for **5-iPrO** are found.



2c **5-Me**

Scheme 4.15

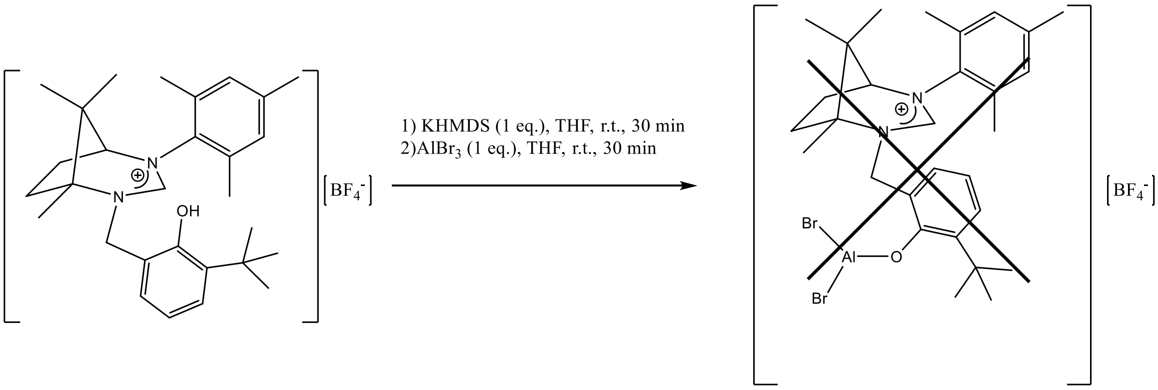
In a schlenk under inert athmosphere trimethyl aluminium 2M in hexane (0.007 g, 47.8 µl, 9.61 • 10^{-5} mol) is dissolved in 15 ml of dried toluene followed by **2c** (0.050 g, 9.61 • 10^{-5} mol) while mix is under stirring. Reaction runs overnight at room temperature. At the end of reaction solution is filtered by using a cannula. Both batches are kept under inert atmosphere and dried under vacuum. Both crude solids are characterized using a J. Young tube by ^{1}H-NMR, ^{13}C-NMR, ^{19}F-NMR and ^{27}Al-NMR but no evidence for **5-Me** are found.



2c **5-Me**

Scheme 4.16

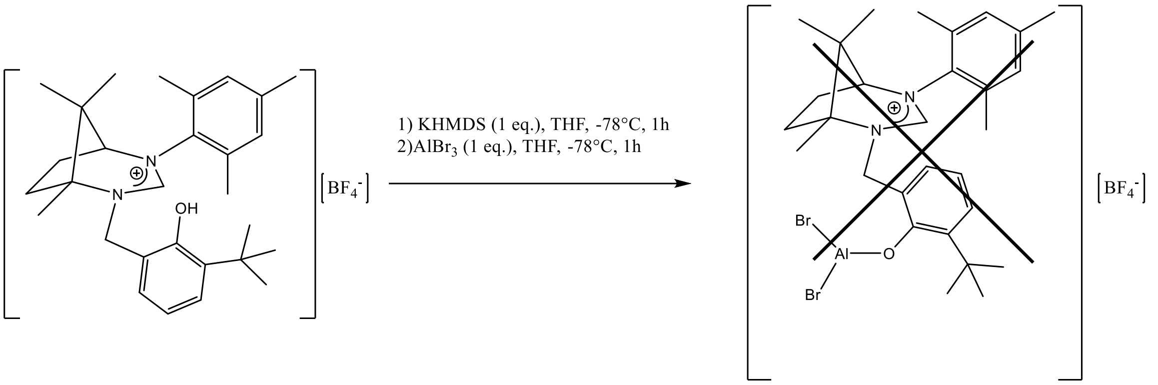
In a schlenk under inert athmosphere trimethyl aluminium 2M in toluene (0.007 g, 47.8 μl, 9.61 • 10^{-5} mol) is dissolved in 15 ml of dried toluene followed by **2c** (0.050 g, 9.61 • 10^{-5} mol) while mix is under stirring. Reaction runs for 4 hours under reflux. At the end of reaction solvent is evaporated under vacuum and crude solid yellow product is characterized using a J. Young tube by ^{1}H-NMR, ^{13}C-NMR, ^{19}F-NMR and ^{27}Al-NMR but no evidence for **5-Me** are found.



2c **5-Br**

Scheme 4.17

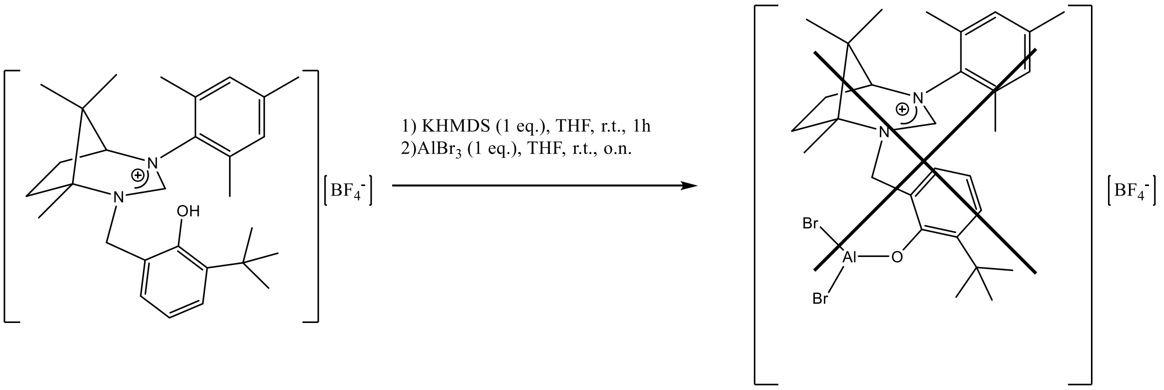
In a schlenk under inert atmosphere **2c** (0.050 g, 9.61 • 10^{-5} mol) is dissolved in 15 ml of dried THF and KHMDS (0.019 g, 9.61 • 10^{-5} mol) is added to stirred mix. After 30 minutes of reaction at room temperature $AlBr_3$ (0.026 g, 9.61 • 10^{-5} mol) is added to stirred mix. After 30 minutes solvent is evaporated under vacuum and crude solid yellow product is characterized using a J. Young tube by ^{1}H-NMR, ^{13}C-NMR, ^{19}F-NMR and ^{27}Al-NMR but no evidence for **5-Br** are found.



2c **5-Br**

Scheme 4.18

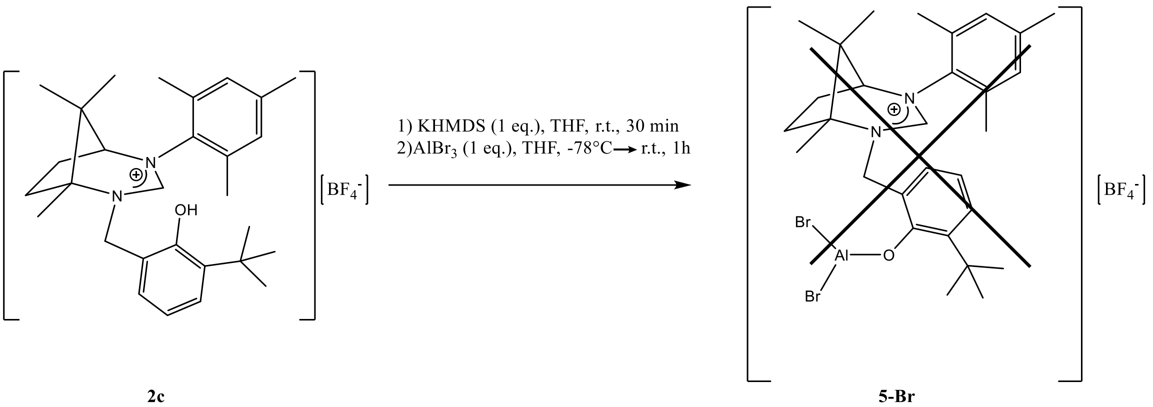
In a schlenk under inert atmosphere **2c** (0.050 g, 9.61 • 10^{-5} mol) is dissolved in 15 ml of dried THF and KHMDS (0.019 g, 9.61 • 10^{-5} mol) is added to stirred mix. After one hour of reaction at -78°C $AlBr_3$ (0.026 g, 9.61 • 10^{-5} mol) is added to stirred mix. After one hour of reaction at -78°C solvent is evaporated under vacuum and crude solid yellow product is characterized using a J. Young tube by ^{1}H-NMR, ^{13}C-NMR, ^{19}F-NMR and ^{27}Al-NMR but no evidence for **5-Br** are found.



