1. General Introduction

1.1. Introduction

Organometallic compounds are defined as materials which possess direct, more or less polar bonds between metal and carbon atoms.[1] Since Zeise synthesized the first organometallic compound in 1827, $K[PtCl_3(CH_2=CH_2)]$, organometallic chemistry has grown enormously although most of its applications have only been developed in recent decades. Some of the key points in the fast expansion of organometallic chemistry are the selectivity of organometallic complexes in organic synthesis (discovered with Grignard reagents at the end of the 19th century),[2] and the interesting role that metals play in biological systems (e.g. enzymes, haemoglobin, etc.).[3]

One of the most interesting things about organometallic compounds is that they can be used as homogeneous catalysts in processes where all the reacting partners are present in one phase, usually the liquid one. Transition metal complexes act in different ways within the catalytic reaction: they bring the substrates together, activate the substrates by coordinating to the metal, and lower the activation energy of the reaction between substrates. In general the use of a homogeneous catalyst in a reaction provides a new pathway, because the reactants interact with the metallic complex. These interactions make it possible for thermodynamically favoured reactions, which need long time to reach equilibrium, to be accomplished within hours. Therefore, homogeneous catalysts can be used to synthesize compounds which can hardly be obtained by conventional methods.

One interesting application of homogeneous catalysis is enantioselective (asymmetric) catalysis. It deals with the synthesis of enantiopure compounds, which are active ingredients of pharmaceuticals, agricultural products, flavours, fragrances and some advanced materials.[4]

Life itself depends on chiral recognition because living systems identify the enantiomers as different substances and interact with them in different ways. For example, for many drugs only one of these enantiomers has a beneficial effect, being the other enantiomer either inactive or even toxic. Although the resolution of racemates is a way of obtaining enantiopure compounds, enantioselective synthesis enables just a single enantiomer to be obtained. The advantage that enantioselective

catalysis has over stoichiometric synthesis is that one organometallic catalyst molecule can generate millions of chiral product molecules. Catalytic synthesis generally also generates smaller amounts of chemical waste than stoichiometric organic synthesis. Therefore, the search for homogeneous enantioselective catalysts is one of the most interesting trends in organometallic chemistry.[5]

The success of organometallic catalysts lies on the easy modification of their environment by ligand exchange. A very large number of different types of ligands can coordinate to transition metal ions. Once the ligands are coordinated, the reactivity of the metals may change dramatically. In fact the rate and selectivity of a given process can be optimized to the desired level by controlling the ligand environment. Understanding the role played by the different ligands coordinated to a metal is one of the main themes in homogeneous catalysis.[6] Because organometallic complexes are highly soluble in organic solvents, their behavior throughout the catalytic reaction can be studied using different techniques by performing *in-situ* measurements. Fundamental knowledge about the catalytic systems and studies about the steps of the catalytic processes can help to improve the efficiency of the catalysts. In this respect, kinetic studies and stoichiometric model reactions with well-defined transition metal complexes are used to elucidate the steps of the catalytic cycle. The use of labelled compounds allows the spectroscopic identification of intermediates.

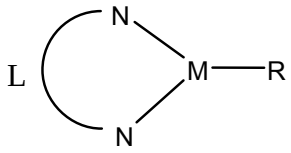
1.2. Amide complexes for catalysis

The design of an appropriate ligand sphere is the most important part in catalysis. The nature of ligand (type, size, basicity, capabilities of hard/soft ligand functionalities) promptly affects something such as mononuclearity, cation size, Lewis acidity, in which co-determine the reactivities of the complexes. These can be used for the activation of well defined reaction centers, allowing to adopt the useful resulting compounds for different applications. As for example, the activation of small unreactive molecules, homogeneous catalysis and some organic transformation can be named.[7]

Over the past few years, an intense search has therefore developed, in both academic and industrial research laboratories, for new-generation catalysts. Beside the well established cyclopetadienyl ligand, nowadays most significant recent

developments have occurred with non-cyclopentadienyl ligand complexes particularly amide ligand complexes as catalyst for hydroamination, hydrosilylation, polymerization and Tishchenko reaction. Hill and co-workers[8] reported a series of mononuclear (bisphospinimino)-methyl [{HC(C(Me)$_2$N-2,6-*i*Pr$_2$C$_6$H$_3$)$_2$}$_2$] derivatives of the bistrimethylsilylamide of heavier alkaline earth metals (Ca, Sr, Ba) and its catalytic activity for hydroamination. In separate work Doye and co-workers developed group IV amide complexes for catalytic hydroamination and sequential hydroamination/hydrosilylation.[9]

