Synthesis and Application of Nano-Structured Metal Catalysts

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General Introduction

Chapter 1

Abstract

This chapter provides a general overview about metal nanoparticles, methods for their synthesis, and their catalytic applications. Also, general aspects and recent advances in Ullmann and Hiyama coupling, and click chemistry are discussed. The motivation and objective for the research presented in this thesis are presented at the end of the chapter.

1.1. Catalysis

Catalysis is a key phenomenon in chemical transformations. The importance of catalytic processes can be summarized by two facts: no life form would exist without enzymes, and the modern society could not have reached the actual degree of development without the catalysts. Catalytic reactions were already used in ancient times, e.g. the sugar fermentation to produce ethanol is a reaction catalyzed by enzymes (biocatalysts), used since always for the wine production. However, the underlying principle of catalysis was not recognized at the time. The scientific development of catalysis only began about 200 years ago, and its importance has grown up to the present day.

The term 'catalysis' comes from the Greek noun 'katalyein' (κατάλυσις = *katá* (down) and *lyein* (split)) and it was introduced as early as 1835 by Berzelius in order to explain various decomposition and transformation reactions.[1] However, the definition that is still valid today is due to Ostwald[2]: "a catalyst accelerates a chemical reaction without affecting the position of the equilibrium." Apart from accelerating reactions, catalysts have another important property: they can influence the selectivity of chemical reactions. This means that completely different products can be obtained from a given starting material by using different catalyst systems. Industrially, this targeted reaction control is often even more important than the catalytic activity.

Catalysts have been successfully used in the chemical industry for more than 100 years; e.g. the synthesis of sulfuric acid or the conversion of ammonia to nitric acid. The growing environmental concern demands the development of "green" production methods, the automobile exhaust control and purification of off-gases from power stations. Catalysis is the solution to this problem. In fact 75 % of all chemicals are produced with the aid of catalysts; in newly developed processes, the figure is over 90 %. Many organic intermediate products, required for the production of plastics, synthetic fibers, pharmaceuticals, dyes, crop-protection agents, resins, and pigments, can only be produced by catalytic processes.[3] In summary, without catalysts, the chemical industry would not have developed the way it has, and the world would not be as we know it.

1.2. Carbon–Carbon coupling reactions

Carbon–carbon coupling reactions are among the most important transformations in organic synthesis, as they make it possible to build up complex structures, as bio-active molecules developed for drugs and agrochemicals, from readily available components in diverse ways. Since the first carbon–carbon bond forming in the acetic acid synthesis 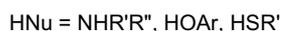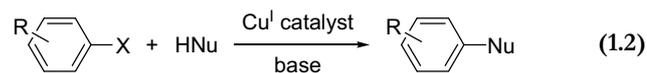by Kolbe in 1845,[4] a large number of metal-catalyzed reactions has been developed over the last forty years.[5] These methods acquired efficiently the ability to forge carbon–carbon bonds between or within functionalized and sensitive substrates. Moreover, it provided new opportunities in total synthesis but also in medicinal and process chemistry, chemical biology and nanotechnology. Few examples of the reactions that are transition metal-catalyzed include the carbonylation of alkenes, the allylic alkylation, the co-polymerization of alkenes and CO, the hydroarylation, cross-coupling reactions, the Sonogashira reaction, the 1,4-addition to dienes, etc. Numerous reviews[6-8] and books[5,9] have covered the topic in the last years.

The metal-mediated carbon–carbon coupling reactions can be classified into two main groups:

(1) *The homocoupling of aryl halides or Ullmann reaction.* The "classic" Ullmann reaction (**Equation 1.1**) is the stoichiometric coupling between two molecules of aryl iodide with one of copper metal to form a symmetric biaryl.

$$2 \ R\text{—}\langle \rangle\text{—}I \ + \ 2\,Cu \ \xrightarrow{\ \Delta\ } \ R\text{—}\langle \rangle\text{—}\langle \rangle\text{—}R \ + \ 2\,CuI \qquad (1.1)$$
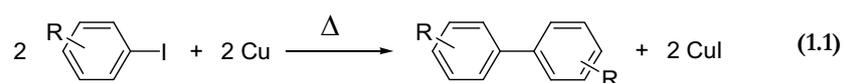
There are also the so-called 'Ullmann-type' reactions consisting on the copper-catalyzed nucleophilic aromatic substitution in aryl halides (**Equation 1.2**). The most common of these is the 'Ullmann ether synthesis' between substituted phenoxides and aryl halides.[10]

$$R\text{—}\langle \rangle\text{—}X \ + \ HNu \ \xrightarrow[\text{base}]{Cu^I \ \text{catalyst}} \ R\text{—}\langle \rangle\text{—}Nu \qquad (1.2)$$

HNu = NHR'R'', HOAr, HSR'

Copper mediated Ullmann reactions have been used for the formation of aryl–carbon and aryl–heteroatom bonds. Despite their several limitations, remain the reactions of choice in large and industrial scale. An overview in the mechanistic details and the development of alternative copper-catalyzed methodologies for the Ullmann reactions will be examined later in this chapter.

(2) *Cross-coupling reactions*. Here, an organometallic reagent R'-M reacts with an organic compound R-X (where X is a leaving group) and is catalyzed often by a transition-metal complex of e.g. palladium or nickel (**Scheme 1.1**).

$$R\text{-}X \; + \; R'\text{-}M \; \xrightarrow[\text{catalyst}]{\text{Pd or Ni}} \; R\text{-}R' \; + \; M\text{-}X$$

R, R' = aryl,   M = MgY Kumada
     vinyl BY_2 Suzuki
     benzyl ZnY
     allyl AlY_2 } Negishi
     alkyl SnY_3 Stille
                      SiY_3 Hiyama

X = Cl, Br, I, sulfonate
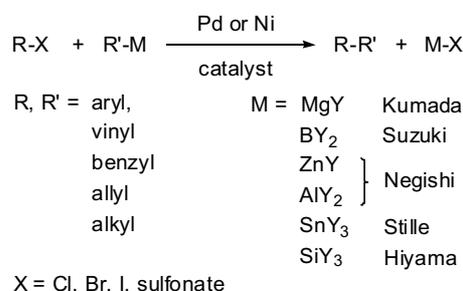
Scheme 1.1. Overview of palladium- and nickel-catalyzed cross-coupling reactions.

