Towards a sustainable synthesis of aromatic isocyanates : by the palladium diphosphane catalyzed reduction of nitrobenzene; a first step

Mooibroek, T.J.

Chapter 1

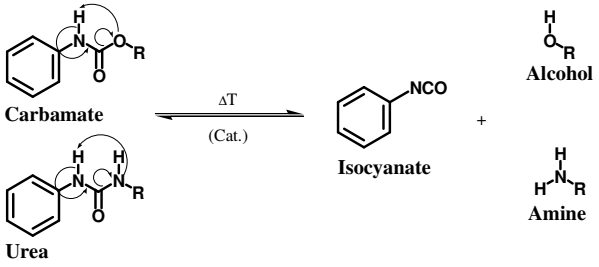
General Introduction

Abstract. In this chapter the chemistry for the synthesis of aromatic isocyanates is reviewed and discussed. First, the industrially applied route to the polymer precursors MDI and TDI is discussed and the drawbacks are emphasized. Several alternative routes to aromatic isocyanates are considered with an emphasis on catalytic alternatives. The prior art in one of these routes, namely the Pd-catalyzed reductive carbonylation of nitro aromatic compounds, is reviewed and some mechanistic proposals are discussed. Finally, a description of the aim of the research and the contents of this thesis is given.

1.1. The industrial synthesis of aromatic isocyanates

1.1.1. Isocyanates, carbamates and ureas

Aromatic isocyanates, carbamates and ureas are related compounds (Scheme 1.1). Carbamates can be considered as 1:1 adducts of isocyanates and alcohols, and thermal cracking of the carbamate results in the related isocyanate and alcohol. Analogously, thermal cracking of a urea yields the related isocyanate and amine. These molecules find their application both in organic synthesis and in industry.[1] Initially, the discovery of isocyanates in 1849 by Wurtz,[2] did not lead to an application, although afterwards this class of compounds was thoroughly studied by the academic community. The discovery of polyurethanes by Bayer in 1937, triggered the interest in isocyanates and eventually resulted in the application of mono- and diisocyanates in a variety of polyurethane (flame-retarding) foams,[3-8] (bio-degradable) plastics,[9-12] pesticides,[13-17] adhesives,[18-20] and coatings.[14, 21-25] Carbamates and ureas are intermediates for the preparation of pesticides and fertilizers.[26, 27] The market for these molecules is vast (several million tons/year) and increasing,[28] since economies like Japan, China and India are expanding at an incredible rate.[29-32] Commercially, isocyanates are the most important class of these compounds, and in particular toluenediisocyanate (TDI) and 4,4'-diphenylmethanediisocyanate (MDI) are of great interest to industry.[33, 34]

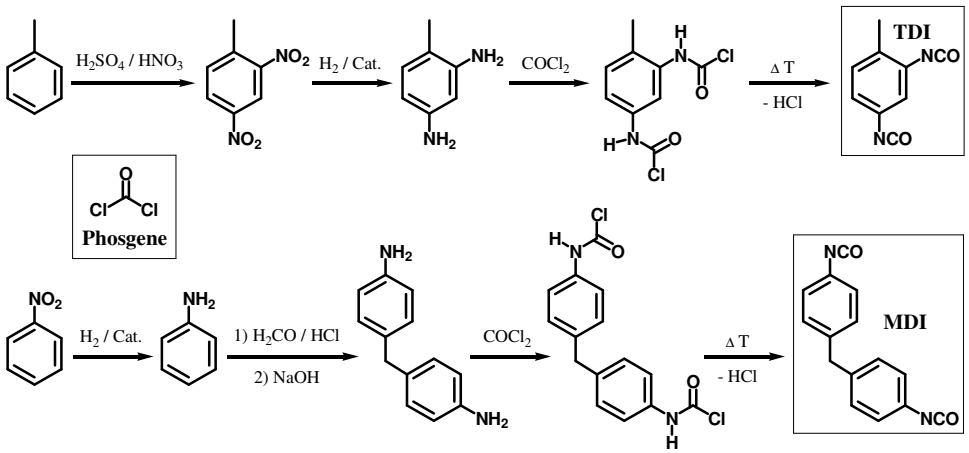


Scheme 1.1. Isocyanates, carbamates and ureas are related compounds.

1.1.2. Traditional route towards isocyanates

The traditional (and currently used) route to make TDI and MDI, as well as a variety of other isocyanates is often referred to as the 'phosgene route' (Scheme 1.2). This route roughly involves three relatively simple organic reactions, wherein a nitro-substituted substrate is first reduced to the corresponding amine

with a Ni or Pd catalyst in 98-99% yield.[35] The amine is then treated with phosgene to yield the intermediate carbamoyl chloride, which is subsequently dehydrochlorinated almost quantitatively above 50 °C, into the corresponding isocyanate. In order to minimize the formation of ureas in the second step, this process is carried out at high dilution (20%) and with an excess of phosgene (50-200%).



Scheme 1.2. Traditional synthetic pathway to toluenediisocyanate (TDI) and 4,4'-diphenylmethane-diisosyanate (MDI); the 'phosgene route'.

1.1.3. Major drawbacks of the phosgene route

Despite the high yields and good selectivity obtained with the phosgene route, there are essentially four major drawbacks. The first and most pronounced is the extreme toxicity (see Table 1.1) and flammability of phosgene and isocyanates, which make these chemicals extremely difficult to handle in bulk quantities and give them a high ranking in government lists of pollutants and eagerly forbidden chemicals. Phosgene was used as a chemical weapon in World War I, and around 36,600 tonnes of the gas were manufactured during this war, out of a total of 190,000 tonnes for all chemical weapons (19%), making it second only to chlorine gas (93,800 tonnes) in the quantity manufactured.[36] In total around 1.3 million people were injured and over 90,000 killed by the use of poisonous gases,[37] of which phosgene is acknowledged to have claimed most deaths.[38] A tragic methylisocyanate leaking accident in the night of 2nd/3rd December 1984 in a Union Carbide plant in Bhopal, India, clearly stressed the drawback of working with toxic chemicals on an industrial scale. Thousands of people were gassed to

death and more than 150,000 people were left severely disabled - of whom 22,000 have since died of their injuries - in a disaster now widely acknowledged as the world's worst-ever industrial disaster. More than two decades after the disaster, at least 50,000 people in Bhopal are too ill to work for their living, and the drinking water of at least 20,000 people is still contaminated.[39, 40]

The second major drawback in this reaction is that per mole of nitro group, two moles of corrosive hydrochloric acid are formed, rendering the medium very aggressive with time, thus allowing other side reactions to occur and to result in reactor degradation. The high dilution in which the reaction is carried out is the third limiting factor, since ideally concentrations should be high and volumes as low as possible, thus avoiding recycling and concentration costs. The final drawback is the unavoidable inclusion of chloride-containing compounds in the final product which can be detrimental for the further processing of the isocyanate.[3, 41]

Table 1.1. LD50 data (Lethal dose (mg/kg) at which 50% of a population dies) of phosgene, some isocyanates and some carbamates

Chemical	**LD_{50}**
Phosgene	1.8 (mice)[42] 1.4 (rats)[42] 1.3 (guinea pigs)[42] 1.0 (rabbits)[42, 43] 0.1 (TLV,[a] humans)[44]
Carbon Monoxide	3000 (mice)[45] 2000 (rats)[45] 6500 (guinea pigs)[45] 50 (TLV,[a] humans)[44]
MDI	5.8 (rats)[2]
TDI	> 31.6 (rats)[2]
Methylisocyanate	71 (rats)[2]
Phenyl isocyanate	940 (rats)[2]
Propham (iso-propyl N-phenylcarbamate)	9000 (rats)[2]
Chloropropham (iso-propyl N-(3-chlorophenyl)carbamate)	5000 – 7000 (rats)[2]

[a] Threshold Limited Value in mg/kg.