In all metallocenes and noncyclopentadienyl rare earth metal catalysts, the cyclopentadienyl, amide or alkoxide act as spectator ligand (L) whereas an alkyl or halide or another amide ligand (R) plays the role as leaving group. Thus these catalysts have the general formula L_2MR or LMR_2. [10]



M = Ln

Scheme 1. Complex design for catalytic reaction

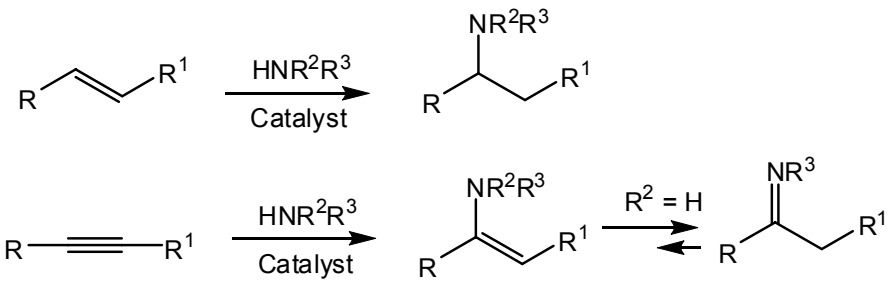
To study the catalytic activity of lanthanide complexes with other bidentate amide ligands such as (bisphosinimino)methanide (BIPM), aminotroponiminate (ATI), 1,2-bis[(2,6-diisopropylphenyl)imino]acenaphthene (DPP-Bian) and *N*,*N*-bis(2,6-dialkylphenyl)formamidine is a great challenge in homogeneous catalysis. Especially lanthanide chemistry is nowadays one of the most extensively studied metal groups in organometallic chemistry because it is versatile and catalyzes a considerable number of organic reactions.[11] The most important lanthanide-catalyzed reactions are those leading to C-C bond formation such as oligomerization and polymerization of alkenes, and to carbon-heteroatom bond formation such as hydroamination, hydrosilylation and Tishchenko reactions.[12]

1.3. Hydroamination

Amines are a highly valuable and relevant class of compounds, both as final products and as versatile intermediates in many processes[13]. Their use ranges from products such as corrosion inhibitors, wetting and surface-active agents, dyes,

dispersing agents, emulsifiers or petroleum additives to highly value-added intermediates for drugs and crops protection agents.[14] With respect to industry, several million tons of amines are produced worldwide per year.[15] The classical well-developed methods for their synthesis are reduction of nitrogen-containing functionalities in higher oxidation states (e.g. reduction of nitriles, imines, azides, nitroso and nitro compounds), nucleophilic substitution of halogens or other potential leaving groups at sp^3 hybridized carbons by ammonia and amines, aminoalkylation, reductive amination of carbonyl compounds.[16] These methods suffer from drawbacks such as by product formation as well as poor selectivity.

Hydroamination, the addition of an N-H bond across carbon-carbon unsaturation, offers an efficient, atom-economical route to primary, secondary and tertiary amines, imines and enamines, by converting readily accessibly alkenes and alkynes into desirable, more highly substituted nitrogen-containing products in a single step (e.g. Scheme 2).[8]



Scheme 2. Hydroamination of alkenes and alkynes.

The hydroamination of alkenes directly provides a convenient access to stable saturated amines, while the hydroamination of alkynes affords relatively reactive amines and imines, which can be used for further synthetic manipulations. However, since alkenes are less reactive and more readily available than alkynes, the hydroamination of alkenes is the more attractive transformation for industrial application.

From a thermodynamical point of view, the direct addition of ammonia or simple amines to alkenes is feasible since corresponding reactions are slightly exothermic or approximately thermoneutral. To illustrate this fact, two representative sets of thermodynamical data for the reactions of ammonia and ethylamine with ethylene are presented in Table 1.[17] Unfortunately, experimental $\Delta H°$ data are not available for the addition of ammonia or amines to alkynes. Therefore, it is not

directly possible to compare the thermodynamics of amine addition to alkynes *versus* that to alkenes. However, the addition of ammonia to acetylene is estimated (AM1-semiempirical calculations) to be ~ 63 kJ mol^{-1} more exothermic than that to ethylene.[18] Regarding this estimation, the hydroamination of alkynes is supposed to be more favorable than the hydroamination of alkenes.