2c **5-Br**

Scheme 4.19

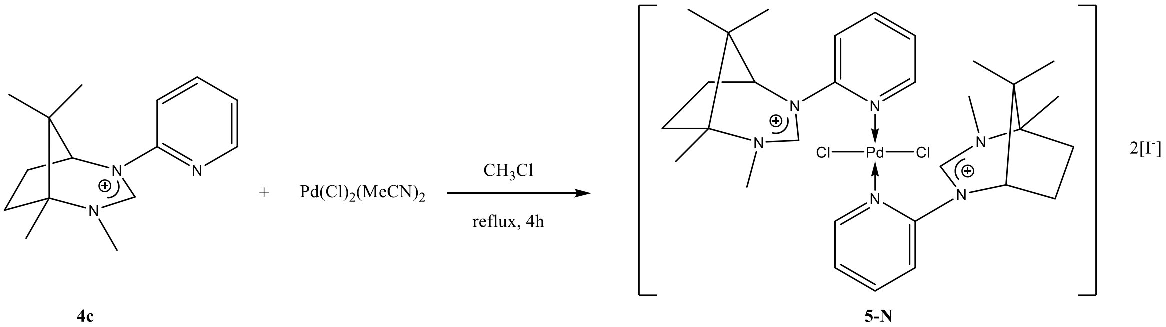
In a schlenk under inert atmosphere **2c** (0.050 g, 9.61 • 10^{-5} mol) is dissolved in 15 ml of dried THF and KHMDS (0.019 g, 9.61 • 10^{-5} mol) is added to stirred mix. After one hour of reaction at room temperature $AlBr_3$ (0.026 g, 9.61 • 10^{-5} mol) is added to stirred mix. Reaction runs overnight at room temperature then solvent is evaporated under vacuum and crude solid yellow product is characterized using a J. Young tube by ^{1}H-NMR, ^{13}C-NMR, ^{19}F-NMR and ^{27}Al-NMR but no evidence for **5-Br** are found.



Scheme 4.20

In a schlenk under inert atmosphere **2c** (0.050 g, 9.61 • 10^{-5} mol) is dissolved in 15 ml of dried THF and KHMDS (0.019 g, 9.61 • 10^{-5} mol) is added to stirred mix. After 30 minutes of reaction at room temperature stirred mix is cooled down to -78°C and $AlBr_3$ (0.026 g, 9.61 • 10^{-5} mol) is added. Reaction runs for 30 minutes at -78°C then room temperature is reached in 30 minutes. At the end of reaction solvent is evaporated under vacuum and crude solid yellow product is characterized using a J. Young tube by ^{1}H-NMR, ^{13}C-NMR, ^{19}F-NMR and ^{27}Al-NMR but no evidence for **5-Br** are found.

4.13. Synthesis of complex 5-N



Scheme 4.21

In a schlenk under inert atmosphere **4c** (0.200 g, 0.54 mmol) and $Pd(Cl)_2(MeCN)_2$ (0.070 g, 0.27 mmol) are dissolved in dried chloroform under stirring. The reaction runs for four hours at reflux. Solution is filtered with a cannula into a schlenk under inert atmosphere and solvent is removed under vacuum. Product is obtained in 74% yield and characterized by ^{1}H-NMR and ^{13}C -NMR.

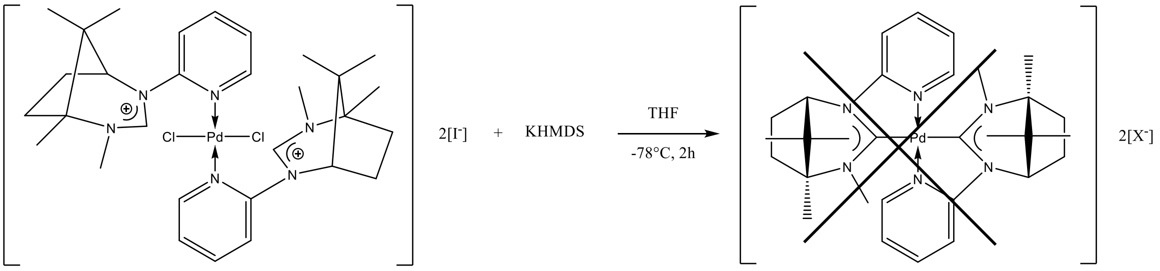
^{1}H-NMR (400.1 MHz, CDCl$_3$):

δ (ppm): 9.83 (s, 1H, N-CH-N), 8.39 (m, 1H, CH$_{pyr}$), 8.28 (m, 1H, CH$_{pyr}$), 8.01 m, 1H, CH$_{pyr}$), 7.28 (m, 1H, CH$_{pyr}$), 4.72 (d, J= 4.97 Hz, 1H, CH), 3.70 (s, 3H, N-CH$_3$), 2.75 (m, 1H, CH$_2$), 2.44 (m, 1H, CH$_2$), 2.34 (m, 1H, CH$_2$), 2.04 (m, 1H, CH$_2$), 1.42 (s, 3H, CH$_3$), 1.26 (s, 3H, CH$_3$), 1.13 (s, 3H, CH$_3$).

^{13}C -NMR (100.61 MHz, CDCl$_3$):

δ (ppm): 152.68 (N-CH-N), 150.34 (C$_{q\ pyr}$), 148.28 (CH$_{pyr}$), 140.46 (CH$_{pyr}$), 122.74 (CH$_{pyr}$), 114.44 (CH$_{pyr}$), 71.85 (C$_q$), 64.73 (CH), 41.07 (C$_q$), 39.02 (N-CH$_3$), 38.60 (CH$_2$), 31.40 (CH$_2$), 21.91 (CH$_3$), 17.00 (CH$_3$), 14.20 (CH$_3$).

4.14. Synthesis of complex 5-CN

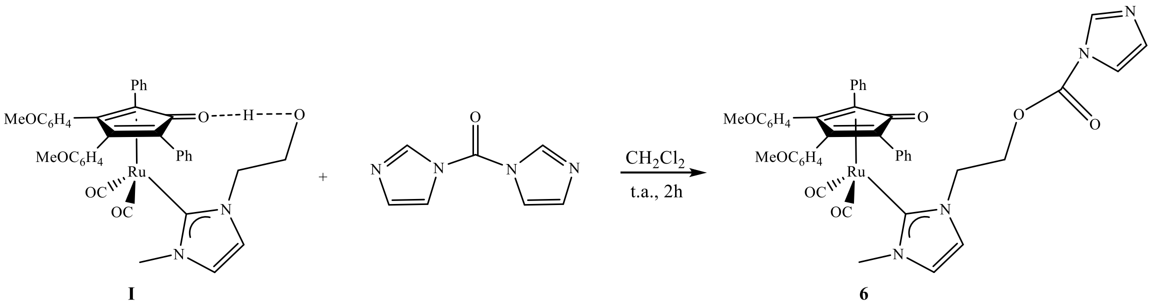


5-N **5-CN**

Scheme 4.22

In a schlenk under inert atmosphere product **5-N** (0.187 g, 0.20 mmol) is dissolved in 15 ml of dried THF. The stirred mix is cooled down to -78°C and KHMDS (0.081 g, 0.41 mmol) is added. After two hours of reaction solvent is removed under vacuum and crude product is characterized by NMR and MS but no evidence for product **5-CN** are found.