1.1.4. Requirements for an alternative isocyanate synthesis

Despite the disadvantages, the phosgene route is still the most lucrative and thus industrially applied procedure to date. In order to replace this procedure, a number of requirements can be thought of in the ideal scenario. First of all, readily accessible chemicals (cheap, large quantity) should be used and second, they should be as harmless as possible. A high overall yield, purity, and selectivity (atom economy) are also obvious requirements. What is more, a reaction

temperature of about 100 °C will be ideal as heat energy is a major waste product in many industrial processes.[46-50] The absence of over- and/or under-pressures and an easy product separation (from the solvent, starting materials and side products) is also logically favored. Finally, a one step (or one pot) synthetic procedure will be the route par excellence.

Most of these requirements could in theory be met by an efficient catalytic system, wherein additional requirements would be: the use of a cheap, fast (a Turn Over Frequency (TOF) in the order of 10^4 mol/mol.h^{-1} or higher), robust (a Turn Over Number (TON) in the order of 10^6 mol/mol or above)[51] and easily recycled catalyst. Naturally, the required TON and TOF strongly depend on the metal involved, since for instance Pd is about 5000 times more expensive than Cu.[52]

1.2. Alternative synthesis of isocyanates

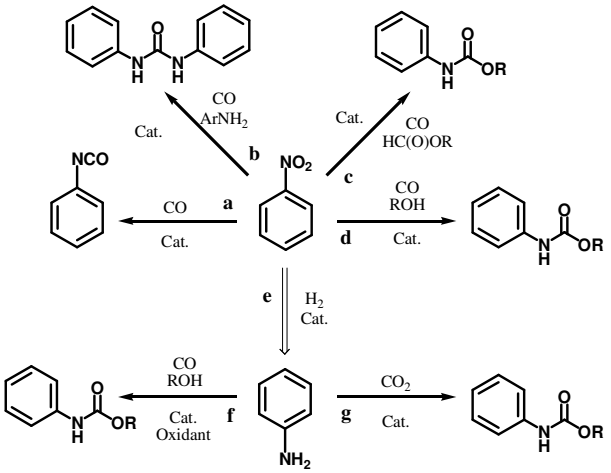
1.2.1. Various organic synthetic pathways to isocyanates

Alternative ways to prepare isocyanates have been studied thoroughly for decades. Innumerable reports such as patents, reviews,[53, 54] and books[55, 56] were published already some decades ago, and more than 22 methods have been reported for the preparation of isocyanates by organic reactions. Although abundant in number, none of these methods is a serious alternative for the current phosgene route, as either stoichiometric quantities of salt or acid are produced, or the starting products are too intricate molecules (i.e. expensive) for this specific purpose. Furthermore, most of the reported pathways are inaccessible when aiming for isocyanates like MDI or TDI, and not all reactions can be conducted in high yields.

1.2.2. Various catalytic synthetic pathways to isocyanates

A promising approach is to synthesize TDI or DMI catalytically, by converting a nitro or amine compound into the corresponding isocyanate (Scheme 1.3). Considerable efforts have been made in studying the oxidative carbonylation[43, 57-63] (Scheme 1.3f) and carboalkoxylation[3, 4, 64-66] (Scheme 1.3g) of aniline, and especially the oxidative carbonylation has been studied with various catalytic systems.[67-85] However, aniline must first be synthesized by hydrogenation of nitrobenzene (Scheme 1.3e), thus the most attractive strategy involves the reaction

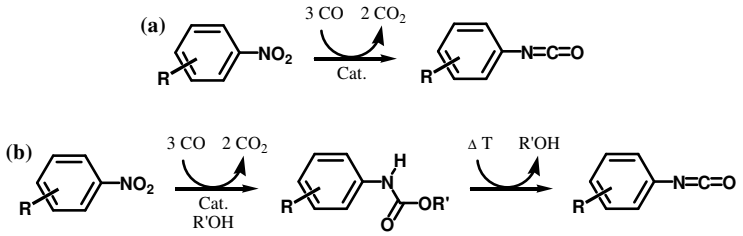
of a nitro compound with carbon monoxide, to yield the isocyanate directly. This conversion is thermodynamically favored ($\Delta H_f^\circ \approx$ -128.8 kcal/mol for nitrobenzene to phenyl isocyanate),[86, 87] but only proceeds in the presence of a metal catalyst.



Scheme 1.3. Catalytic pathways toward isocyanates, starting from nitrobenzene (a-d) or aniline (f-g) which is made from nitrobenzene (e).

1.2.3. The reductive carbonylation of nitro compounds

There are two related pathways in which the reductive carbonylation of nitro compounds can lead to isocyanates, which are commonly referred to as the direct and the indirect method, as depicted in Scheme 1.4(a-b) respectively. In the direct method, a catalyst activates the nitro group and carbon monoxide to form the isocyanate with liberation of carbon dioxide. In the indirect method, the isocyanate is trapped by an additional reagent (alcohol or amine, which can be used as solvent) to form the related carbamate or urea. Thermal cracking then leads to the isocyanate and alcohol or amine, which can thus be recycled.



Scheme 1.4. (a) the direct, and (b) the indirect method for the reductive carbonylation of nitro compounds.

Initially, a variety of elements were investigated as catalyst for the conversion of nitroaromatic compounds to isocyanates, such as sulfur, tellurium and especially selenium, which was reported to be very efficient.[88] However, these derivatives seem to be far too toxic to be applied in industry,[89-91] and it appears difficult to separate the catalyst from the final product.[92, 93] Alternatively, group 8 – 10 metal compounds can be applied, and in 1967, Hardly and Bennett were the first to report the generation of isocyanates from nitro compounds using rhodium, palladium or other noble metal salts as catalyst with a Lewis acid promoter.[94]

Regarding the direct carbonylation of mono- or dinitroaromatic compounds, it has been reported that heterogeneous catalyst precursors such as Pd/C or Rh/C,[95] as well as inorganic polymeric precursors like $PdCl_2$ and $RhCl_3$ give poor results. Although addition of a Lewis acid promoter (such as $MoCl_5$, VCl_4, $FeCl_3$, etc.) strongly increases both the rate and selectivity of the reaction towards isocyanates,[96-101] the catalyst is quite rapidly deactivated, resulting in poor TONs ranging from 5[102] to a maximum of about 150,[103] the selectivity being 52 and 15% respectively. The addition of an aromatic nitrogen base such as pyridine is known to have a positive effect with most metal chlorides.[68, 92, 99, 101, 104-118] Polymetallic carbonyl precursors like $Ru_3(CO)_{12}$ or $[HRu_3(CO)_{12}]^-$ were reported to be virtually inactive.[97, 118, 119] The most active catalytic systems to date however, involve Pd-based catalysts. In one of these ([Pd]/phen/H^+), a chelating diimine ligand like phenanthroline is bound to a homogeneous Pd^{II} precursor and the reaction is co-catalyzed by non-coordinating acids such as 2,4,6-trimethylbenzoic acid.[120]

It must be pointed out, however, that these systems work better for the indirect carbonylations, and (consequently) in the last decades, research has been focused almost exclusively on the indirect carbamate/isocyanate route. One additional advantage is the reduced toxicity of carbamates with respect to isocyanates (Table 1.1), which makes them more viable candidates from a governmental and environmental point of view. Moreover, part of the carbamates produced could be used for other purposes than isocyanate production. For the indirect reductive carbonylation, very similar methods could be employed: solid supported metals in the presence of ligands,[121-125] MCl_n/ligand/Lewis acid (M = Pd, Ru, n = 2,3),[13, 124] or the more active polynuclear precursors like carbonyl clusters of Rh or

Ru[126] in the presence of a co-catalyst like NEt_4Cl.[119, 127] Especially chelating ligands were found to improve the catalytic activity, and both N-[26, 92, 120, 121, 127-165] and P-[166-172] donor ligands have been found to improve this catalytic activity. Since these homogeneous systems comprise the most potential of all, they will be discussed in more detail.