Table 1. Thermodynamic data for the hydroamination of ethylene

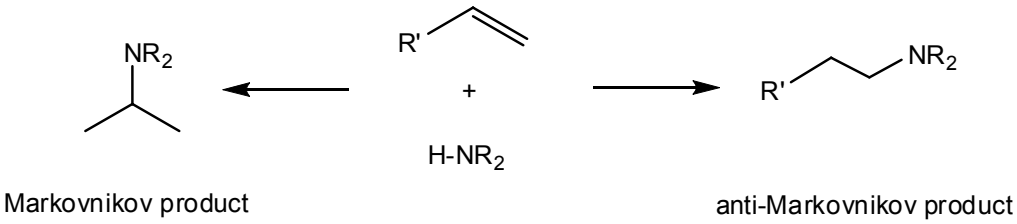
Reaction	$\Delta_R G^\theta$ *(kJ/mol)*	$\Delta_R H^\theta$ *(kJ/mol)*	$\Delta_R S^\theta$ *(kJ/mol K)*
$C_2H_4 + NH_3 \rightleftharpoons EtNH_2$	- 14.7	- 52.7	- 127.3
$C_2H_4 + EtNH_2 \rightleftharpoons Et_2NH$	- 33.4	- 78.7	- 152.6
$C_2H_4 + Et_2NH \rightleftharpoons Et_3N$	- 30.0	- 79.5	- 166.3

In general, a high activation barrier exists for the direct addition of amines across C-C multiple bonds which arise from electrostatic repulsion between the electron lone pair at the nitrogen atom and the electron rich π-bond of the alkene or alkyne.[17, 19] However, it is not possible to overcome this activation barrier simply by performing the hydroamination reaction at elevated temperature. Caused by the general negative reaction entropy $\Delta_R S^\theta$ of the amine addition, the equilibrium of the hydroamination reaction is shifted to the starting materials with increasing temperature. Additionally, in the case of concerted mechanism, there is not a strong interaction between the reactants because of the symmetry forbidden HOMO-LUMO overlapping during the addition of the N-H bond to C-C double bond. Also high energy difference between the orbitals involved, π(C=C)/σ*(N-H) or σ(N-H)/π*(C=C) makes the process unfavourable. Therefore, it is indispensable to identify alternative catalytic procedures for the discussed hydroamination reactions.

Thus, the direct nucleophilic addition of amines proceeds easily only to electron-deficient (activated) systems containing neighbouring functional groups, such as keto, ester, nitrile, sulfoxide, or nitro, usually leading to the anti-Markovnikov products.[20] Catalysis is obligatory for this conversion and hence the functionalization of olefins with anti-Markovnikov regioselectivity is viewed as one of the major challenges of catalysis.[21]

1.3.1. Regioisomer in hydroamination

The specific control for the regioselectivity is a great challenge for the application of catalysts in organic reactions. The hydroamination of asymmetric substituted alkenes can proceed principally with Markovnikov- or anti-Markovnikov regioisomer.[22]



Scheme 3. Regioisomer products in hydroamination.

The former is usually favoured as a consequence of the higher stability of the intermediate carbenium ion. However, the functionally linear anti-Markovnikov product amine is of great interest for large industrial amines. Particularly the use of amine derivatives as detergents is necessary using the linear, branched product to ensure biodegradability.