The most important examples include the Grignard cross-coupling or Kumada coupling,[11] the Suzuki-,[12,13] Negishi-,[6] Stille-,[7] and the Hiyama reaction.[14] A simplified catalytic cycle consists of three elementary steps (**Scheme 1.2**): oxidative addition of an electrophile, typically an organic halide R–X, onto the metal center; transmetallation to produce diorganometallic intermediates; and final reductive elimination to form cross-coupling products and to regenerate the active catalysts.

Throughout the cycle, Pd or Ni is bound with its ligands, and its reactivity is strongly influenced by the steric and electronic properties of these ligands.[9] The electrophile nature is also very important for the reaction success. A wide range of organic electrophiles can be applied in these reactions. Usually, aryl and vinyl halides are employed (iodides and bromides, rarely chlorides),[9] but also other leaving groups, e.g. triflates, can be used. Unfortunately, the more reactive aryl iodides and triflates are less widely available and more expensive than the corresponding bromides, and especially chlorides because of green chemistry issues.

Therefore, lot of effort has been devoted to the development of the catalysts able to convert chlorides substrates under mild conditions.[15]
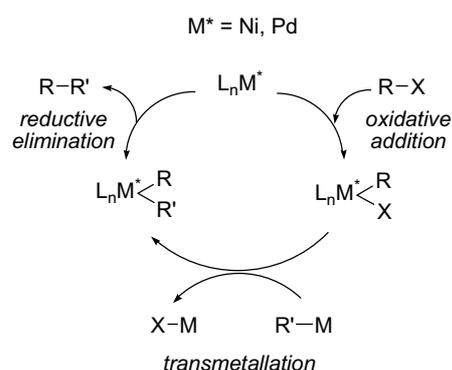
**Scheme 1.2.** Generalized C–C cross-coupling catalytic cycle.

Increasingly, industry seeks more environmentally-friendly C–C coupling processes. Research groups are investigating modifications of the reactions, e.g. trace amounts of catalysts (ppb) that work in water.[16] Also, ligand-free catalysts, solvent-free, or ionic liquids as solvent, are being investigated.[17,18] The work described in this thesis is mainly focused on developing new catalysts or methods for the classic-Ullmann reaction and the Hiyama coupling.

1.2.1. **The Ullmann reaction**

The classic-Ullmann reaction, initially reported in 1901,[19] has been employed for a long time to generate C–C bonds between aromatic nuclei. Typically, two molecular equivalents of aryl halide are reacted with one equivalent of finely divided copper above 200 °C to form a symmetric biaryl and a copper halide. The reaction mechanism has been extensively studied (**Scheme 1.3**). The active species is an organo-Cu^I-complex (Ar–Cu) which undergoes oxidative addition with the second equivalent of halide. This is followed by reductive elimination and the formation of the aryl–aryl carbon bond.

The Ullmann reaction requires harsh reaction conditions such as high reaction temperature and stoichiometric amount of copper. It is also limited to electron deficient aryl halides and has a reputation for erratic yields. This procedure and its variants have been extensively

reviewed in the last decades.[20-24] Since its discovery, some improvements and alternative procedures were introduced.[24] For example, dimethylformamide is a solvent which permits the use of lower temperatures and a lower proportion of Cu. Besides, the use of an activated form of Cu powder, made by the reduction of CuI with potassium, allows the reaction to be carried out at even lower temperatures (~85 °C) with improved yields. As the reaction is heterogeneous, it can also be accelerated considerably using ultrasound.[25]
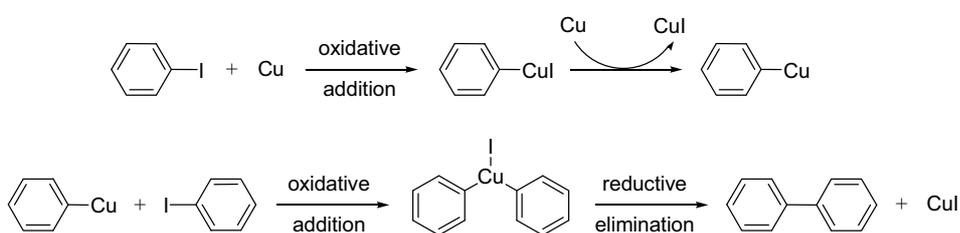

Scheme 1.3. Mechanism for the classic stoichiometric Ullmann reaction.

Another major limitation of the Ullmann reaction is that it gives only symmetrical biaryls. Several attempts to synthesize unsymmetrical biaryls have been made, and some success has been achieved by associating aryl halides of different reactivities. However, these extensions of the original Ullmann reaction to unsymmetrical biaryls formation require the use of a significant excess of the "activated" aryl.[26]

Among the alternatives to the stoichiometric Ullmann reaction with copper, there are several palladium-catalyzed processes, based on both homogeneous[27] and heterogeneous[28,29] systems. Numerous reductive and oxidative mechanisms have been proposed for these palladium-catalyzed coupling protocols. The common factor in all of them is the use of the $Pd^{2+} \leftrightarrow Pd^{0}$ redox cycle.[30] The heterogeneous palladium systems benefit from easy catalyst separation and recycling, but still require a reducing reagent such as isopropanol,[31] formate salts,[29] hydrogen gas,[32] or zinc metal,[33] to complete the catalytic cycle. Intensive research is still being done to find an industrial alternative to the classic-Ullmann reaction.