4.15. Synthesis of Dicarbonyl(η⁴-3,4-bis(4-methoxyphenyl)-2,5-diphenylcyclopenta-2,4-dienone)(1-methyl-3-(2-CO₂Im-ethyl)imidazol-ylidene)ruthenium (6)



Scheme 4.23

Complex **I** synthetized as reported in literature[51] (1.44 g, 1.98 mmol) and 1,1'-carbonyldiimidazole (0.97 g, 5.99 mmol) were reacted under nitrogen atmosphere in of anhydrous CH_2Cl_2 (30 ml). The reaction mixture was stirred at room temperature for 2h. The solution was then extracted with water (3x20 mL). Trace of water were removed from organic phase with anhydrous Na_2SO_4, then the solvent was removed under vacuum and the white/brown product,identified as **6**, was obtained with an yield of 84%.

IR (CH_2Cl_2): ν(CO): 2007cm^{-1}, 1948 cm^{-1}; ν(C=O,-O_2CIm): 1768cm^{-1}.

^{1}H-NMR (399.9 MHz, $CDCl_3$):

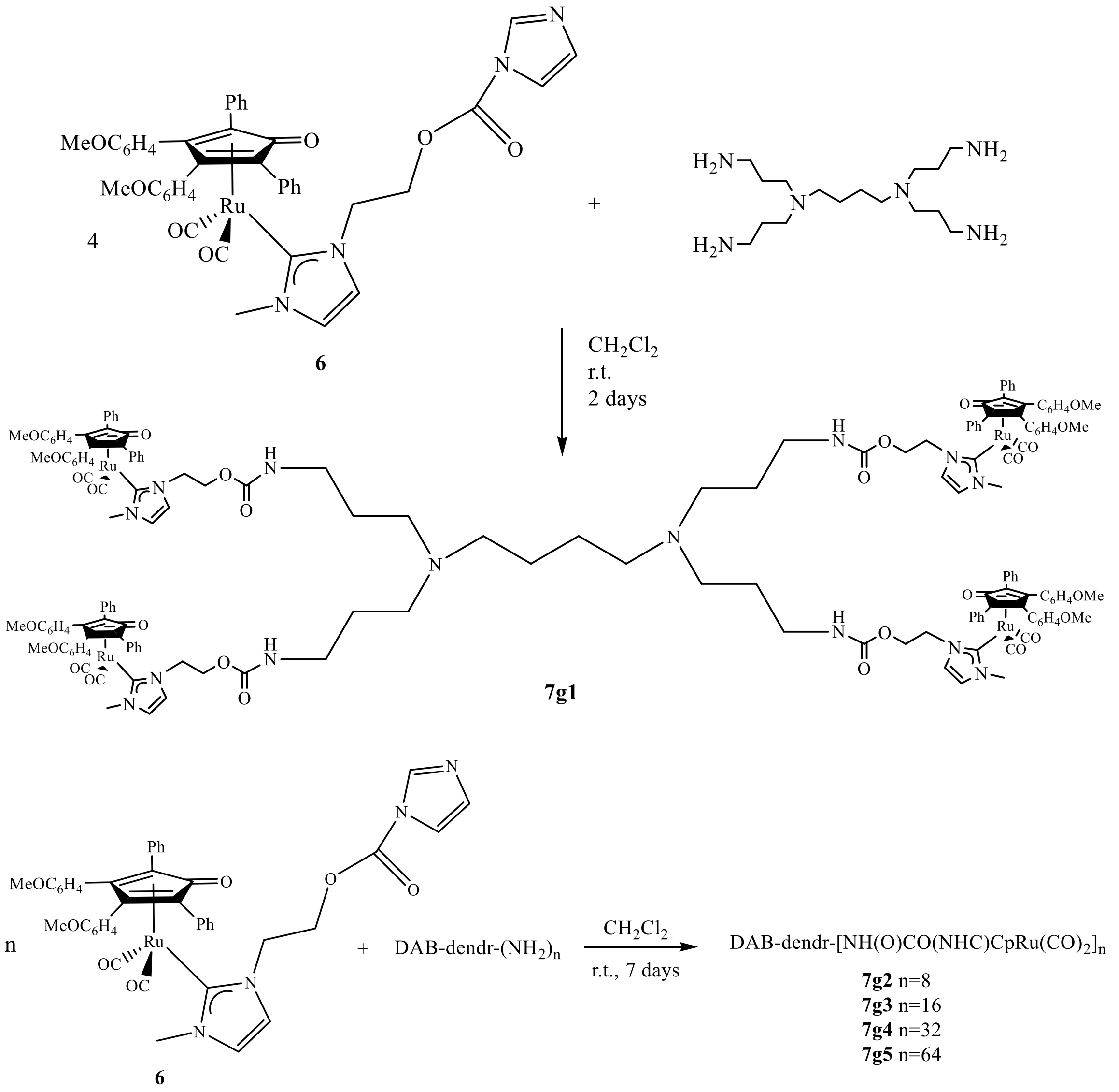
δ (ppm): 8.03 (s, 1H, Im); 7.78 (m, 4H, CH_{aryl}), 7.33 (m, 1H, Im), 7.16-7.12 (m, 8H, CH_{aryl}), 7.08 (m, 1H, Im), 7.06 (m, 2H, CH_{aryl}), 6.96 (d, J = 2.00 Hz, 1H, CH_{NHC}), 6.85 (d, J = 2.00 Hz, 1H, CH_{NHC}), 6.65 (m, 4H, CH_{aryl}), 4.05 (m, 2H,-CH_2-), 3.99 (m, 2H,-CH_2-), 3.72 (s, 6H, -OCH_3), 3.14 (s, 3H, -NCH_3).

^{13}C-NMR (100.6MHz, $CDCl_3$, DEPT):

δ (ppm): 202.15 (CO), 174.80 ($C_{carbene}$), 169.41 (C=O, Cp), 158.64 (-*C*OCH_3), 147.89 (-OC(O)N-), 136.95 (CH, Im), 134.91 (Cq_{aryl}), 133.55 (CH_{aryl}), 130.88 (CH, Im), 129.36 (CH_{aryl}), 127.63 (CH_{aryl}), 125.63 (Cq_{aryl}), 124.70 (CH_{NHC}), 124.37 (CH_{aryl}), 121.76 (CH_{NHC}), 116.97 (CH, Im), 112.96 (CH_{aryl}), 104.09 ($C_{2,5}$, Cp), 78.88 ($C_{3,4}$, Cp), 67.02 (-CH_2-), 55.00 (-OCH_3), 49.20 (-CH_2-), 38.41 (CH_3, NHC).

ESI-MS (m/z) (+): 823 $[M+H]^+$; 845 $[M + Na]^+$.

4.16. Synthesis of DAB-dendr-$[NH(O)CO(NHC)Cp{=}ORu(CO)_2]_n$ {n=4, 8, 16, 32, 64; NHC =[-CH_2CH_2-5-CH_3-imidazol-2-ylidene]; Cp=O =[3,4-$(CH_3O-C_6H_4)_2$-2,5-$Ph_2(\eta^4-C_4CO)$]} (7gn)



Scheme 4.24

DAB-*dendr*-$(NH_2)_4$ (0.02 g, 0.06 mmol) and **6** (0.26 g, 0.31 mmol, 1.13 eq.) were dissolved in CH_2Cl_2 (10 mL) under inert atmosphere. Reaction mixture was stirred at room temperature for two days. The solution was then extracted with water (3x20 mL). Trace of water were removed from organic phase with $MgSO_4$, then the solvent was removed under vacuum and the crude was washed with Et_2O (3x15 mL). The yellow solid was identified as **7g1** and obtained with 42% yield.