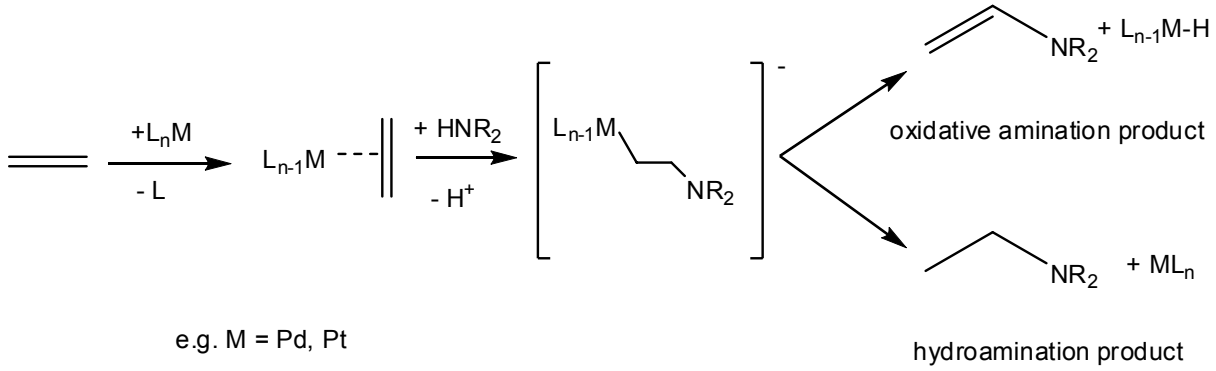
1.3.2. Activation mechanism

The addition of amines to non activated multiple bonds can be promoted by alkali metals, early transition metals (groups 3-5, as well as lanthanides and actinides) or late transition metals (groups 8-10). In principle these metals allow three different strategies for the catalytic activation of aminations. First, activation of the olefin can be effected by π-coordination to a late-transition metal rendering the olefin more susceptible toward nucleophilic attack by the amine. Alternatively, the N-H bond can be activated by deprotonation to the more nucleophilic amide of electropositive alkali or lanthanide metals. Amides are also the key intermediates when an N-H bond is oxidatively added to a transition metal which allows insertion of the alkenes either into the M-N or M-H bond.[9c]

1.3.2.1. Activation of C-C double bond

The activation of a double (C=C) or a triple bond (C≡C) can be made by the coordination to a lewis acidic metal center. Alkene activation is generally accomplished with the late transition-metal catalysts, which render a coordinated π-

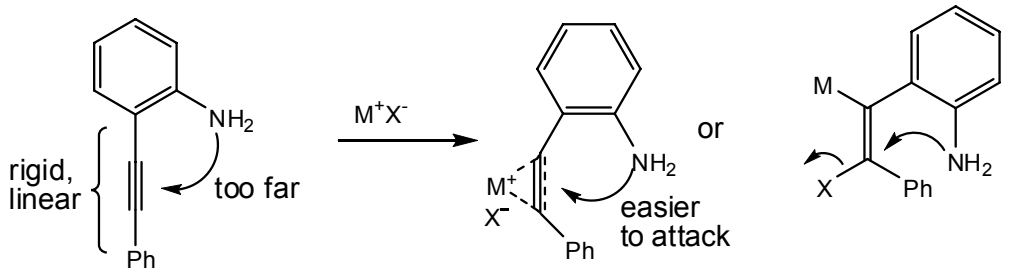
system susceptible to attack by amine nucleophiles. The attack of an amine on a coordinated alkene gives an 2-ammino ethyl complex (Scheme 4). Alkynes are activated in the same way for a nucleophilic attack to yield the corresponding α-ammonio ethenyl complex. ß-hydride elimination from resulting 2-aminoalkyl intermediates leads to the oxidative amination products and protonolysis of the M-C bond releases the hydroamination product. [10c]



Scheme 4. C-C activation by π-coordination to transition metal

Amines -especially aliphatic ones- are strong ligands for electrophilic transition-metal centers and often rather displace than attack coordinated alkenes or alkynes. Thus, their catalytic activation is frequently difficult to achieve in the presence of amines.[23] The stability of amine complexes is typically 2-3 orders of magnitude higher than of alkene and alkyne complexes.[24]

The effectiveness of catalysts like [Pd(triphos)]$(CF_3SO_3)_2$, (triphos = bis-(2-diphenylphosphinoethyl)-phenylphosphine), for cyclization of 2-(phenylethylnyl)-aniline provides evidence for the reaction pathway involving coordination of C-C triple bond to the metal. For this substrate attack of the amine at the alkyne carbon would be impossible without prior coordination to the metal since the molecule is too rigid to bend around. Coordination of C-C triple bond to a metal decreases the bond angle at the alkyne carbons, allowing the amine group to attack the alkyne carbon (eqs. 1).[25]

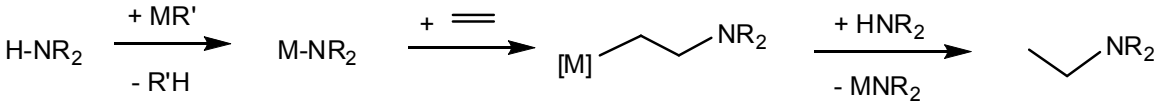


Scheme 5. Facile cyclization of 2-(phenylethynyl)aniline indicating a reaction pathway involving coordination of the C-C triple bond to the metal.

During the nucleophilic attack an electron pair is transferred from the lone pair of the amine to the carbon atom coordinated to the metal. This charge transfer is favored for a positive metal center as compared to a neutral one.