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1.2.2. **Hiyama coupling**

The Hiyama coupling is a metal-catalyzed reaction of organosilanes with organic halides or triflates **(Equation 1.3)**. It was first reported by Hatanaka and Hiyama in 1988.[14] The reaction has became very popular for industrial purposes because of its many advantages such as low environmental impact, high atom efficiency, and safe handling of organosilicon compounds compared with the coupling reactions of organoboron, organozinc, or organotin compounds.[9]
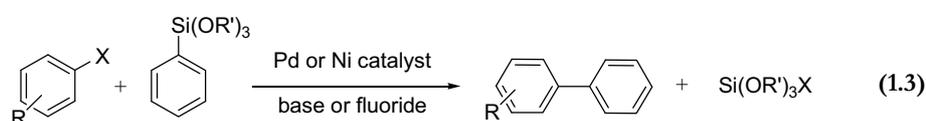
$$X = Cl, Br, I, OTf$$

Typically, the Hiyama reaction is promoted by activation of the organosilane with fluorides or a base. The polarization of the Si–C bond is crucial for the success of reaction.[34] The activation of the silane compound with a base or fluoride ions, e.g. tris-(dimethylamino)-sulfonium trimethyldifluorotrimethylsilicate (TASF) or tetrabutylammonium fluoride (TBAF) leading to a pentavalent silicon compound is a first necessary step (see **Scheme 1.4**).[9] This intermediate is more active for transmetallation. Without the added fluorine the organosilicon compound is simply too stable. The reaction mechanism proceeds through the usual oxidative addition, transmetalation and reductive elimination sequence.
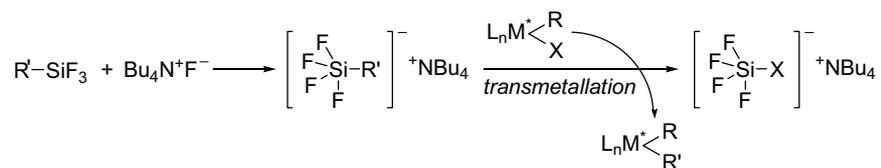
Scheme 1.4. Activation of the silicon compound by fluorine compounds for the transmetallation step.

The reaction rate can be increased by using silanes with R' groups such as fluoro or alkoxy instead of alkyl.[35,36] Another approach uses silacyclobutanes.[37] These small-ring silanes offer enhanced Lewis acidity because angle strain is released when the silicon undergoes transition from tetrahedral to pentavalent, which favors the activation.⁻

Although many improvements in the reaction conditions have been reported, the usual catalysts for Hiyama coupling are organometallic Pd^{2+} complexes, where a large mol% of catalyst and big excess of base is used.[37,38] For these reasons, intensive research is done to make the Hiyama coupling a better alternative to the Suzuki- or the Stille coupling.

1.3. Click Chemistry

'Click chemistry', a term introduced by Sharpless in 2001,[39] describes chemistry tailored to generate substances quickly and reliably by joining small units together. This is inspired by the fact that nature also generates substances by joining small modular units. Proteins are made from repeating amino acid units and sugars are made from repeating monosaccharide units. The connecting units are based on carbon–heteroatom bonds rather than carbon–carbon bonds. A computational study by Guida *et al.*[40] suggests that the pool of 'drug-like' compounds (<30 non-hydrogen atoms, <500 Daltons; only H, C, N, O, P, S, F, Cl and Br; likely to be stable in the presence of water and oxygen) is as large as 10^{63}. Click chemistry in combination with combinatorial chemistry, high-throughput screening and building chemical libraries speeds up the organic synthesis of new pharmaceuticals[41] due to the large number of possible structures.[39]

The following criteria are encouraged by click chemistry: modular application and wide in scope; high chemical yield and atom economy; single reaction product and inoffensive by-products; stereospecific; simple reaction conditions; readily available starting materials and reagents; no solvent involved or a benign solvent, preferably water; easy product isolation; fast reaction; and strong thermodynamic driving force (exothermic reactions make reactants "spring loaded"). Many of the criteria are subjective; and even if measurable and objective criteria could agree upon, it is unlikely that any reaction will be perfect for every situation and application.

However, several reactions have been identified which fit the bill better than others (**Scheme 1.5**); e.g. addition reactions to carbon–carbon double bonds like epoxidation[42] and dihydroxylation;[43] and the consecutive nucleophilic substitution to the small strained rings to form difunctionalized compounds.[39] Among these reaction are also, cycloadditions such as the Huisgen 1,3-dipolar addition to give 5-memebered heterocyles;[44] and the formation of aromatic heterocycles, oximes ethers and hydrazones from carbonyl compounds.