1.3. The indirect reductive carbonylation of nitro compounds using Pd^{II}–catalysts stabilized by P or N donor ligands

1.3.1. Phosphorus and nitrogen as donor atoms

Both phosphorus and nitrogen ligands with the general formula YR_3 (Y = P, N) (called phosphanes and amines respectively) can be described as sp^3 hybrids in a (close to) tetrahedral geometry, having a lone pair on the central atom, capable of donating its electron density to an empty (transition) metal d-orbital. Amines are more electronegative than their phosphane analogues, so one would expect them to bind stronger to a metal. However, unlike amines, phosphanes can act as a π acid with their σ^* orbitals, so they can be involved in π-backbonding (provided that the metal ion has available d-electrons), rendering the overall bond strength larger than would be expected intuitively (Figure 1.1). So, the overall metal-phosphate bond strength is determined by an interplay of σ donation and π backbonding, the first having an increasing contribution when electropositive / donating substituents are employed, the latter when electronegative / withdrawing substituents are used.[51]

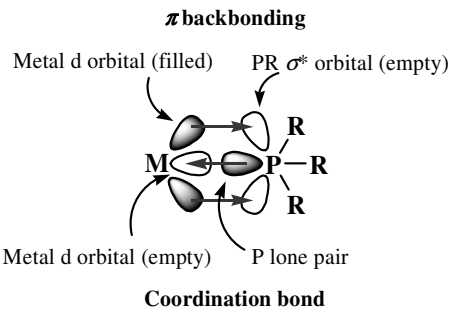


Figure 1.1. Schematic representation of the two factors governing the bond strength in a M-P bond: the donation of a lone pair (regular coordination bond), and the π backbonding of metal d electrons into PR σ^* orbitals. Shading represents orbital occupation.

1.3.2. Mono- and bidentate phosphane ligands

Due to their π backbonding capability, phosphanes (PR_3) are a very important class of ligands, as they can stabilize redox metal catalysts in high and low oxidation states. Especially zero-valent d^{10}-metals such as nickel and palladium

are known to bind strongly with phosphane ligands and not at all with amines. In addition, phosphanes constitute one of the few series of ligands in which both electronic and steric properties can be altered systematically. A useful classification of the electronic (υ_{CO})[173] and steric (θ)[174] nature for a series of monodentate phosphane ligands was described by Tolman, and selected examples are shown in Table 1.2.

The electronic parameter was defined using the carbonyl stretching frequency (υ_{CO} in cm^{-1}) of a 0.05 M solution of $Ni(CO)_3(PR_3)$ in CH_2Cl_2.[173] When R in PR_3 is electron donating, the electron density on nickel is increased, and some of the electron density is donated to the COs by back-donation. As a result, the υ_{CO} is lowered. Likewise, the use of electron withdrawing R-groups results in a higher υ_{CO}. Tolman defined the steric parameter of a monodentate phoshane ligand as the so-called cone angle (θ in º). This angle was obtained from space-filling models of a $M(PR_3)$ group with M–P distances fixed at 2.28 Å (Figure 1.2). The angle of the cone that just fits all atoms of the ligand is the cone angle (the metal is at the apex of the cone).

Table 1.2. Electronic and steric properties of monodentate phosphane ligands according to Tolman. [173, 174]

Ligand	ν_{CO} (cm^{-1})	$\Delta\nu$	θ (º)
P(*t*-Bu)$_3$	2056.1	0.0	182
P(*o*-MeOPh)$_3$	2058.3	2.7	-
PMe_3	2064.1	3.7	118
P(*p*-MeOPh)$_3$	2066.1	10.2	-
PPh_3	2068.9	12.9	145
$P(OEt)_3$	2076.6	20.4	109
PF_3	2110.8	54.6	104

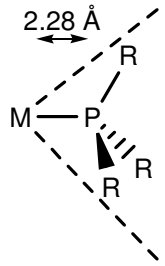


Figure 1.2. Schematic representation of the cone angle as defined by Tolman.[174]

A possible drawback of monodentate phosphane ligands is the lack of control over cis coordination, which is of the utmost importance in some catalytic reactions.[51, 175] This can be overcome by using a backbone spacer between two phosphorus donors thus ensuring a cis-coordination. In addition, fine-tuning the length of the backbone will enforce a specific geometry to the complex, as reflected in the P–M–P angle. This geometric parameter can be seen as a compromise between the metal preferred angle (for example 90º in a square planar Pd^{II} complex) and the ligand preferred angle[176, 177] (or bite-angle, β). Thus,

for a series of $Pd^{II}(ligand)Cl_2$ complexes with cis-coordinated bis(diphenylphosphane) ligands, the P–Pd–P angle increases from 72.7º to 85.8º to 90.6º for using a methylene (dppm), ethylene (dppe), or propylene backbone (dppp).[178] When the backbone is further extended to a butylene spacer in $Pd^{II}(dppb)(C_6F_5)_2$, the P-Pd-P angle is 96.8º.[179]

The effect of the P-M-P angle is both steric (size of the catalyst pocket) and electronic (M-P orbital overlap) in nature. In both cases, the effect is the stabilization or destabilization of intermediates and transition states in a catalytic cycle. The effect of ligand bite-angles on catalytic reactions such as the hydroformylation, CO-ethene copolymerization, allylation and C-C bond forming reactions is widely acknowledged, as reflected in several (review) articles on the topic.[175, 176, 180-183]

1.3.3. Catalytic systems based on phosphorus ligands

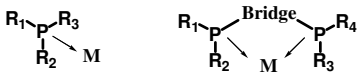
There are basically five research groups that have reported on the use of phosphorus ligands in the catalytic reduction of nitrobenzene, both in the patent and in the academic literature. Table 1.3 provides an overview of the ligands and metals reported, as well as their highest TOF (mol/mol.h^{-1}) and carbamate or urea selectivity (%) achieved. In 1982, Drent and van Leeuwen[92] patented the use of divalent Pd salts in combination with some mono- and bidentate phosphorus ligands (as well as some N-donating ligands, see next section) in the presence or absence of an acid as co-catalyst in the indirect carbonylation of nitro compounds to the corresponding carbamates or ureas. Relatively good results were obtained: TOFs up to 400 mol/mol.h^{-1} and selectivities for carbamate or urea of up to 95% were reported.

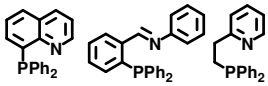
Thereafter, in 1986, Grate, Hamm, and Valentine[184] first patented their own catalytic systems with similar monodentate ligands, but with Ru^0 compounds in stead of Pd^{II} salts and only employing an amine as co-reagent, thus exclusively producing urea. Only moderate results were obtained: TOFs up to 30 mol/mol.h^{-1} and the selectivity for urea of less than 80%. Application of bidentate ligands and an alcohol improved performance, ensuing TOFs of up to 72 mol/mol.h^{-1} and carbamate selectivities of about 88%.[167, 185] In their third patent that year, they claimed ethanol to be a better reagent than methanol (obtaining a TOF of 41 mol/mol.h^{-1} and a carbamate selectivity of 74% with ethanol and none with

methanol). Finally, they extended their phosphane/Ru^0 library, claiming them in a 1987 WO patent,[186] only improving the TOF to about 72 mol/mol.h^{-1}. None of these patents reported on the addition of a Brønsted acid as co-catalyst, but Lewis acids were found to quench the reactivity.

Table 1.3. Schematic representation of (a) monodentate and (b) bidentate, or chelating phosphorus ligands that were used by several groups in the past decades, together with the highest turn over frequencies (TOF's) in h^{-1} and the highest selectivity in carbamate or urea in percentages (depending whether the indirect method involved an alcohol or amine respectively). Please note that these values are not necessarily derived from identical experiments. See text for comments and references.