1.3.2.2. Activation of N-H bond

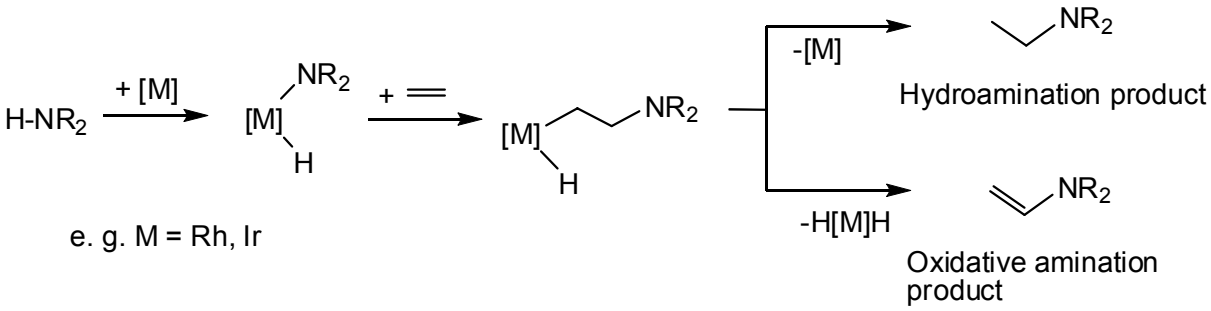
Another approach to amine activation utilizes alkali-, alkaline earth metals or lanthanides to deprotonate the amine to the corresponding amide which is highly nucleophilic and directly attacks an alkene (Scheme 6). The electronic repulsion between the negatively charged amide and the electron rich π-system of the alkene which leads to a high activation energy for the nucleophilic attacks is weakened in the vicinity of the metal ion.



Scheme 6. Amine activation via metal bond formation

1.3.2.3. Amine activation by oxidative addition

An alternative amine activation route uses oxidative addition of an H-NR_2 bond to an electron rich, coordinatively unsaturated, metal center ML_n. The reaction process forms a hydrido amido complex [$MH(NR_2)$] which enables the subsequent insertion of the alkene into M-N bond generating a hydrido 2-aminoalkyl complex. Reductive elimination of the product alkylamine regenerates the metal center in the low oxidation state (Scheme 7). The oxidative addition requires that an electron pair of the metal is available for the formation of one of the two new metal-ligand bonds.



Scheme 7. Mechanism for the coupling promoted by electrophilic late transition metals.

1.3.3. Hydroamination and oxidative amination of alkenes

A lot of examples have been reported in term of amine- or alkene activation. The possibilities and the limits of applied catalyst systems were introduced in the following. Beside the single reports about the hydroamination of alkenes with e. g. zeolite-,[26] Copper-,[27] Ruthenium-,[28] and Iron[29] catalysts could be emphasized five catalyst systems in particular for hydroamination: Lanthanide-, Alkalimetalamide catalyst type systems, which use the late transition metals Palladium, Iridium or Rhodium.

1. 3.3.1. Organolanthanide-catalyzed hydroamination

Marks *et al.* reported the first intramolecular hydroamination/cyclization of aminoalkenes and aminoalkynes by using organolanthanide catalysts.[30] They showed that organometallic rare earth metal complexes e.g. $(Me_5Cp)_2LnE$, $Me_2Si[(\eta^5\text{-}C_5Me_4)(^tBuN)]LnE$ (E = H, $N(SiMe_3)_2$, $CH(SiMe_3)_2$, Ln = La, Nd, Sm, Y, Lu)[30] and homoleptic $Ln[N(SiMe_3)_2]_3$ [31] are suitable for the hydroamination/cyclization of terminal alkenes, 1,3-dienes, allenes and alkynes to corresponding cyclic amines, enamines or imines with highly efficient, regiospecific corresponding five- and six-membered nitrogen heterocycles.[32] In most reactions high turnover frequencies (TOF) were achieved at room temperature, however the formation of six and seven membered rings required elevated temperature.

The highest TOF occurred in the five membered ring syntheses and it can be enhanced by the insertion of alkyl substituent at internal carbon atom on the ß-position from amine of the substrate (Thorpe-Ingold effect).[33] The systematic study showed that not only terminal olefins, but also C-C unsaturated compounds, such as 1,2-disubtituted internal aminoalkenes,[34] 1,1-disubstituted aminoalkenes,[35] aminoalkynes[31,32], aminoallenes [36] and conjugated aminodienes [37] can be catalytically hydroaminated (Table 2). Hydroamination of aminoalkynes exhibited much higher turnover frequencies than terminal aminoalkenes (entries 5). The cyclization of aminoalkynes showed that the reactivity is dependent on the alkyne terminal substituents. The reactivity decreases in descending order R = $SiMe_3$>H>Me>Ph.

Kinetic study indicates that the reaction rate is zero order in the amine subtrates and first order in the catalyst concentration. Isotope labelling experiments