The Huisgen 1,3-dipolar cycloaddition between azides and terminal alkynes,[45] has rapidly become the most popular click reaction to date.[46] Fokin and Sharpless independently described it as *"the cream of the crop"* of click chemistry, firmly placing it among the most reliable processes fitting the click criteria.[39] Although azides and alkynes display high mutual reactivity, individually these functional groups are two of the least reactive in organic synthesis. They have been termed bio-ortogonal because of their stability and inertness towards the functional groups typically found in biological molecules.[46]
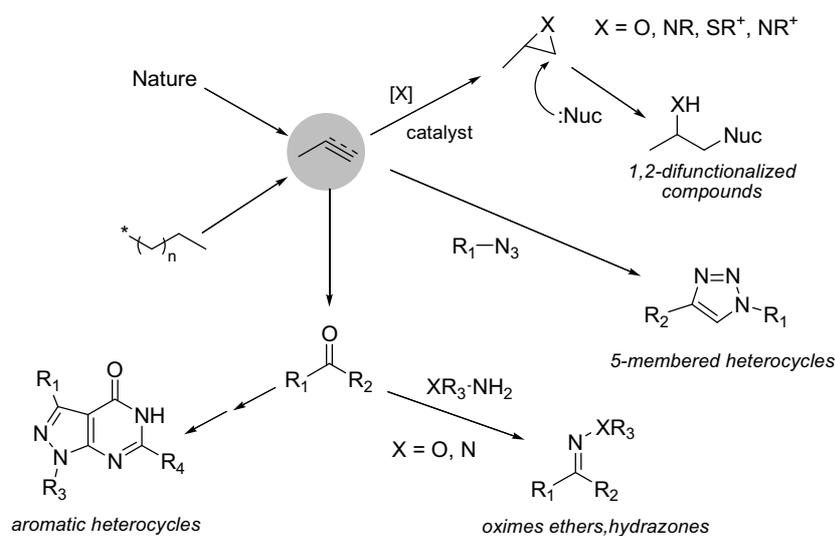
Scheme 1.5. The most common click reactions; where the starting materials are obtained from nature or by simple synthetic methods.

The formation of triazoles *via* the cycloaddition of azide and [47]mechanism of these cycloadditions was not fully realized until the 1960's.[45] The reaction generates a mixture of

1,4- and 1,5-disubstituted triazoles (**Equation 1.4**). Various attempts to control the regioselectivity have been reported without much success until the discovery of the Cu^I-catalyzed reaction in 2002,[48,49] which exclusively yields the 1,4-disubstituted 1,2,3-triazole.

$$R\overset{-}{\underset{}{N}}-\overset{+}{N}{\equiv}N \quad + \quad R'\text{---}\equiv \quad \longrightarrow \quad R\text{-}N\overset{N\diagdown N}{\underset{R'}{}} \quad + \quad R\text{-}N\overset{N\diagdown N}{\underset{R'}{}} \qquad (1.4)$$
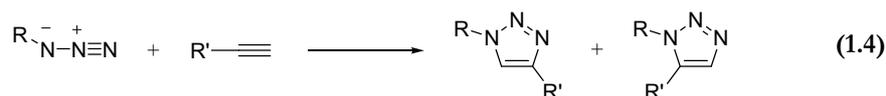
Several commercial sources of Cu^I such as cuprous bromide or iodide, can be employed but the reactions generally must be run with acetonitrile as co-solvent, require a nitrogen base, and sometimes generate unwanted diacetylene and bis-triazole by-products.[48] The reaction works better using the *in situ* reduction of Cu^{II} (e.g. CuSO$_4$) to Cu^I with sodium ascorbate in aqueous alcoholic solvents allows the formation of 1,4-triazoles at room temperature in high yield with less than 2 mol% catalyst loading.[47] As Cu^I is unstable in aqueous solvents, stabilizing ligands are effective for improving the reaction outcome, especially if *tris*-(benzyltriazolylmethyl)amine (TBTA) is used. The reaction can be run in a variety of solvents, and mixtures of water and a variety of miscible organic solvents including alcohols, DMSO, DMF, *t*-BuOH and acetone work well.[50] Owing to the powerful coordinating ability of nitriles towards Cu^I it is best to avoid acetonitrile as the solvent. Primary, secondary, and tertiary substituted azides as well as aromatic azides can be utilized. Numerous terminal acetylene components participate in the transformation and the reaction is compatible with various functional groups such as esters, acids, alkenes, alcohols, and amines. The copper-catalyzed reaction was later expanded by Yamamoto and coworkers using a bimetallic catalyst so that triazoles could be obtained from seemingly internal alkynes.[51]

The copper-catalyzed reaction is thought to proceed in a stepwise manner starting with the generation of Cu^I–acetylide (**Scheme 1.6**). Density functional theory calculations[52] show a preference for the stepwise addition ($5 \rightarrow 6 \rightarrow 7 \rightarrow 8$) over the concerted cycloaddition ($5 \rightarrow 8$) by approximately 12 to 15 kcal mol^{-1}, leading to the intriguing six-membered metallocycle.

Due to the reliability and generality of the Cu^I-catalyzed azide-alkyne cycloaddition to generate N-heterocyclic pharmacophores, the reaction has been utilized for various aspects of drug discovery.[46] The development of the Cu^I-catalyzed cycloaddition reaction between

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azides and terminal alkynes has led to many interesting applications of click reactions including the synthesis of natural product derivatives, target guided synthesis[53] and activity-based protein profiling.[54] They are also receiving widespread use in materials and surface science.[55] Most variations in coupling polymers with other polymers or small molecules have been explored.[56] Current shortcomings are that the terminal alkyne appears to participate in free radical polymerizations. Similarly, the use of organic solvents, Cu^I and inert atmospheres to do the cycloaddition with many polymers makes the "click" label inappropriate for such reactions. An aqueous protocol for performing the cycloaddition with free radical polymers is highly desirable.
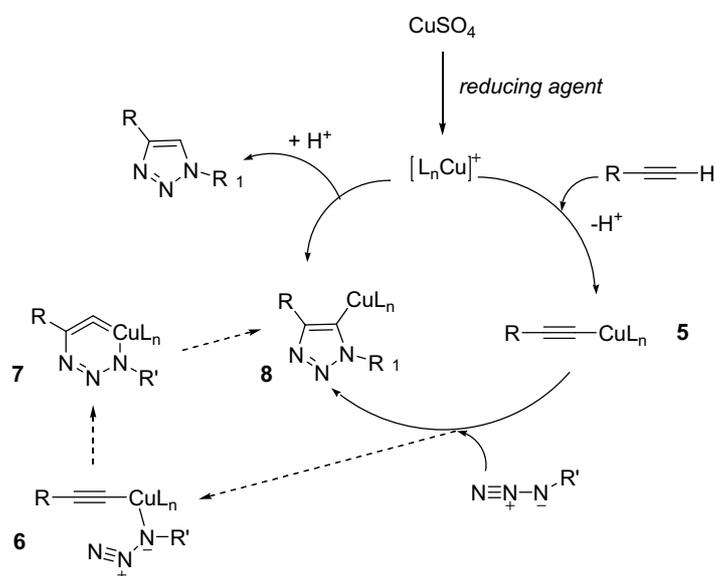
Scheme 1.6. Postulated catalytic cycle for the azide-alkyne coupling.