(a) **(b)**



Ligands used	Reported by:	Max. TOF (h^{-1})	Max. carbamate or urea selectivity (%)
R_{1-4} = Me, CF_3, Et, Pr, Bu, Ph, C_6F_5, Ph(Me) **Bridge =** $(CH_2)_n$, C_2H_2, C_6H_4 **M =** Pd(II)	Drent *et al.* 1982	400	95
R_{1-4} = Me, Pr, Ph, o-Ph(Cl), p-Ph(OMe), C_6H_{11} **Bridge =** C_2H_4, C_3H_6, C_6H_4 **M =** Ru(0)	Grate *et al.* 1986/1987	70	88
R_{1-4} = Ph **Bridge =** CH_2, C_2H_4, C_3H_6, **M =** Ru(0)	Cenini and Ragaini *et al.* 1988	70	67
R_{1-4} = Me, Ph, o-Ph(Me), Bz, C_6H_{11} (only b) **Bridge =** CH_2, C_2H_4 **M =** Ru(0)	Gladfelter *et al.* 1991-1997	10	60
R_{1-4} = Ph (only b) **Bridge =**CH_2, C_2H_4, C_3H_6, C_4H_8, C_6H_4, Napht **M =** Pd(II)	Wehman *et al.* 1995	70	78
 + Pd(II)	Wehman *et al.* 1995	20	66

After these reports, the academic world ensued these initial findings, and especially Gladfelter *et al*. spent a considerable amount of research on the Ru/P catalytic system in the 1990s. [168, 169, 171, 172, 187-192] Initially they reported some catalytic data concerning the Ru_2(bis(dimethylphosphanyl)methane)$_2(CO)_5$ dimer as catalyst (TOF of 7 mol/mol.h^{-1}, carbamate selectivity of 60%),[187] in their later studies they focused solely on the mechanistic aspects of the alcohol-assisted indirect carbonylation of nitro compounds. These studies mainly involved the

complex Ru(1,2-bis(diphenylphosphanyl)ethane)$(CO)_3$ as catalyst precursor,[168, 169, 171, 172, 188-190, 192] but other ligands/catalyst systems were also investigated.[168, 187, 191]

In 1988, Cenini and Ragaini *et al*. also reported on the use of almost identical Ru^0/P catalytic systems, resulting in similar TOFs and selectivities.[193] In the same paper, they also reported on the use of chelating N-donor ligands with which they continued their work (see section 1.3.3).

Notably, in 1995 Wehman *et al*. [194] reported on the use of some bidentate phosphane / Pd^{II} catalysts as well as on some bidentate P and N / Pd^{II} catalysts.[194, 195] She found that the use of bis(diphenylphosphanyl) ligands with a flexible bridge gave more efficient catalyst systems than their rigid counterparts, resulting in a TOF of about 68 mol/mol.h^{-1} and a carbamate selectivity of about 78% for the propylene-bridged ligand. The catalytic systems with P/N ligands showed almost no activity (TOF <20 mol/mol.h^{-1}, carbamate selectivity <65%).

1.3.4. Catalytic systems based on nitrogen ligands

The catalytic systems based on ligands with nitrogen-donor atoms have been intensively studied by essentially five groups. In Table 1.4, an overview is presented regarding the ligands and metals used by these groups, as well as the highest TOF (mol/mol.h^{-1}) and carbamate or urea selectivity (%) achieved. Since there are many papers on the topic, dealing with different aspects of the reaction, in this section only the molecular components of the applied catalytic system are mentioned together with their best achievements.

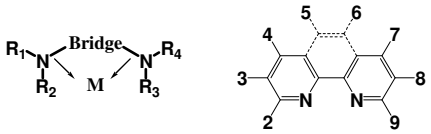
Similar to the research focused on phosphane ligands, the venture was initiated by the pioneering work of Drent and van Leeuwen in their 1982 patent,[92] mentioned earlier. They claimed the use of a variety of bidentate N-donor ligands wherein the amine/imine donors are bridged by different spacers.

Markedly, the use of 2,2'-bipyridine and 1,10-phenanthroline was preferred, the latter of which was found to result in one of the best catalytic systems to date (!), when combined with a strong Brønsted acid such as para-toluene sulfonic acid as co-catalyst (TOF = 1980 mol/mol.h^{-1}, carbamate selectivity = 95%). Five years

later, Drent patented a similar catalytic system,[131, 142] wherein the 1,10-phenanthroline/Pd^{II} was combined with a Lewis acid such as $Cu(PhSO_3)_2$, $Cu(ClO_4)_2$, or $VOSO_4$ as the co-catalyst. The use of $VOSO_4$ was found to result in the most active system of the series tested (TOF = 490 mol/mol.h^{-1}, carbamate selectivity = 88%).

Table 1.4. Schematic representation of (a) bidentate, or chelating, and (b) dipyridine / phenanthroline ligands that were used by several groups in the past decades, together with the highest turn over frequencies (TOFs) in h^{-1} and the highest selectivity in carbamate or urea in percent (depending whether the indirect method involved an alcohol or amine respectively). * Indicates that dinitrotoluene was used as substrate in stead of nitrobenzene. Please note that these values are not necessarily derived from identical experiments. See text for comments and references.

(a) **(b)**



Catalyst systems used:	Reported by:	Max. TOF (h^{-1})	Max. carbamate or urea selectivity (%)
R_{1-4} = Me, Et, t-Bu, Ph **Bridge =** $(CH_2)_n$ n = 1-4 **(b) =** 2,2'-bipyridine and 1,10-phenentroline **M =** Pd(II) **Acid =** Brønsted or Lewis	Drent *et al.* 1982/1987	2000	95
(b) = (4,7-Me_2, 4,7-$(OMe)_2$, 4,7-Ph_2, 3,4,7,8-Me_4) 1,10-phenentroline **M =** Pd(II) or Pd/C(5%) **Acid =** None or Brønsted	Mestroni *et al.* 1984-1987 1999	130 260*	97 82*
(b) =(4,7-Cl_2, Me_2, OMe_2, $(NMe_2)_2$) 1,10-phenantroline, (4,4'-CF_3, Cl, Me, OMe, NMe_2) 2,2'-bipyridine **M =** Pd(II) **Acid =** None or Brønsted	Wehman and van Leeuwen *et al.* 1994-1996	380 180*	92 31*
(b) =(2,9Me_2, 4,7Me_2, 3,4,7,8-Me_4) 1,10-phenantroline, 2,2'-bipyridine **M =** Pd(II) or Pd/C(5%) **Acid =** None or Brønsted	Cenini and Ragaini *et al.* 1988-present	7900 580*	88 78*

From that time on, the academic world showed interest to fundamentally explore these remarkable findings, in order to improve these catalysts, and four groups worked on the subject in the past three decades. The group of Paul (who wrote a review on the topic in 2000)[196] and Osborn only reported on mechanistic studies.[153-155, 197] Other groups active in the field are the groups of Mestroni,[26, 120, 130, 135, 152, 156, 159, 198-205] Cenini and Ragaini,[120, 150, 157, 160-165, 193, 206-212] and van

Leeuwen,[144-146, 194, 195] the first of whom was the initial group to study similar N-donor based systems.

In the early eighties, Mestroni *et al*. worked for some time on a reaction closely related to the catalytic reductive carbonylation of nitroaromatics, i.e., the catalytic reduction of nitrobenzene to aniline in the presence of water and carbon monoxide. In these studies Ir, Rh or Os salts were used in combination with bipyridine or phenanthroline and KOH as the catalytic system.[198-200] Since this system is similar to the ones used for the reductive carbonylation of nitroaromatics, they employed their catalytic system also for this reaction.[26, 130, 135, 202] The metal mainly used was Pd, either immobilized on carbon or as Pd^{II} salt, and a bulky Brønsted acid was added (2,4,6-trimethylbenzoic acid (TMBA)). Remarkably, identical results were obtained for 3,4,7,8-tetramethyl-1,10-phenanthroline/Pd/C(5%)/TMBA[130] and [Pd(3,4,7,8-tetramethyl-1,10-phenanthroline)$_2$](PF_6)$_2$,[26] namely a TOF of 125 mol/mol.h^{-1} and a carbamate selectivity of 97%. After a 'break' of about twelve years, they reported the reductive carbonylation of 2,4-dinitrotoluene leading to TDI to proceed in high conversion (100%), selectivity (82%), and fair TOF (260 mol/mol.h^{-1}). In this study the cationic complex [Pd(1,10-phenanthroline)$_2$](PF_6)$_2$ was used with an excess of free ligand, hexafluoridophosphoric acid as co-catalyst, and a substrate/Pd ratio of 520. [152]