The other dendrimers respectively functionalized with 8 **7g2**, 16 **7g3**, 32 **7g4** and 64 **7g5** ruthenium complexes were prepared with the same procedure, but they required seven days of reaction time.

The quantities of reagents used for other generations are:

7g2: 0.02 g (0.03 mmol) of DAB-*dendr*-$(NH_2)_8$ and 0.26 g (0.31 mmol) of **6**;

7g3: 0.02 g (0.01 mmol) og DAB-*dendr*-$(NH_2)_{16}$ and 0.17 g (0.21 mmol) of **6**;

7g4: 0.02 g (6.00 µmol) of DAB-*dendr*-$(NH_2)_{32}$ and 0.20 g (0.25 mmol) of **6**;

7g5: 0.02 g (3.00 µmol) of DAB-*dendr*-$(NH_2)_{64}$ and 0.20 g (0.25 mmol) of **6**.

The functionalized dendrimers **7g2**, **7g3**, **7g4** e **7g5** were obtained with yield respectively of 25%, 32%, 41% e 43% and were characterized by IR, ^1H-NMR e ^{13}C-NMR.

7g1

IR (CH_2Cl_2): ν(C=O): 2006 cm^{-1}, 1947 cm^{-1}; ν(C=O, -NHC(O)O-): 1718 cm^{-1}; ν(C=C): 1601 cm^{-1}, 1518 cm^{-1}; ν(C=O, Cp): 1582 cm^{-1}.

^1H-NMR (399.9 MHz, $CDCl_3$):

δ (ppm): 7.72-6.60 (CH_{aryl}), 6.81 (m, 4H, CH_{NHC}), 6.62 (m, 4H, CH_{NHC}), 3.77 (m, 8H, -CH_2-), 3.68 (s, 24H, -OCH_3), 3.59 (m, 8H, -CH_2-), 3.09 (s, 12H, -NCH_3), 3.06, 2.97, 2.36, 1.57, 1.36 (br, 32H, CH_2, DAB-dendr).

^{13}C-NMR (100.6 MHz, $CDCl_3$):

δ (ppm): 202.05 (C=O), 172.66 ($C_{carbene}$), 169.55 (C=O, Cp), 158.53 (-*C*OCH_3), 155.99 (-OC(O)N-), 135.04 (Cq_{aryl}), 133.55 (CH_{aryl}), 129.39 (CH_{aryl}), 127.45 (CH_{aryl}), 125.49 (Cq_{aryl}), 124.44 (CH_{aryl}), 124.35 (CH, NHC), 121.74 (CH, NHC), 112.85 (CH_{aryl}), 103.72 ($C_{2,5}$, Cp), 78.97 ($C_{3,4}$, Cp), 63.29 (-CH_2-), 54.96 (-OCH_3), 49.75 (-CH_2-), 38.25 (CH_3, NHC), 53.74, 51.74, 39.57, 26.99, 24.88 (CH_2, DAB-dendr).

ESI-MS (m/z) (+): 3355 [M + Na]$^{+}$

7g2

IR (CH_2Cl_2): ν(C=O): 2008cm^{-1}, 1948 cm^{-1}; ν(C=O, -NHC(O)O-): 1719cm^{-1}; ν(C=C): 1603 cm^{-1}, 1518 cm^{-1}; ν(C=O, Cp): 1577 cm^{-1}.

^{1}H-NMR (399.9 MHz, $CDCl_3$):

δ (ppm): 7.75-6.60 (CH_{aryl}), 6.96 (m, 8H, CH_{NHC}), 6.79 (m, 8H, CH_{NHC}), 3.78 (m, 16H, -CH_2-), 3.70 (s, 48H, -OCH_3), 3.59 (m, 16H, -CH_2-), 3.10 (s, 24H, -NCH_3), 3.20-2.80, 2.60-2.20, 1.96-1.42 (br, 80H, CH_2, DAB-dendr).

^{13}C-NMR (100.6 MHz, $CDCl_3$):

δ (ppm): 202.17 (C=O), 173.95 ($C_{carbene}$), 169.45 (C=O, Cp), 158.60 (-*C*OCH_3), 156.15 (-OC(O)N-), 135.00 (Cq_{aryl}), 133.57 (CH_{aryl}), 129.48 (CH_{aryl}), 127.59 (CH_{aryl}), 125.78 (Cq_{aryl}), 124.55 (CH_{aryl}), 124.29 (CH, NHC), 122.38 (CH, NHC), 112.95 (CH_{aryl}), 103.64 ($C_{2,5}$, Cp), 78.68 ($C_{3,4}$, Cp), 63.65 (-CH_2-), 55.02 (-OCH_3), 50.04 (-CH_2-), 38.31 (CH_3, NHC), 53.40, 51.51, 38.43, 26.84, 23.66 (CH_2, DAB-dendr).

7g3

IR (CH_2Cl_2): ν(C=O): 2008cm^{-1}, 1949 cm^{-1}; ν(C=O, -NHC(O)O-): 1718cm^{-1}; ν(C=C): 1602 cm^{-1}, 1517 cm^{-1}; ν(C=O, Cp): 1577 cm^{-1}.

^{1}H-NMR (399.9 MHz, $CDCl_3$):

δ (ppm): 7.76-6.61 (CH_{aryl}), 6.96 (m, 16H, CH_{NHC}), 6.78 (m, 16H, CH_{NHC}), 3.77 (m, 32H, -CH_2-), 3.71 (s, 96H, -OCH_3), 3.69 (m, 32H, -CH_2-), 3.10 (s, 48H, -NCH_3), 3.20-1.50 (br, 176H, CH_2, DAB-dendr).

^{13}C-NMR (100.6 MHz, $CDCl_3$):

δ (ppm): 202.17 (C=O), 173.93 ($C_{carbene}$), 169.45 (C=O, Cp), 158.60 (-*C*OCH_3), 153.57 (-OC(O)N-), 135.00 (Cq_{aryl}), 133.57 (CH_{aryl}), 129.29 (CH_{aryl}), 127.59 (CH_{aryl}), 125.52 (Cq_{aryl}), 124.55 (CH_{aryl}), 124.29 (CH, NHC), 122.38 (CH, NHC), 112.94 (CH_{aryl}), 103.97 ($C_{2,5}$, Cp), 78.68 ($C_{3,4}$, Cp), 63.70 (-CH_2-), 55.02 (-OCH_3), 49.45 (-CH_2-), 38.31 (CH_3, NHC), 53.40, 51.41, 38.42 (CH_2, DAB-dendr).

7g4

IR (CH_2Cl_2): ν(C=O): 2009cm^{-1}, 1947 cm^{-1}; ν(C=O, -NHC(O)O-): 1718cm^{-1}; ν(C=C): 1603 cm^{-1}, 1518 cm^{-1}; ν(C=O, Cp): 1576 cm^{-1}.

^{1}H-NMR (399.9 MHz, $CDCl_3$):

δ (ppm): 7.75-6.60 (CH_{aryl}), 6.96 (m, 32H, CH_{NHC}), 6.78 (m, 32H, CH_{NHC}), 3.77 (m, 64H, -CH_2-), 3.71 (s, 192H, -OCH_3), 3.67 (m, 64H, -CH_2-), 3.10 (s, 96H, -NCH_3), 3.20-1.50 (br, 368H, CH_2, DAB-dendr).