1.4. Nanoparticles

The 21st century is in many ways the century of nanotechnology. Promises and possibilities range wide: nanometric catalysts open new routes to a variety of products,[57,58] nanomagnets will store information for superfast computers,[59] nanowires will string together nanoelectronic circuits,[60,61] and nanomachines will transform modern medicine.[62] Whether these promises will be fulfilled or not depends also on our understanding of what makes nanoparticles

In the nanoscale regime (**Figure 1.1**), somewhere between the bulk solid and molecular state, nanoparticles show unique properties. Nanoparticles (nanoclusters or nanocolloids) are defined as any type of metallic species with a size between 1-25 nm. They have attracted attention from a wide range of fields, including physics, chemistry, material science, biology and medicine.

Although, generally nanoparticles are considered an invention of modern science, they actually have a very long history, e.g. metal nanoparticles were already used by Roman artisans as far back as in the 4th century for generating a glittering effect on the surface of pottery (**Abstract figure**).[63] They have been also exploited for centuries in diverse areas ranging from pigments and paints to medicines, as well as in photography, agriculture, etc.[64]
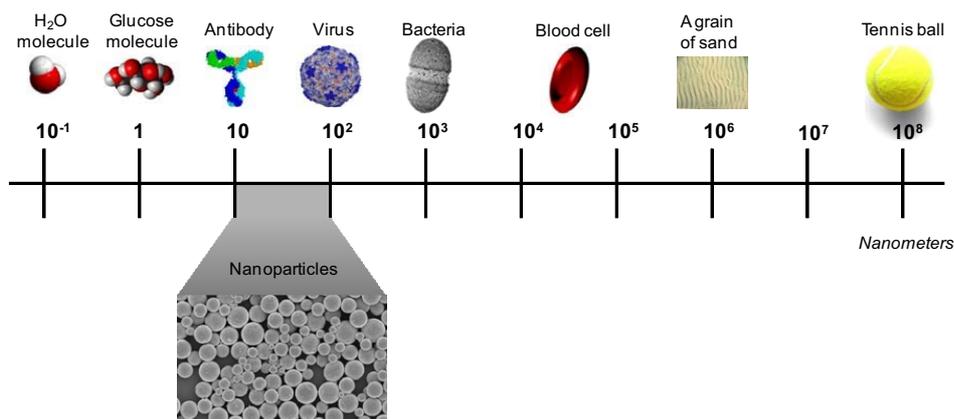

Figure 1.1. Nanoparticles in the nanoscale regime.

But the first scientific study on metal nanocolloids was done by Michael Faraday in 1857.[65] Faraday believed that the bright red color of the colloidal gold was due to the extremely small sizes of the individual particles, which interacted with light in a different manner compared to metallic gold. However, colloid science kept unpopular during many years. The theoretical works of Mie,[66] Gans,[67] and Kubo[68] which were successful in predicting the optical properties and electronic structure of metal particles, Einstein's success in relating Brownian motion to diffusion coefficient,[69] were largely ignored. But thanks to visionaries such as Feynman[70] and his famous lecture *"there are plenty of room at the bottom",* the science of colloids staged a gradual revival in the 1980s. Since then, significant advances in both experimental and theoretical aspects have led to an explosion of interest in the areas of nanoscience and nanotechnology. This is reflected by the number of books and review articles that have been published in the last years.[71-75]

Nanoparticles, owing to their dimensions, exhibit quantum size effects. Physicists predicted that when the particle sizes of clusters are reduced to about 1-10 nm the properties of the cluster would be intermediate between that of individual atoms/molecules and that of the bulk material. Some examples of these properties are lower melting points, increased solid-solid phase transition pressure decreased ferroelectric phase transition temperature, higher self-diffusion coefficient, changed thermophysical properties, and of course a unique catalytic activity, that will be explain in detail further in this chapter.

1.4.1. Stabilization and formation mechanism of nanoparticles

This section will focus in the formation of stable suspension of nanoparticles required for catalysis in liquid phase. The formation of nanoparticles in solution occurs by chemical reactions that result in the formation of stable nuclei and subsequent particle growth. For nucleation to occur, the solution must be supersaturated either by directly dissolving the solute at higher temperature and then cooling to low temperatures or by adding the necessary reactants to produce a supersaturated solution during the reaction.[76,77] When the concentration drops below the critical level, nucleation stops and the particles continue to grow until the equilibrium concentration of the precipitates is reached.

Uniformity of the size distribution is achieved through a short nucleation period. The smaller particles grow more rapidly than the larger ones because of the free energy driving force.