Van Leeuwen and Wehman[194] systematically studied the influence of electron donating or withdrawing substituents on the 4,4'-positions of 2,2'-bipyridine (R = CF_3, Cl, H, CH_3, OCH_3, $N(CH_3)_2$); it was found that electron donating substituents rendered [Pd(R_2bipy)$_2$](CF_3SO_3)$_2$–type catalysts more reactive whereas electron withdrawing substituents resulted in an inactive catalyst. Moreover, it was shown that replacement of one of the triflate anions by a chloride anion inhibited the catalytic reaction and, additionally, the presence of water reduced the selectivity for carbamate.[144] A selectivity of more than 99% for carbamate was achieved, but only a very low TOF of 28 mol/mol.h^{-1} was reached, using the preformed compound [Pd((NMe_2)$_2$bipy)$_2$](CF_3SO_3)$_2$ as catalyst precursor. Subsequently, a similar study was conducted for a series of 4,7-disubstituted 1,10-phenanthroline ligands (R = Cl, H, CH_3, OCH_3, $N(CH_3)_2$), confirming the benefit of electron-donating substituents.[145] Furthermore, they compared two non-coordinating anions in the preformed catalyst (CF_3SO_3 and

BF_4) and found a subtle balance in activity when using a certain ligand together with a certain anion. The best results in this paper were reported for the $[Pd(Me_2phen)_2](CF_3SO_3)_2$ catalytic system: a TOF of 311 mol/mol.h^{-1} and a carbamate selectivity of 84%. After this, the electronic and steric properties of the nitroaromatic substrate was systematically explored using in a series of p-substituted nitrobenzenes (R = CF_3, Cl, Br, H, CH_3, OCH_3, $N(CH_3)_2$), and the abovementioned catalyst.[194] It was found that electron-donating substituents decreased the conversion and increased the selectivity to carbamate. Introduction of (bulky) o-substituents (R = H, Cl, Me, Ph CF_3, OCH_3, $CH(CH_3)_2$, $C(CH_3)_3$) proved detrimental for both conversion and selectivity. Noteworthy, no acid co-catalyst was added during these studies. However, in another study, they reported on the influence of aromatic carboxylic acids as co-catalyst in this $[Pd(Me_2phen)_2](CF_3SO_3)_2$ system.[146] Although the pK_a-value of the acid used did not seem to make a difference, its concentration was found to be of the utmost importance for both the conversion of the substrate and the selectivity towards carbamate. Furthermore, the anion of the acid was found affect the results: weakly coordinating benzoate anions were believed to stabilize various palladium intermediates. However, if the concentration or the coordinating ability of the anions becomes too high, a negative effect was observed. The acid yielding the best results was found to be 2,4,6-trichlorobenzoic acid, yielding a TOF of 378 mol/mol.h^{-1} and a selectivity to carbamate of 92%. Moreover, they also found the presence of aniline to have a promoting effect on the TOF. Finally, the catalytic system ($[Pd(phen)_2](CF_3SO_3)_2$/4-chlorobenzoic acid) was tested with some commercially more interesting aromatic dinitro compounds, wherein TOFs of 73-183 mol/mol.h^{-1} and carbamate selectivities of 30 to 100% were achieved.[194]

The best results to date have been reported by Cenini and Ragaini *et al*., who started in the mid 1980s with a $Ru_3(CO)_{12}/H^+$ catalytic system.[119, 127] Thereafter they too added some bidentate ligands (N and P, see previous section), obtaining only poor results.[193] Subsequently, in 1990, it was reported that Pd and Rh supported on alumina (which are inactive as such) could be 'activated' by the addition of chelating N-donor ligands like 2,2'-bipyridine, 1,10-phenanthroline (and derivatives thereof) with or without a Brønsted acid (TMBA). The system Pd/Al_2O_3/bipy/H^+ was studied for the direct route, giving very poor results (TOF = 21 mol/mol.h^{-1}, isocyanate selectivity = 65%). The Rh/Al_2O_3/phen catalyst was studied for the indirect route, also resulting in poor results (TOF = 45 mol/mol.h^{-1},

carbamate selectivity = 68%). Since it was evidenced that a homogeneous catalyst, formed in situ from the heterogeneous precursor, was the active species, they continued their efforts by solely studying homogeneous systems. After a period of thirteen years (i.e. in 2003), they reported a study of the reaction involving the $[Pd(phenanthroline)_2](BF_4)_2$ system, co-catalyzed by an aromatic carboxylic acid (by then known to yield the best results). Moreover, since aniline had been reported to enhance the reactivity, they found that combining the two promoters (e.g. benzoic acid and aniline) in the molecule 2-NH_2PhCOOH, had a positive effect when compared to benzoic acid alone, resulting in a TOF of about 1400 mol/mol.h^{-1} and a carbamate selectivity of about 70%.[161] In the same year, they reported a TOF of roughly 6000 mol/mol.h^{-1} and a carbamate selectivity of 88%, using $[Pd(phenanthroline)_2][BF_4]_2$ as catalyst and H_3PO_4 (85%) and aniline as co-catalysts and working at temperatures as high as 170 ºC.[160, 162] These high values were obtained by increasing the CO pressure up to 100 bar, whereas the initially used CO pressure of 60 bar gave a TOF of 'only' 4130 mol/mol.h^{-1} and a selectivity for carbamate of 87%. In fact, a linear trend wherein the conversion is dependant in the CO pressure, without loss of selectivity, was disclosed. It is worth mentioning that analytically pure H_3PO_4 gave significantly poorer results than the cheaper 85% variant and other phosphorus acids, for reasons still not known.[162] Furthermore, they made use of the reactive drying agent 2,2-dimethoxypropane, that is known to be beneficial in similar reactions.[139, 140, 151, 152] How it is possible that these two reagents together (i.e. 85% H_3PO_4 and a drying agent) can be beneficial, is not clear. Nonetheless, it seems to work, and in the year after, this catalytic system was studied for the conversion on 2,4-dinitrotoluene instead of the model compound nitrobenzene, and some distinct parameters were optimized. The best acid co-catalysts for the reductive carbonylation of this molecule seemed to be phenylphosphonic or 4-tolylphosphonic acid. Furthermore, the addition of the aniline analogue of the substrate was found to be beneficial as well, and again the CO pressure was found to be an important parameter. Moreover, they reported an important 'extra feature' concerning the isolation of the carbamates involved: they precipitate from the solvent (methanol) when cooled to 0 °C, and after one recrystallization the 99% pure product could be isolated. Under their optimized conditions, they obtained unprecedented (for 2,4-dinitrotoluene) results, expressed in a TOF of 580 mol/mol.h^{-1} with 78% selectivity for the corresponding dicarbamate. Also in the year 2005, they reported on the indirect method using aniline as co reactant

for the production of ureas, and studied the effect of chloride anions on this reaction.[211] Although some positive effects of Cl^- were found for the conversion of nitrobenzene, an inhibiting effect was observed for the conversion of 2,4-dinitrotoluene. In both cases only poor results were obtained, however (TOF ~50 mol/mol.h^{-1}, urea selectivity ~50-98%). It is important to note, however, that these results were obtained using CO pressures of only 40 bar, whereas their previous (outstanding) results were obtained applying CO pressures up to 100 bar.[162, 163] The highest TOF reported to date, namely 7900 mol/mol.h^{-1} at 100 bar (5710 mol/mol.h^{-1} at 60 bar), has been reported very recently (2010) by using the unsymmetrical ligand 4-methoxyphenanthroline.[213]

1.4. Mechanistic considerations

1.4.1. Frequently reported side-products

Frequently reported side-product in the transition-metal catalyzed reductive carbonylation of nitrobenzene in methanol are azobenzene, azoxybenzene, aniline, isocyanate oligomers, metallacyclic compounds, *N,N'*-diphenylurea (DPU) and Pd^0 or palladium black (Figure 1.3). Although never isolated, nitrosoaromatic compounds (Ph-NO) are sometimes believed to be intermediate species for other side products since they are easily further deoxygenated.[53, 214, 215] Azo- and azoxyaromatic compounds are common byproducts and have been reported to poison the catalyst when present in high enough concentrations.[151] Aniline was first thought to be a mere side product,[119, 144, 146, 216] but has also been reported to act as co-catalyst.[160] Isocyanate oligomers are well known to be formed through either assisted or spontaneous self-coupling reactions.[214, 217-219] Metallacyclic compounds can be seen as either reaction intermediates (for the product or a byproduct) or a way to deactivate the catalyst; if the species is too stable it removes the metal from the catalytic cycle.