^{13}C-NMR (100.6 MHz, $CDCl_3$):

δ (ppm): 202.15 (C=O), 173.87 ($C_{carbene}$), 169.38 (C=O, Cp), 158.60 (-*C*OCH_3), 153.57 (-OC(O)N-), 134.96 (Cq_{aryl}), 133.57 (CH_{aryl}), 129.31 (CH_{aryl}), 127.59 (CH_{aryl}), 125.54 (Cq_{aryl}), 124.52 (CH_{aryl}), 124.30 (CH, NHC), 122.38 (CH, NHC), 112.94 (CH_{aryl}), 103.96 ($C_{2,5}$, Cp), 78.75 ($C_{3,4}$, Cp), 63.69 (-CH_2-), 55.02 (-OCH_3), 49.46 (-CH_2-), 38.32 (CH_3, NHC), 52.47, 51.23, 38.44, 24.09, 19.74 (CH_2, DAB-dendr).

7g5

IR (CH_2Cl_2): ν(C=O): 2006cm^{-1}, 1950 cm^{-1}; ν(C=O, -NHC(O)O-): 1717cm^{-1}; ν(C=C): 1602 cm^{-1}, 1518 cm^{-1}; ν(C=O, Cp): 1577 cm^{-1}.

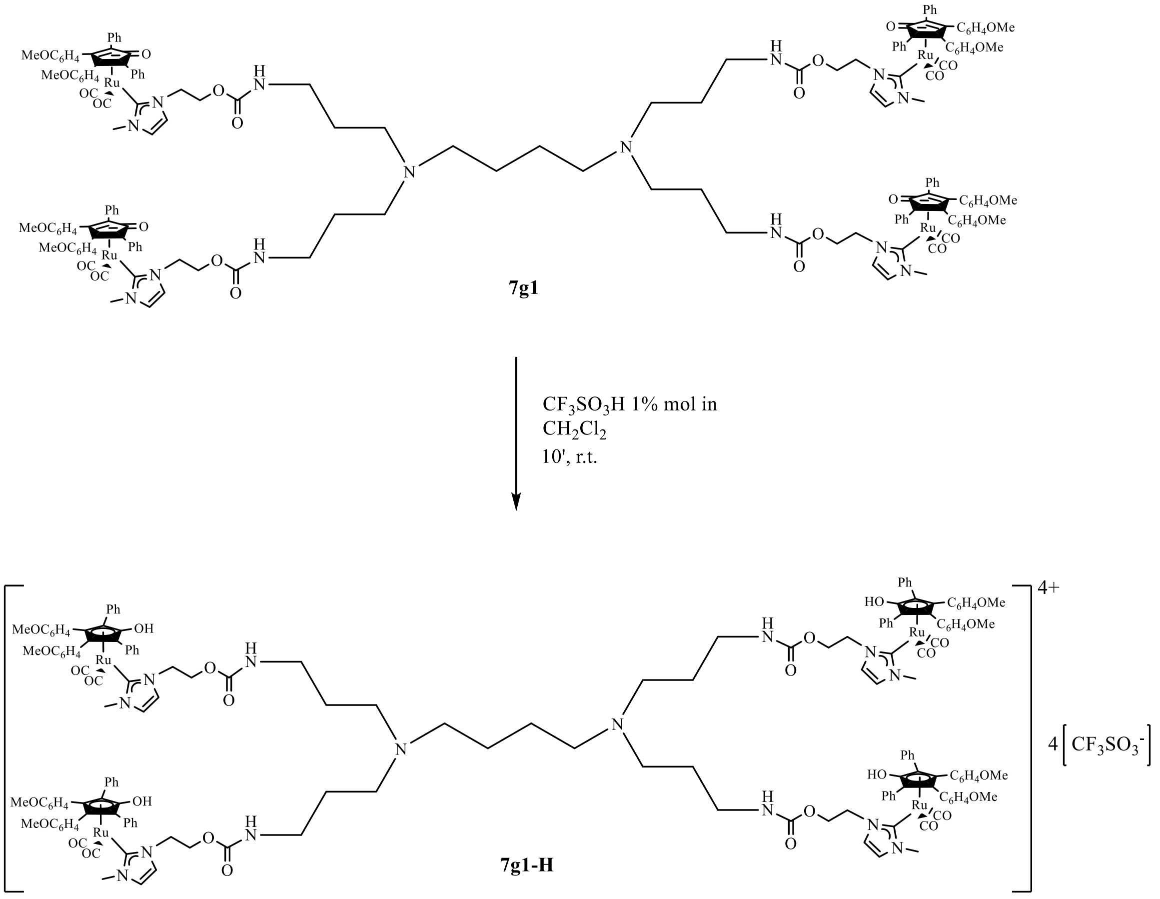
^{1}H-NMR (399.9 MHz, $CDCl_3$):

δ (ppm): 7.75-6.58 (CH_{aryl}), 6.96 (m, 64H, CH_{NHC}), 6.78 (m, 64H, CH_{NHC}), 3.77 (m, 128H, $-CH_2-$), 3.71 (s, 384H, $-OCH_3$), 3.66 (m, 128H, $-CH_2-$), 3.10 (s, 192H, $-NCH_3$), 3.21-1.50 (br, 752H, CH_2, DAB-dendr).

^{13}C-NMR (100.6 MHz, $CDCl_3$):

δ (ppm): 202.16 (C=O), 173.91 ($C_{carbene}$), 169.43 (C=O, Cp), 158.60 (-*C*OCH_3), 153.57 (-OC(O)N-), 134.98 (Cq_{aryl}), 133.57 (CH_{aryl}), 129.30 (CH_{aryl}), 127.59 (CH_{aryl}), 125.53 (Cq_{aryl}), 124.54 (CH_{aryl}), 124.30 (CH, NHC), 122.38 (CH, NHC), 112.95 (CH_{aryl}), 103.97 ($C_{2,5}$, Cp), 78.70 ($C_{3,4}$, Cp), 63.80 ($-CH_2-$), 55.02 ($-OCH_3$), 49.45 ($-CH_2-$), 38.31 (CH_3, NHC), 52.46, 51.35, 38.39, 26.70, 24.09 (CH_2, DAB-dendr).

4.17. Synthesis of DAB-dendr-[NH(O)CO(NHC)Cp-OHRu(CO)$_2$]$_n^+$[CF$_3$SO$_3$]$_n^-$ {n = 4; NHC = [-CH$_2$CH$_2$-3-CH$_3$-imidazol-ilidene]; Cp-OH = [3,4-(CH$_3$O-C$_6$H$_4$)$_2$-2,5-Ph$_2$(η^5-C$_4$COH)]} (7g1-H)



Scheme 4.25

Frist generation functionalized dendrimer (**7g1**) (0.150 g, 45 μmol) was dissolved in anhydrous CH_2Cl_2 (10ml) under inert atmosphere. HCF_3SO_3 1% in CH_2Cl_2 (0.019 ml, 216 μmol, 1.2 eq.) was added to stirred solution. After ten minutes of reaction the solvent was removed under vacuum. The product was obtained in quantitative yield and was identified as **7g1-H**.

IR (CH_2Cl_2): ν(C=O): 2038 cm^{-1}, 1987 cm^{-1}; ν(C=O, -NHC(O)O-): 1725 cm^{-1}, 1701 cm^{-1}; ν(C=C): 1610 cm^{-1}, 1520 cm^{-1}.

^{1}H-NMR (399.9 MHz, $CDCl_3$):

δ (ppm): 7.36-6.40 (CH_{aryl}), 7.02 (m, 4H, CH_{NHC}), 6.65 (m, 4H, CH_{NHC}), 3.87 (m, 8H, -CH_2-), 3.70 (m, 24H, -OCH_3), 3.56 (m, 8H, -CH_2-), 3.31 (s, 12H, -NCH_3), 3.10, 1.84, 1.73, 0.85 (br, 32H, CH_2-DAB-dendr).