Monodisperse size distribution can be obtained at this stage by either stopping the reaction quickly or by supplying reactant source to keep a saturated condition during the course of the reaction

"Naked" nanoparticles are kinetically unstable in solution, with respect to agglomeration to the bulk. Thus, all preparation methods involve the use of stabilizing agents, which adsorb at the particle surface. The charge or solubility properties keep the clusters suspended, and thereby prevent their aggregation. Stabilization can be achieved by two methods:

(1) *Electrostatic stabilization*. Anions and cations from the starting materials remain in solution, and associate with the metal nanoparticles. The particles are surrounded by an electrical double layer. This results in a Coulombic repulsion between particles that varies exponentially with the interparticle distance as shown schematically in **Figure 1.2**, **left**. The minimum in potential energy at short interparticle distance defines a stable arrangement of particles. Thus, if the electric potential associated with the double layer is sufficiently high, electrostatic repulsion will prevent particle agglomeration.
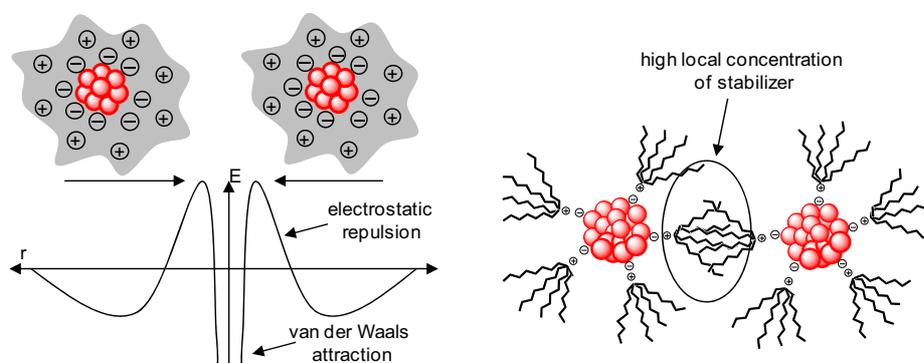
Fig 1.2. Electrostatic stabilization (*left*) and steric stabilization of metal nanoparticles (*right*).

(2) *Steric stabilization*. A second method by which metal particles can be prevented from aggregating is by the adsorption of large molecules such as polymers or surfactants at the surface of the particles, providing a protective layer. The way in which adsorbed large molecules prevent aggregation can be seen in a simplified manner by visualizing the close approach of two particles, each with long chain molecules adsorbed at their surfaces as

shown in **Figure 1.2**, **right**. In the interparticle space the adsorbed molecules would be restricted in motion, fewer conformations will be accessible, causing a decrease in entropy and thus an increase in free energy.

1.4.2. Synthesis of metal nanoparticles

The various methods for synthesizing metal nanoparticles were extensively reviewed by Bönnemann,[78] Schmidt,[74] Finke,[72] Roucoux,[79] Wilcoxon,[80] Chaudret,[81] and Cushing.[82] Big steps have been made in nanoparticles synthesis in the last decade. There are reproducible methods for making structured nanoparticles, with good control over size, shape, and composition. In this respect, nanoparticles fulfill yet the promises of nanotechnology with regard to bottom-up synthesis and device manufacturing. In general, there are four main categories of nanoparticles synthesis:

(1) *Reduction of transition metal salt precursors.* Discovered 150 years ago by Michael Faraday, the 'wet chemical' reduction has become the most common method for making nanoparticles.[83] The first reproducible synthesis was done by Turkevich and co-workers, who prepared 20 nm Au particles by citrate reduction of $[AuCl_4]^-$.[84,85] They also proposed a mechanism for the stepwise formation of nanoparticles based on nucleation, growth and agglomeration.[86]

$$x M^{n+} + nxe^- + \text{stabilizer} \rightarrow M^0_{n\,(\text{cluster})} \qquad (1.5)$$
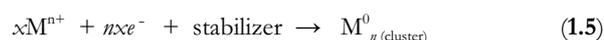
In this approach, (**Equation 1.5**) the reducing agent (e.g. hydrogen, alcohol, hydrazine or borohydride) is mixed with the metal precursor salt in the presence of stabilizing agents (ligands, polymers or surfactants). The latter prevent the undesired agglomeration and formation of metal powders (**Figure 1.3**). The actual size of the nanoparticles depends on many factors, including the type of reducing agent, metal precursor, solvent, concentration, temperature and reaction time.[78,87]
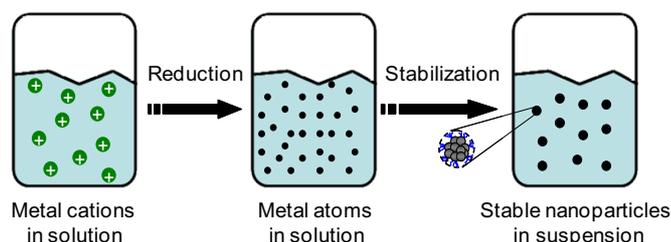
Figure 1.3. Formation of nanoparticles *via* reduction of metal salt precursors.

(2) *Electrochemical synthesis*. This method was developed by Reetz in the 1990s.[88,89] The overall process includes five steps (see **Figure 1.4**):

1. Oxidative dissolution of the sacrificial metal bulk anode.

2. Migration of metal ions to the cathode.

3. Reductive formation of zerovalent metal atoms at the cathode.

4. Nucleation and growth of metal particles.

5. Arresting of the growth process and stabilizing of the particles by protecting agents, e.g., tetraalkylammonium ions.

The electrochemical pathway avoids contamination with by-products resulting from chemical reducing agents, and the products are easily isolated from the precipitate. Further, it allows size-selective particle formation by tuning the current density: high current densities lead to small nanoparticles, and *vice versa*. The particle size can also be controlled by adjusting the distance between the electrodes, the reaction time and temperature, or the solvent polarity.[78]