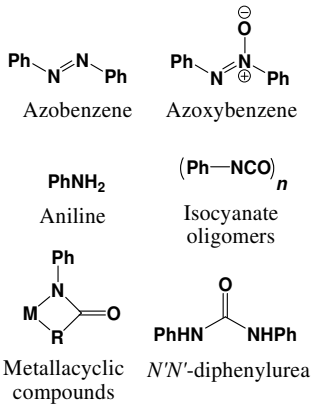


Figure 1.3. Frequently reported side-products in the reductive carbonylation of nitrobenzene.

Paul *et al.* elegantly proved that in non-alcoholic conditions phenylisocyanate reacts with a metallacyclic intermediate Pd species thus poisoning the catalyst.[155] This is schematically shown in Figure 1.4, wherein (a) is a reaction intermediate, (b) proved to be a very stable compound and (c) and (d) decomposed into

N,N',N''-triphenylbiurea (TPB) and DPU respectively, with liberation of the active species. Alternatively, these compounds can be formed by reacting aniline with isocyanate and the thus formed urea with (again) isocyanate, thus forming the diurea. However, in the presence of an alcohol, the corresponding carbamate is favored on thermodynamic grounds, thus ureas are only rarely isolated in high yields. The same reaction sequence may occur in the indirect pathway, but, since the concentration of isocyanate is low, catalyst degradation will be much slower via this route, thus allowing for relatively higher TON and TOF values to be reached, as is generally observed.

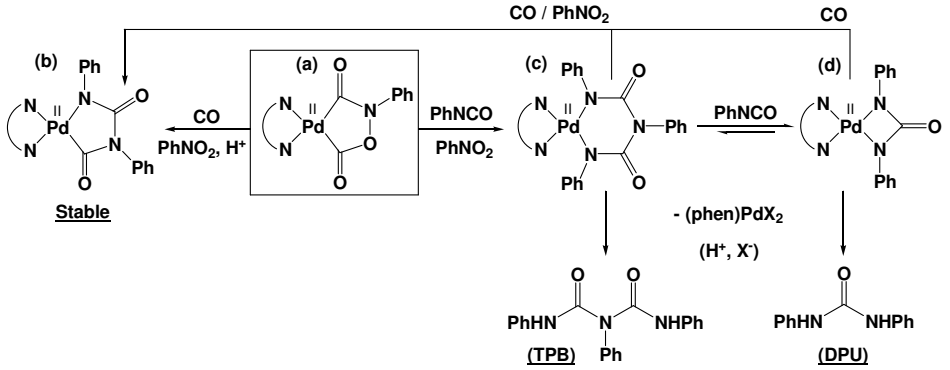


Figure 1.4. Palladacyclic structures studied by F. Paul *et al.*.[155] (a) is believed to be a key intermediate in the Pd/Phen/H^+ catalyzed reductive carbonylation of nitrobenzene, and (b) is a very stable species that can be formed thereof, thus poisoning the catalyst. (c) and (d) can also form from (a) and decompose into the active species and one of the byproducts often detected. See reference for exact reaction conditions and stoichiometry.

1.4.2. Interrelated proposals of the mechanism, in a historical context

1.4.2.1. Introduction

Although several papers have claimed otherwise,[150, 220, 221] the catalytic system in the carbonylation reaction of nitrobenzene is usually a homogeneous one. Even when a 'heterogeneous' catalyst is used, the active species is generally believed to be homogeneous,[120, 123, 124, 134] almost without exceptions.[222] The mechanism was initially (1970s) thought to proceed via a similar mechanism as the direct carbonylation, with subsequent reaction of the isocyanate with the alcohol employed. This idea was abandoned in the mid 1980s, as evidence suggesting a different mechanism was found,[119, 223-227] in which the alcohol is interacting with

the catalyst. Though the carbonylation reaction was discovered more than 50 years ago, still no clear-cut mechanism has been proposed so far. In fact, it seems likely to assume that different mechanisms may be operative in different catalytic systems. It lies outside the scope of this introductory chapter to discuss all mechanistic proposals in great detail; only some key-proposals will be briefly discussed.

Five groups have proposed a mechanism for the reductive carbonylation of nitrobenzene, and in an important review by Paul in 2000,[196] the proposed mechanisms are summarized of both the direct and indirect reductive carbonylation of nitro aromatics of all catalyst systems of which the mechanism have been studied. The five proposals for the Pd/phen/H^+ system by the different groups are provided in chronological order (the most recent proposal of each group is given).

1.4.2.2. The Pd/phen/H^+ mechanism

In nearly all proposed catalytic cycles, palladacyclic intermediates (see e.g. Figure 1.5a) play a crucial role and the active species that enters the catalytic cycle is believed to be a zeo-valent palladium complex (see e.g. **1** in Figure 1.6, hence rationalizing the similar activity when employing Pd/C and phen, as was done in the early days).[26, 130] Furthermore, the palladium compounds **2** – **4** (see Figure 1.6) were all characterized crystallographically (see Figure 1.5a-c) and form the basis of all proposed mechanisms. The first of these intermediate palladacyclic structures was isolated and characterized already in 1990 by Leconte *et al.*[153] (Figure 1.5a, see also **2** in Figure 1.6 and).

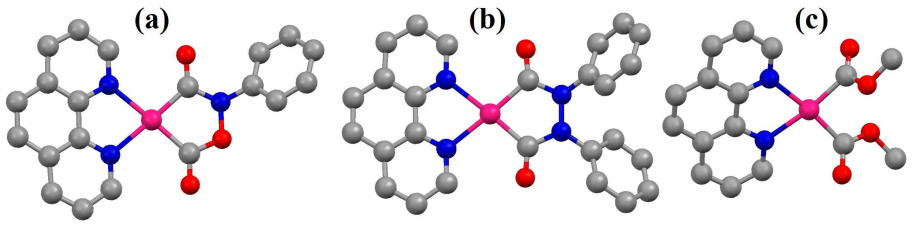


Figure 1.5. Perspective views of the crystal structures that are believed to be intermediates in the catalytic reductive carbonylation of nitro aromatic compounds based on the Pd/phen catalytic system. Their molecular structure is also shown in Figure 1.6 as compounds (2) – (4) respectively. Carbon is grey, nitrogen is blue, oxygen is red, palladium is pink, and hydrogen and solvent molecules are omitted for clarity.

Based on these structural data, the knowledge of the promoting influence of an acid and their own observations concerning the formation of aniline, Wehman *et al*. proposed the catalytic cycle as depicted in the top left of Figure 1.6. Despite the attractive simplicity of this cycle, empirical evidence for this proposal was minimal.[146]

The catalytic cycle proposed by Mestroni *et al*.[159] (top right in Figure 1.6) is based on their crystallographically characterized metallacycle **3**, which they proposed to be a key-intermediate in the catalytic cycle. In this proposal, azo- and azoxybenzene are considered to be formed as intermediates. However, they had no empirical evidence to prove this, nor did they explain the initial formation of azoxybenzene or the role of aniline in the process.

Another proposal was brought forth by Paul *et al*.[3, 16, 155, 196] (bottom left in Figure 1.6) and also involved a series of stepwise deoxygenation/carbonylation steps. This proposal is very similar, but more complicated than the one proposed by Wehman *et al*., forming the carbamate by a (stepwise) proton-catalyzed alcoholysis of **2**. Although one could argue in favor of the stability of the different metallacycles proposed here, as well as the likelihood of certain individual steps, here too the empirical evidence is lacking and it does not account for the formation/role of aniline or other byproducts/intermediates.