^{13}C-NMR (100.6 MHz, $CDCl_3$):

δ (ppm) 198.72 (CO), 160.81 ($C_{carbene}$), 159.47 (*C*OCH_3), 141.63 (C-OH, Cq), 133.34 (CH_{aryl}), 130.48 (CH_{aryl}), 128.66 (CH_{aryl}), 127.81(Cq_{aryl}), 126.21 (Cq_{aryl}), 121.66 (CH_{NHC}), 120.62 (CH_{aryl}), 118.49 (CH_{NHC}), 113.38 (CH_{aryl}), 104.14 ($C_{2,5}$, Cp), 87.79 ($C_{3,4}$, Cp), 62.71 (CH_2), 55.06 (OCH_3), 51.87 (CH_2), 51.11 (CH_2), 49.90 (CH_2), 38.93 (NCH_3), 37.49 (CH_2), 23.67 (CH_2), 19.85 (CH_2).

^{19}F-NMR (282.4 MHz, $CDCl_3$) δ (ppm): -78.67 (CF_3SO_3).

ESI-MS (m/z) (+): 833 $[M + 4H]^{4+}$

ESI-MS (m/z) (-): 149 $[CF_3SO_3]^-$

4.18. General method for hydrogenation

Functionalized dendrimer (3.75 µmol for **4g1** and **4g1-H** , 5% mol [Ru]), additive (1 eq. per metal centre when needed) and *i*PrOH (3 mL) were stirred at reflux for 15 min. Then 4-fluoroacetophenone (36 µL, 300 µmol) was added and samples were taken at regular intervals. Aliquots (ca. 0.05mL) were diluted with $CDCl_3$ (0.5 mL) and conversions were determined by ^{19}F-NMR spectroscopy.

4.19. General method for dehydrogenation

Functionalized dendrimer (3.75 μmol for **4g1** and **4g1-H** , 5% mol [Ru]), additive (1 eq. per metal centre when needed) and solvents (dioxane or toluene) (3 mL) were stirred at reflux for 15 min. Then 4-fluorobenzylalcohol (33 μL, 300 μmol) was added and samples were taken at regular intervals. Aliquots (ca. 0.05mL) were diluted with $CDCl_3$ (0.5 mL) and conversions were determined by ^{19}F-NMR spectroscopy.

4.20. Characterization of dendrimer DAB-dendr-[NH(O)COCH$_2$CH$_2$Im(CH$_3$)]$_4$ (g1-Imid):

^1H-NMR (400 MHz, D_2O):

δ (ppm) 8.81 (m, 4H, NCHN), 7.57 (m, 4H, CH_{Im}), 7.46 (m, 4H, CH_{Im}), 4.52 (m, 8H, -CH_2-), 4.47 (m, 8H, -CH_2-), 3.92 (s, 12H, -NCH_3), 3.15, 1.92, 1.78, 0.85 (br, 32H, CH_2-DAB-dendr).

^1H-NMR (400 MHz, acetone-d_6):

δ (ppm) 9.06 (m, 4H, NCHN), 7.79 (m, 4H, CH_{Im}), 7.70 (m, 4H, CH_{Im}), 4.61 (m, 8H, -CH_2-), 4.42 (m, 8H, -CH_2-), 4.05 (s, 12H, -NCH_3), 3.38-0.85 (br, 32H, CH_2-DAB-dendr).

4.21. Characterization of Dicarbonyl(η^4-3,4-bis(4-methoxyphenyl)-2,5-diphenylcyclopenta-2,4-hydroxycyclopentadienyl)(H)ruthenium (A):

^1H-NMR (399.9 MHz, $CDCl_3$):

δ (ppm): 7.46-6.54 (m, 18H, CH_{aryl}), 3.71 (s, 6H, -OCH_3), -9.88 (s, 1H, hydride).

4.22. Characterization of Dicarbonyl(η^4-3,4-bis(4-methoxyphenyl)-2,5-diphenylcyclopenta-2,4-hydroxycyclopentadienyl)(Cl)ruthenium (B):

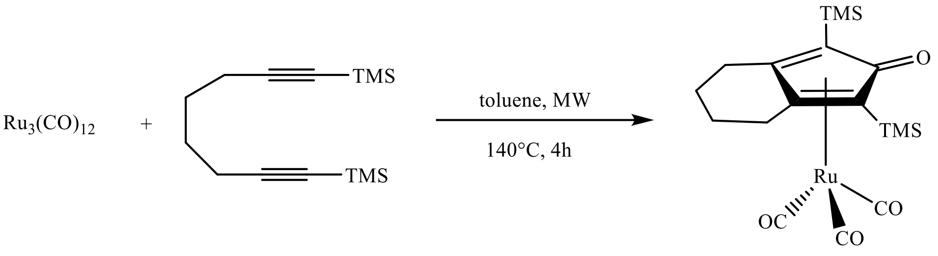
^1H-NMR (399.9 MHz, $CDCl_3$):

δ (ppm): 7.44-6.61 (m, 18H, CH_{aryl}), 3.74 (s, 6H, -OCH_3).

^{13}C-NMR (100.6MHz, $CDCl_3$, DEPT):

δ (ppm): 197.48 (CO), 159.49 (-*C*OCH_3), 140.44 (-C-OH), 132.99-113.35 (CH_{aryl}), 99.25 ($C_{2,5}$, Cp), 88.52 ($C_{3,4}$, Cp), 55.14 (-OCH_3). IR (CH_2Cl_2): ν(CO): 2038 cm^{-1}, 2018 cm^{-1}.

4.23. Triscarbonyl-(2,4-bis(trimethylsilyl)bicyclo[3.3.0]nona-1,4-dien-3-one)ruthenium (8)



8

Scheme 4.26

In a 75 mL Teflon tube equipped with magnetic stirrer, 3,4-Bis(4-methoxyphenyl)-2,5-diphenylcyclopenta-2,4-dienone 0.150 g (0.6 mmol) and $Ru_3(CO)_{12}$ 0.191 g (0.3 mmol) were dissolved in 40 mL of toluene. The container is closed with a cap, equipped with a temperature sensor, and placed into microwave. The reaction is heated to 140 °C for 4h. Upon removal of the solvent, the crude was purified by neutral alumina column chromatography eluting, at first, with hexane, then with dichloromethane and finally with ethyl acetate to afford the yellow triscarbonyl-(2,4-bis(trimethylsilyl)bicyclo[3.3.0]nona-1,4-dien-3-one)ruthenium complex (**8**). Yield = 52%.

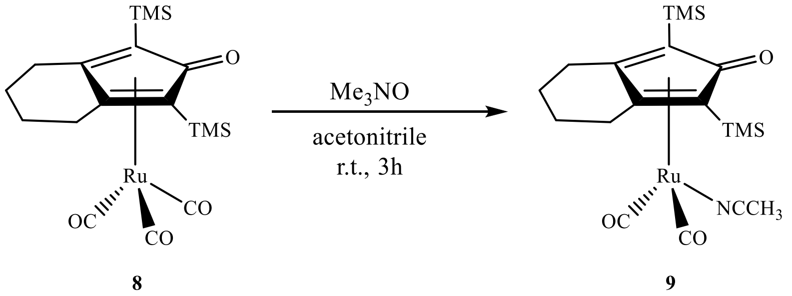
IR (CH_2Cl_2, cm^{-1}): (ν CO) 2076, 2017, 2000, (ν C=O) 1614.

^{1}H-NMR (399.9 MHz, $CDCl_3$):
δ (ppm): 2.65 (m, 4H, CH_2), 1.80 (m, 4H, CH_2), 0.26 (s, 18H, CH_3, TMS).