This method was successfully applied in the preparation of a number of monometallic nanoparticle organosols and hydrosols, including Pd, Ni, Co, Fe, Ti, Ag, and Au. Bimetallic alloys (e.g. Pd/Ni, Fe/Co, or Fe/Ni) are accessible if two sacrificial metal anodes are used simultaneously.[90]

$$M^0 \text{ } anode \quad \rightarrow \quad M^{n+} \text{ } + \text{ } ne^-$$

$$M^{n+} \text{ } + \text{ } ne^- \text{ } + \text{ } stabilizer \quad \rightarrow \quad M^0 \text{ } (nanoparticle)$$

$$M^0 \text{ } anode \text{ } + \text{ } stabilizer \quad \rightarrow \quad M^0 \text{ } (nanoparticle)$$
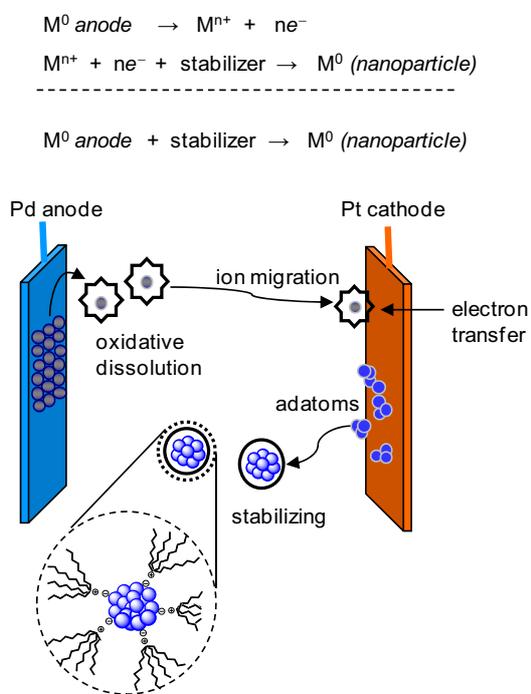
Figure 1.4. Electrochemical formation of $NR_4^+Cl^-$-stabilized Pd nanoparticles.

(3) *Reduction of organic ligands in organometallic precursors.* Starting from low-valent metal complexes, the ligands are reduced typically with H_2 (**Equation 1.6**) or carbon monoxide. The reduced ligands leave the M^0 centre, allowing the clustering of metal atoms.[91]

$$n M(L)_x \text{ } + \text{ } x H_2 \text{ } + \text{ } stabilizer \quad \rightarrow \quad M^0_{n \text{ (cluster)}} \text{ } + \text{ } x L H_2 \qquad (\textbf{1.6})$$
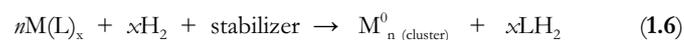
(4) *Metal vapour chemistry.* The atomic vapour of a metal is condensed into a cold liquid, containing a stabilizer. Upon warming, the dissolved metal atoms form nanoparticles. When the liquid itself acts as a stabilizer, the metal vapor can condense with the solvent vapour, giving a solid matrix.[92]

Other less common methods include   redox surface techniques, thermal[93] and photochemical[94] decomposition of metal complex precursors, sonochemical synthesis,[95] and

laser ablation.[96] Alternatively, one can anchor the nanoparticles on a solid support. This approach is popular as a method for catalyst preparation and heterogenization.[87,97]

1.4.3. Catalysis with nanoparticles

Because of the small size, a high percentage of the atoms are surface atoms, leading to increased catalytic activity.[98] Homogenous catalysts are molecularly dispersed with the reactants in the same phase, which gives easy access to the catalytic site but make the separation of the catalyst difficult. Heterogeneous catalysts are in a different phase from the reactants, which facilitates separation but limits access to the active site due to diffusion resistance. Thus, metal nanoparticles, as intermediate case, are attractive catalysts. Since industrial catalysts usually work on the surface of metals, the metal nanoparticles, which possess much larger surface area per unit volume or weight of metal than the bulk metal, have been considered as promising materials for catalysis.

Metal nanoparticles have been used in heterogeneous catalysis for over 50 years.[99] One of the first process using such catalysts is the catalytic reforming for the production of reformulated gasolines.[100] Industrial catalysts containing nanoparticles of 1 nm-Pt on chlorinated alumina were introduced in the 1960s[101] and Pt-Re or Pt-Su bimetallic catalysts (1 nm particles) in the 1970s.[102] In hydrogenation, hydrocracking and aromatization processes, zeolites exchanged with noble[103,104] and non-noble metals[105] are currently used. More recently metal catalysts were successfully employed in automotive catalytic converters.[106] In homogenous catalysis, as early as 1986, Lewis *et al.* envisaged the participation of Pt nanoparticles in catalytic hydrosylilation reactions.[107] Since then, noble-metal nanoparticles catalysts appeared in numerous reports and reactions, from hydrogen peroxide decomposition[108] all the way to Heck cross-coupling.[88,109] Several reviews cover the catalytic applications of nanoparticles.[72,79,110]

A key issue in nanoparticles research is the nature of the cluster catalysis. Various groups have reported in the last years that often the nanoparticles suspension is simply a reservoir for metal atoms/ions that leach into solution. In C–C coupling, for example, leaching of Pd atoms and/or ions has been extensively investigated. There has been much scientific argument regarding the actual catalytic species. Bradley and co-workers,[111] and El-Sayed,[112] reported that low coordination sites on the clusters catalyse the reaction. Shmidt,[113] Arai,[114]

de Vries,[115-117] and Reetz,[118] suggested a homogeneous mechanism in which the nanoparticles act as "reservoirs" of active Pd atoms or ions. Conversely, Dupont and co-workers[119] argued for the participation of nanoparticles in Heck coupling reactions in ionic liquids. Several papers show, mainly for hydrogenation reactions, that soluble metal precursors often form metal nanoparticles as the actual catalysts.[120,121] Currently, there are three promising approaches for dealing with the leaching problem: The first is by immobilizing the nanoparticles on a solid surface. This cuts down the leaching, but also reduces substrate accessibility.[122] Alternatively, biphasic separation using ionic liquids can minimize leaching while still keeping the nanoparticles accessible.[123] Another strategy employs nanoparticles suspensions knowing that leaching occurs, and thereby maintaining a low concentration of very active homogeneous ligand-free catalysts in solution. The de Vries group at DSM has recently demonstrated this approach for Pd-catalysed Heck reactions.[117]