In their latest proposal[211] (centre right in Figure 1.6), which is partially based on their own crystallographically characterized Pd intermediate **4**,[208] Cenini *et al*. 'divide' the catalytic cycle into two distinct pathways: 1) the initial formation of a (metallacyclic) intermediate and the subsequent (proton-catalyzed) liberation of phenyl isocyanate and the active species (**2** and **1** in the Figure respectively); 2) a catalytic cycle involving the intermediate production of aniline and the acyl complex **4**, from which nucleophilic attack of aniline on **4** is thought to produce phenyl isocyanate and methanol. In both cases, phenyl isocyanate is thought to react with aniline to *N,N'*-diphenylurea, which is then converted to the carbamate to release aniline. This does seem to explain the promoting role of aniline[160] and merges the routes which can be envisaged with the two intermediary Pd structures **2** and **4**. However, here too, little evidence was brought forth to verify this experimentally, and no detailed mechanism was provided for the formation of aniline or other side-products.

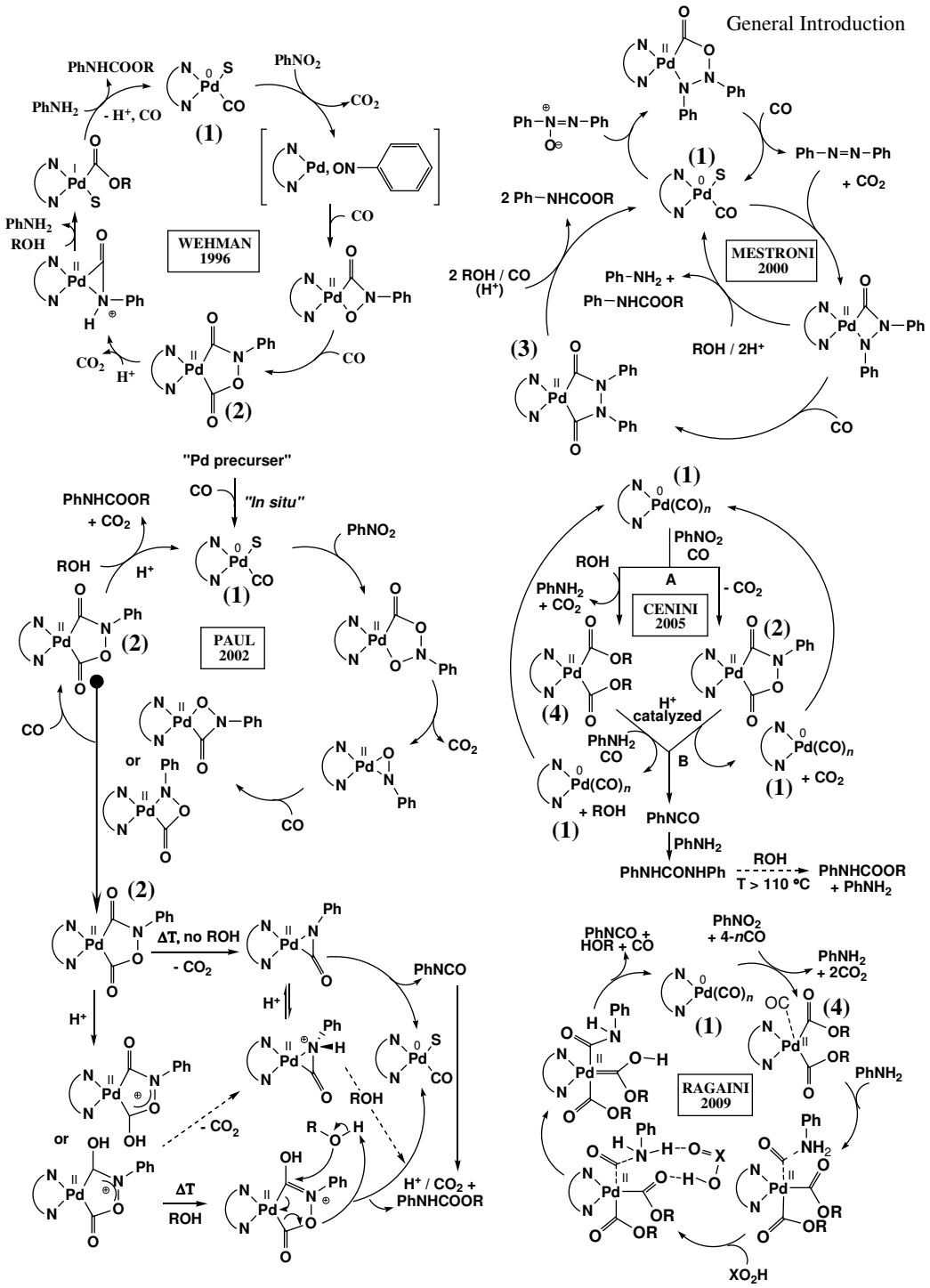
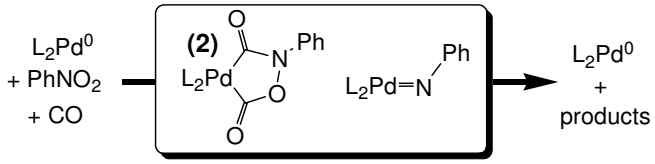


Figure 1.6. Different interrelated catalytic cycles for the Pd/phen/H^+ catalytic system as proposed by Wehman in 1996 (top left), Mestroni in 2000 (top right), Paul in 2002 (bottom left), and Cenini in 2005 (bottom right). The structures 2 – 4 were all characterized crystallographically (see Figure 1.5a-c). (1) is believed to be the active species and 2 – 4 are believed to be key-intermediates. S = solvent molecule. See text for further explanation.

Finally, Ragaini and co-workers very recently put forward a (bottom right in Figure 1.6) which shows strong resemblance to the mechanism proposed by Gladfelter *et al*. [168, 169, 171, 172, 187-190, 192] for the almost inactive (max. TOF of 7 h^{-1}) Ru/diphosphane catalytic system (not discussed further in this chapter). Like the proposal of Cenini, the palladium-diacyl complex **4** is also thought to be formed first, while reducing nitrobenzene to aniline. Aniline is then thought to attack on a CO molecule that is associating with Pd via one of the axial coordination sites, where after a carbonic acid (RO_2H) works as a co-catalyst to assist proton transfer from aniline to one of the acyl ligands, resulting in a carbene species. The carbene ligand in this pentacoordinate Pd-complex is thought to decompose to CO_2 and methanol, and then further to phenyl isocyanate, methanol, and the starting zero-valent palladium compound **1**. What is unclear however, is again how aniline is formed first, how exactly nitrobenzene is deoxygenated, and again very little experimental evidence has been put forth to verify this proposal; e.g. the proposed carbene intermediate is a formal Pd^{II} species surrounded by two anionic acyl-type ligands and three strong sigma-donor atoms (two phen-N and one carbene-C); clearly a situation that will not be favorable for a d^8 palladium complex.

1.4.3. Opportunities to generate mechanistic insight

Overall, the above mechanistic proposals rationalize the formation of carbonylation products such as phenyl isocyanate, methyl phenylcarbamate and *N,N'*-diphenylurea, and most of them rationalize the co-catalytic effect of added acid. There is however, not one unified and generally accepted mechanism to explain the formation of all these products, or of other observed products such as azo(xy)benzene and aniline. Moreover, the mechanism for nitrobenzene reduction/de-oxygenation is not well-understood, it is generally *assumed* to proceed by a series of carbonyation/decarboxylation steps to palladacycles such as **2** (see Scheme 1.5). However, a complete deoxygenation of nitrobenzene may also result in an imido-complex ('L_2Pd=NPh', see Scheme 1.5), from which products may then evolve.



Scheme 1.5. Proposed crucial intermediates in the reductive carbonylation of nitrobenzene discussed in this thesis: a palladacyclic compound and a palladium-imido compound.