^{13}C-NMR (150.8 MHz, $CDCl_3$, g-HSQC, g-HMBC):
δ (ppm): 195.06 (CO), 184.54 (C=O), 112.62 ($C_{2,5}$, Cp), 68.69 ($C_{3,4}$, Cp), 24.96 (CH_2, 2C), 22.59 (CH_2, 2C), 0.14 (CH_3, TMS, 6C).

ESI-MS (m/z) (+): 465 $[M+H]^+$; 487 $[M + Na]^+$; 503 $[M+K]^+$.

4.24. Dicarbonyl-(2,4-bis(trimethylsilyl)bicyclo[3.3.0]nona-1,4-dien-3-one)[acetonitrile]ruthenium (9)



Scheme 4.27

In a dried 10 mL Schlenk flask, triscarbonyl-(2,4-bis(trimethylsilyl)bicyclo[3.3.0]nona-1,4-dien-3-one)ruthenium (**8**) 0.065 g (0.140 mmol) and trimethylamine-N-oxide 0.016 g (0.210 mmol) were dissolved in 3 mL of anhydrous acetonitrile. Reaction mixture was stirred at room temperature and protected from light for 3 hours. A pale-yellow precipitate appeared. The solid was filtered and washed with cold hexane to afford the complex dicarbonyl-(2,4-bis(trimethylsilyl)bicyclo[3.3.0]nona-1,4-dien-3-one)[acetonitrile]ruthenium (**9**). Yield : 75%.

IR (CH_2Cl_2, cm^{-1}): (ν CO) 2010, 1948, (ν C=O) 1591.

^{1}H-NMR (399.9 MHz, $CDCl_3$):

δ (ppm):

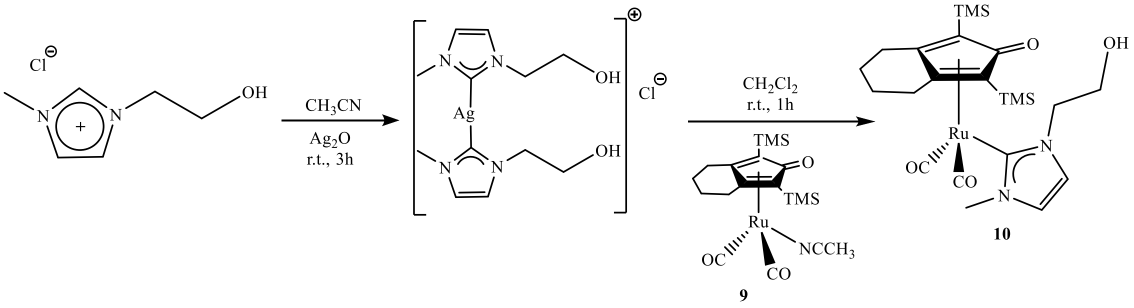
2.42 (m, 4H, CH_2), 2.25 (s, 3H, CH_3), 1.60 (m, 4H, CH_2), 0.26 (s, 18H, CH_3, TMS).

^{13}C-NMR (150.8 MHz, $CDCl_3$, g-HSQC, g-HMBC):

δ (ppm): 199.10 (CO), 182.47 (C=O), 124.51 (Cq, -$CH_3\mathit{C}N$), 107.27 ($C_{2,5}$, Cp), 67.99 ($C_{3,4}$, Cp), 25.17 (CH_2, 2C), 22.44 (CH_2, 2C), 4.09 (-$\mathit{C}H_3CN$), 0.14 (CH_3, TMS, 6C).

ESI-MS (m/z) (+): 478 $[M+H]^+$; 500 $[M + Na]^+$.

4.25. Dicarbonyl-(2,4-bis(trimethylsilyl)bicyclo[3.3.0]nona-1,4-dien-3-one)[1-(2-hydroxyethyl))-3-methylilidene]ruthenium (10)



Scheme 4.28

1-methyl-3-(2-hydroxyethyl) imidazolium chloride (0.014g, 0.096mmol) was reacted with Ag_2O (1.2eq., 0.027g, 0.115mmol) in dry CH_3CN under inert atmosphere and with protection from light. The reaction mixture was stirred for 3h at room temperature in order to reach complete conversion to the corresponding silver carbene complex. Then, the solvent was removed under vacuum, the solid obtained dissolved in CH_2Cl_2 and 0.046g (0.096mmol) of dicarbonyl-(2,4-bis(trimethylsilyl)bicyclo[3.3.0]nona-1,4-dien-3-one)[acetonitrile]ruthenium precursor (**9**) was straightforwardly added to the *in situ* prepared silver complex solution. After stirring for 1h at room temperature, the reaction mixture was filtered on a celite pad and the solvent removed under vacuum leading to the quantitative formation of the dicarbonyl-(2,4-bis(trimethylsilyl)bicyclo[3.3.0]nona-1,4-dien-3-one)[1-(butyl-3-(2-pyridinyl)-imidazol-2-ylidene]ruthenium complex (**10**).

IR (CH_2Cl_2, cm^{-1}): (ν CO) 2003, 1939, (ν C=O) 1525.

^{1}H-NMR (399.9 MHz, $CDCl_3$):

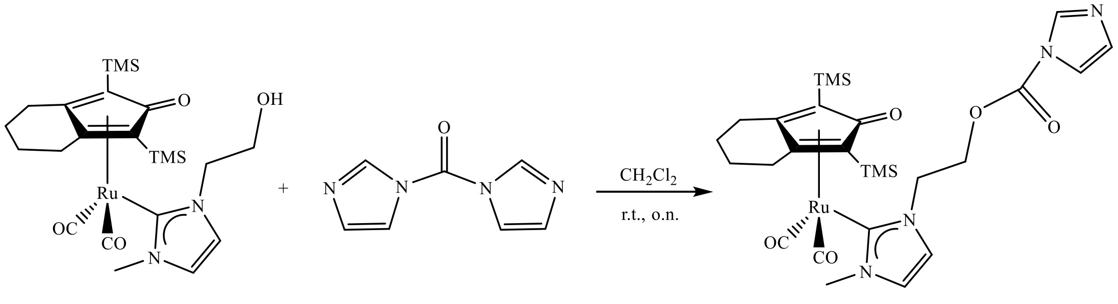
δ (ppm): 7.24 (s, 1H, CH_{NHC}), 7.06 (s, 1H, CH_{NHC}), 4.23 (t, 2H, $-NCH_2$), 3.92 (t, 2H, CH_2OH), 3.87 (s, 3H, $-NCH_3$), 2.59 (m, 4H, CH_2), 1.77 (m, 4H, CH_2), 0.19 (s, 18H, CH_3, TMS).

^{13}C-NMR (150.8 MHz, $CDCl_3$, g-HSQC, g-HMBC):

δ (ppm): 202.94 (CO), 176.47 ($C_{carbene}$), 175.68 (C=O), 124.22 (CH_{NHC}), 120.17 (CH_{NHC}), 105.64 ($C_{2,5}$, Cp), 70.04 ($C_{3,4}$, Cp), 59.16 ($-NCH_2$), 53.91 ($-CH_2OH$), 40.65 ($-NCH_3$), 25.12 (CH_2, 2C), 22.87 (CH_2, 2C), 1.00 (CH_3, TMS, 6C).

ESI-MS (m/z) (+): 563 $[M+H]^+$; 585 $[M + Na]^+$.