1.5. Metallo-organic hybrid materials

At every significant step in the astronomical advance that mankind has made since the nomadic age lays the discovery of better materials. Besides the materials themselves, the process involved in utilizing these materials are also critical for the advancement of the civilization. One way to improve the material properties is to mix two or more compounds and its properties are either improved or entirely new compared with the nature of each compounds separately, or its qualities are a direct result of the simply added up properties of the compounds used. This is the generally accepted definition for composites.

A prominent example concerns the sol-gel doped materials. They are porous metal oxides confining active species. The initial discovery was made by Avnir and Reisfeld,[124] who first conceived the alkoxide gelation process and to verify the activity of the glass. It was rapidly established that any organic molecules, including enzymes, could be entrapped and dispersed within the *inner* porosity of such glasses with full retention of the chemical activity and marked stabilization of the entrapped dopant molecules. The domains of organic chemistry and ceramic materials were merging and the new era of inorganic-organic hybrid materials

had started.[125,126] These materials found useful applications practically all across modern chemistry and biochemistry.[127-130]

The next step for Avnir and co-workers from a similar approach was the doping of metals with organic molecules. The motivation is based on the fact that organic and bioorganic molecules represent a very rich library of properties that metals are devoid of. The traditional properties and applications of metals will then merge with the diverse properties of organic molecules. The incorporation of a molecule within the sea of electrons of a metal, will affect its physical and chemical properties. Various useful applications have been already demonstrated, including the physical alteration of metal properties, the formation of new catalysts with superior performances, as well as the induction of new unorthodox properties to the metals.

$$dopant + MX + red + H_2O \rightarrow dopant@M^0 + oxid + HX$$

△ Metal precursor (MX)	∿ Dopant
◆ Reducing agent	● M^0
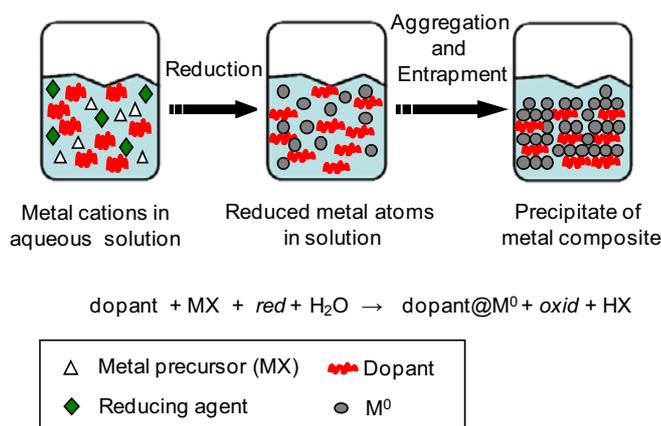
Figure 1.5. Entrapment procedure, where the doped metal is represented by 'dopant@metal', e.g. Nafion@Ag.

The general method of preparation of these metallic composites involves a room temperature metal synthesis by the chemical reduction of the cation, which is carried out in the presence of the desired organic molecule, with a carefully selected reducing agent **Figure 1.5**. The entrapment methodology can be applied for different types of molecules including hydrophilic (Congo-red, Safranin-O and Thionin) and hydrophobic (Sudan-III) dyes and polymers (Nafion, PVA, PVBA and PSSA). So far, the feasibility of the entrapment has been

proven on silver, copper and gold. Studies on the material structure showed physical caging inside partially closed pores, the walls of which are the faces of nanocrystallites. The entrapped molecules showed an interesting feature: they remain accessible to reaction with substrates diffusing in through the pore nano-network. This was proven by applying the material to the catalysis of typical organic reaction. e.g. Congo-red@Ag, in which Congo-red improved the performance of Ag as catalyst in the methanol oxidation to formaldehyde.

In summary, these new composite materials, at the border between metals and organic molecules, comprise the practical opening of a new field within materials science. These materials are expected to have an impact wherever metals are used such as catalysis, electrochemistry, magnetism, corrosion protection, etc.

1.6. Motivation and aim of the thesis

In the past, industrial chemical processes were mainly driven by the demands of cost and efficiency, in the absence of true awareness of the adverse effects on the environment. Since then, considerable knowledge has been gained in homogeneous, heterogeneous, supported, and biphasic catalysis, which now helps to minimize the environmental impact. In this context, metal nanoparticles catalysts can enhance selectivity, efficiency and atom economy.

The main goal of this thesis was to synthesize, characterize and develop different metal nanoparticles systems as alternative ligand-free catalysts for important reactions in the synthesis of fine chemicals. We also developed a new synthetic method for core/shell nanoclusters catalysts combining an inexpensive nickel core with a palladium shell.

Detailed knowledge of the catalysis nature is essential for processes optimization. Thus, the mechanistic understanding of the cluster catalysis was a strong motivation in the work done in every chapter of this thesis, since a better insight into the catalytic reaction mechanism can help us to design better catalysts.

Finally, the challenge of tailoring and developing new and better materials motivated us to move all the way to the organically-doped metals (the opposite concept of organometallic

complexes). The properties of metal catalysts are tailored by ligands around their coordination sphere, in the case of homogenous catalysis, or by the solid support, in the case of heterogeneous catalysis. By doping a metal with small organic impurities, an exciting and simple methodology is opened to induce new properties to the metals.

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