4.26. Dicarbonyl-(2,4-bis(trimethylsilyl)bicyclo[3.3.0]nona-1,4-dien-3-one)[1-(2-(imidazolcarbonyloxy)ethyl)-3-methylilidene]ruthenium (11)



10 **CDI** **11**

Scheme 4.29

Dicarbonyl-(2,4-bis(trimethylsilyl)bicycle[3.3.0]nona-1,4-dien-3-one)[1-(2(imidazolcarbonyloxy)ethyl)-3-methylilidene]ruthenium (**10**) (0.029 g,52 μmol) was dissolved in 5 ml of CH_2Cl_2 under inert atmosphere. Three equivalent of carbonyldiimidazole (**CDI**) (0.025 g, 156 μmol) were added to the solution and the reaction mixture was stirred for 24h at room temperature. The solution was then extracted with water (3x20ml). Water traces were removed from the organic solution with $MgSO_4$ and the solvent was removed under vacuum. The yellow solid was characterized by IR, ^{1}H-NMR, ^{13}C-NMR and ESI-MS and identified as Dicarbonyl-(2,4-bis(trimethylsilyl)bicyclo[3.3.0]nona-1,4-dien-3-one)[1-(2-(imidazolcarbonyloxy)ethyl)-3-methylilidene]ruthenium (**11**) obtained with 79% yield.

IR (CH_2Cl_2): ν(C=O): 1998 cm^{-1}, 1935 cm^{-1}; ν(C=O, -NHC(O)O-): 1768 cm^{-1}; ν(C=C): 1605 cm^{-1}, 1566 cm^{-1}.

^{1}H-NMR (599,7 MHz, $CDCl_3$):

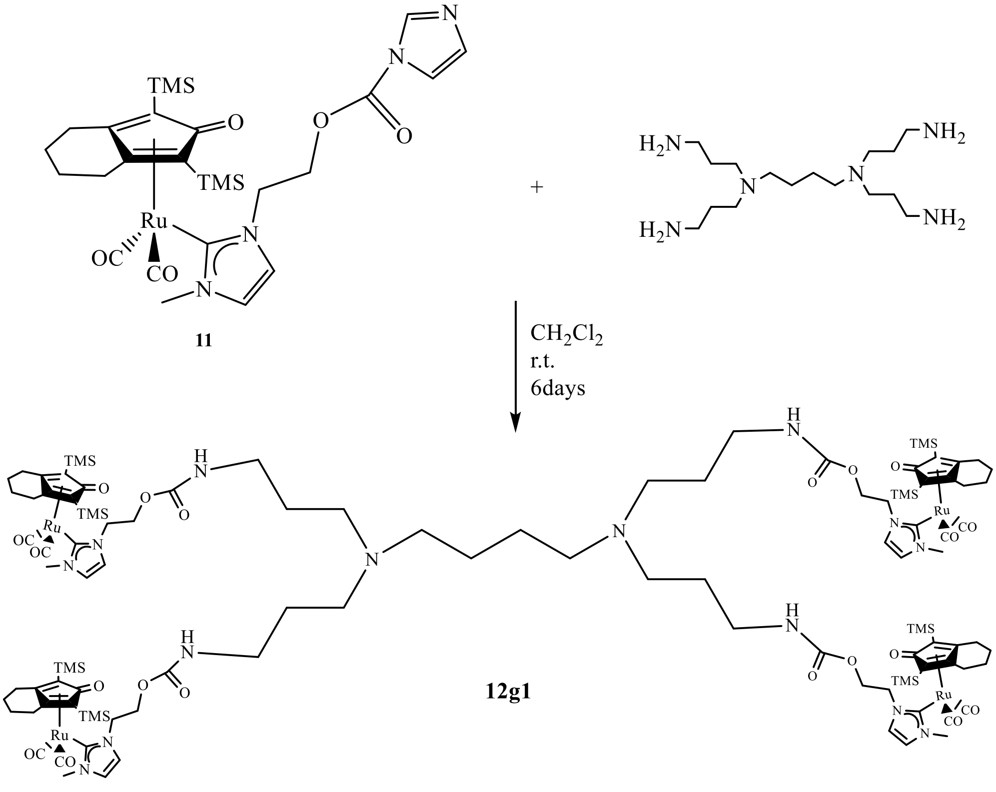
δ (ppm): 8.12 (s, 1H, CH_{Imid}), 7.41 (s, 1H, CH_{Imid}), 7.12 (s, 1H, CH_{NHC}), 7.09 (s, 1H, CH_{Imid}), 7.06 (s, 1H, CH_{NHC}), 4.75 (s, 4H, $CH_{2\ LINKER}$), 3.91 (s, 3H, $-NCH_3$), 2.58 (m, 4H, CH_2), 1.78 (m, 4H, CH_2), 0.19 (s, 18H, TMS).

^{13}C-NMR (150.8 MHz, $CDCl_3$):

δ (ppm) 202.74 (CO), 181.03 ($C_{carbene}$), 179.01 (CO, C_p), 148.15 (-OC(O)N-), 137.00 (CH, Imid), 131.04 (CH, Imid), 124.19 (CH, NHC), 121.66 (CH, NHC), 117.02 (CH, Imid), 106.07 ($C_{2,5}$, C_p), 68.83 ($C_{3,4}$, C_p), 66.93 ($-NCH_2-$), 50.74 ($-CH_2O-$), 40.77 (NCH_3), 24.91 (CH_2), 22.81 (CH_2), 0.60 (CH_3, TMS).

ESI-MS (m/z) (+): 657 $[M+H]^+$; 679 $[M + Na]^+$.

4.27. Synthesis of DAB-dendr-[NH(O)CO(NHC)Cp=ORu(CO)$_2$]$_4$ {NHC =[-CH$_2$CH$_2$-5-CH$_3$-imidazol-2-ylidene]; Cp=O =[2,4-bis(trimethylsilyl)bicyclo[3.3.0]nona-1,4-dien-3-one]} (12g1)



Scheme 4.30

DAB-*dendr*-(NH_2)$_4$ (2.91 mg, 9.2 μmol) and Dicarbonyl-(2,4-bis(trimethylsilyl)bicyclo[3.3.0]nona-1,4-dien-3-one)[1-(2-(imidazolcarbonyloxy)ethyl)-3-methylilidene]ruthenium (**11**) (0,027 g, 41.2 μmol) was dissolved in 5 ml of CH_2Cl_2

under inert atmosphere. The reaction mixture was stirred at room temperature for six days. At the end solvent was removed under vacuum and the brown solid was washed with water (3x20mL). The product, obtained in quantitative yield was identified as (**12g1**).

IR (CH_2Cl_2): ν(CO):1999 cm^{-1}, 1937 cm^{-1}; ν(C=O, -NHC(O)O):1760 cm^{-1}.

^{1}H-NMR (399.9 MHz, $CDCl_3$):

δ (ppm) 7.15 (m, 4H, CH_{NHC}), 6.99 (m, 4H, CH_{NHC}), 4.52 (s, 8H, $CH_{2\ linker}$), 4.33 (s, 8H, $CH_{2\ linker}$), 3.87 (s, 12H, $-NCH_3$), 3.19, 2.43, 238, 1.61, 1.41 (br, 32H, CH_2, DAB-dendr), 2.53 (s, 16H, CH_2), 1.76 (s, 16H, CH_2), 0.18 (s, 72H, TMS).

^{13}C-NMR (150.8 MHz, $CDCl_3$, g-HSQC, g-HMBC):

δ (ppm) 202.51 (CO), 181.10 ($C_{carbene}$), 177.28 (CO, C_p), 155.96 (-OC(O)N-), 123.63 (CH, NHC), 122.22 (CH, NHC), 106.20 ($C_{2,5}$, C_p), 68.41 ($C_{3,4}$, C_p), 63.57 ($-NCH_2-$), 51.61 ($-CH_2O-$), 40.52 ($-NCH_3$), 24.74 (CH_2), 22.79 (CH_2), 0.63 (CH_3, TMS).

ESI-MS (m/z) (+): 2669 $[M+H]^+$.

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