Speculations concerning the intermediacy of palladium–imido compounds in catalytic reactions have been put forward in literature of the 1960's and 1970's. The existence of such imido compounds has been postulated in the context of nitrobenzene reduction to aniline with CO/H_2O,[228, 229] in the carbonylation of nitrobenzene to phenyl isocyanate,[103, 230] and also speculatively proposed in the palladium/phen/H^+ catalyzed nitrobenzene carbonylation in methanol as the reaction medium.[146, 147] It has also been proposed that the palladium-catalyzed reduction of functionalized nitroarenes with CO proceeds via a palladium–imido intermediate to yield N-heterocyclic compounds.[231, 232] Moreover, a series of bidentate phosphane stabilized Ni–imido complexes has been isolated, characterized crystallographically, and were shown to react with CO to form isocyanates.[233-235]

Despite these indications, Pd-imido complexes are not generally considered as intermediates in the reductive carbonylation of nitrobenzene in an alcoholic solvent. This clearly presents an opportunity for further research, especially by applying diphosphane ligands to stabilize the palladium catalyst. Not only have Pd/diphosphane catalytic systems been scarcely studied, the steric and electronic properties of phosphane ligands are much easier to fine-tune than those of 1,10-phenanthroline (see also section 1.3.1.). This allows for a correlation to be established between the catalyst performance and its structure; allowing valuable information to be gained into the mechanism of the title reaction. Such knowledge is long overdue and clearly a prerequisite for the further rational development of new, possibly more active and selective, catalyst system for the alternative synthesis of aromatic isocyanates as outlined in section 1.2.

1.5. Aim and outline of this thesis

As discussed in detail in this chapter, the current industrially applied route to prepare aromatic isocyanates has several drawbacks, and alternative –phosgene free– strategies have been explored to replace this dangerous process. In particular strategies involving transition metal catalysts have arisen as potential alternatives. The most promising of these is the palladium-catalyzed indirect reductive carbonylation of nitro aromatic compounds, where the palladium metal is stabilized by phosphorus or nitrogen donor ligands. In particular the Pd/phen/H^+ catalytic system has been extensively studied over the years.

Despite these efforts, a clear, unified, and generally agreed upon mechanism for this reaction has still to emerge, yet such understanding is critical for the development of catalysts of optimal performance.

The aim of the research described in this thesis is therefore to gain understanding into the molecular mechanism of the palladium(/diphosphane) catalyzed reductive carbonylation of nitrobenzene in methanol. It is expected that such molecular understanding will –in the long run– allow the design of catalyst structures for optimal performance. In particular, the molecular connection between the steric and electronic properties of the catalyst complexes and their respective catalytic performances needs to be revealed. The research described in the subsequent chapters of this thesis is aimed at acquiring this knowledge.

The catalytic reactions reported in this thesis (but also in many other studies) are performed using in situ synthesized catalyst precursor complexes. It is known however, that this (Ligand)Pd(Anion)$_2$ complex formation process is not always straightforward, sometimes resulting in the formation of inactive complexes.[236] This process has therefore been studied in depth using palladium salts and various bidentate diarylphosphane ligands in methanol, acetone and dichloromethane, and the findings of these studies are condensed in **Chapter 2** of this thesis. Also presented in this chapter are the structural characteristics of selected complexes in the solid state and in solution.

Chapter 3 reports on selected catalytic nitrobenzene carbonylation experiments and a thorough qualification and quantification of the products formed. These products not only comprise the expected nitrobenzene reduction products, but also large amounts of methanol oxidation products. Based on these data, and partially on other carefully chosen catalytic experiments, a comprehensive conceptual analysis is given of the likely molecular processes that underlie the formation of the various products observed. This analysis leads to the postulation of a palladium-imido complex ('P_2Pd=NPh') as the central intermediate species in an unprecedented complex network of catalytic reactions. This hypothesis not only allows the rationalization of the products formed, but moreover allows for an accurate simulation of the observed product distributions and –to some extent– relate the catalyst performance to the structure of the catalyst as imposed by that of the ligand.

In the studies described in **Chapter 4**, a more comprehensive library of functionalized phosphane ligands has been applied in the title reaction, together with variations in reaction conditions. It is shown that the 'imido-hypothesis' as developed in Chapter 3 can indeed explain, on the molecular level, the effects that the catalyst structure and reaction conditions may have on the conversion of nitrobenzene and the observed selectivities. Moreover, additional spectroscopic evidence for the existence of this proposed 'P_2Pd=NPh' complex is presented. As an alternative intermediate for the production of nitrobenzene carbonylation products, a palladacyclic intermediate (see Scheme 1.5) was considered. It appeared however, that when supported by phosphane ligands, the palladacycle decomposes not to give carbonylation products but yielding a variety of –mainly unidentified– products via the palladium-imido complex. These data thus also point strongly into the direction of a 'P_2Pd=NPh' complex as centrally important product-releasing intermediate.

In **Chapter 5**, the mechanistic knowledge gained in the foregoing two chapters is applied to understand the evolution of methanol oxidation products during the nitrobenzene reduction process. In particular, the chapter focuses on the evolution of the useful methanol oxidative carbonylation products dimethyl carbonate (DMC) and dimethyl oxalate (DMO). Based on the effects that different functionalized phosphane ligands and different reaction conditions have on the activity and selectivity for DMC / DMO production, a more detailed molecular mechanism is proposed for their formation, involving –besides the P_2Pd=NPh complex– the dimethoxido complex $P_2Pd(OCH_3)_2$ and the acyl complex $[PdC(O)OCH_3]^+$.

Chapter 6 reports on a (catalytic and DFT) comparative study between palladium catalysts stabilized by the N-donor ligand phen and those stabilized by bidentate P-donor ligands, in particular one that displays a nearly identical selectivity for the nitrobenzene reduction products as the phen-supported system. The similarities and differences between these two catalytic systems could all be rationalized using the mechanism developed in Chapters 3–5. For example, also for the Pd/phen catalytic system the palladacyclic intermediate (Scheme 1.5) is most likely not a product releasing species. Our hypothesis centered around the Pd=NPh intermediate thus seems to provide a mechanistic understanding of the

title reaction that is generally applicable, irrespective of the supporting ligand. Under acidic conditions however, the palladacycle may become a product-releasing species in the Pd/phen/H^+ system, whereas this is not likely to be the case in Pd/diphosphane/H^+ systems.

The application of other nucleophiles than methanol (i.e. *p*-cresol, *i*-propanol, 2,2,2,-trifluoroethanol (TFE), and aniline) in the title reaction is explored in **Chapter 7**. Here too, it seems that the mechanism developed in chapters 3–5 can be applied to understand the experimental data. Moreover, TFE will be highlighted as a very promising nucleophile and solvent.

Finally, in **Chapter 8** is presented a detailed summary of the most important findings established in this thesis, together with some general conclusions and an outlook.

Parts of this thesis have been published,[237-239] have been submitted for publication,[240] or are soon to be submitted.[241, 242]

References

[1] R. H. Richter, R. D. Priester, *in: J.L. Kroschmitz, M. Howe-Grand (Eds.), Kirk-Othmer Encyclopedia of Chemical Technology, Vol. 14*, Wiley, New York, **1995**.
[2] H. Ulrich, *Ullmann's Encyclopedia of Industrial Chemistry, Vol. A14*, VCH publishers, New York, **1989**.
[3] S. Fukuoka, M. Chono, M. Kohno, *Chemtech* **1984**, *14*, 670.
[4] S. Fukuoka, M. Chono, M. Kohno, *J. Chem. Soc.-Chem. Commun.* **1984**, 399.
[5] S. V. Levchik, E. D. Weil, *J. Fire Sci.* **2006**, *24*, 345.
[6] S. V. Levchik, E. D. Wei, Recent progress in flame retardancy of polyurethane and polyisocyanurate foams in *Fire And Polymers Iv: Materials And Concepts For Hazard Prevention, Vol. 922*, Am. Chem. Soc., Washington, **2006**, pp. 280.
[7] J. Q. Wang, W. K. Chow, *J. Appl. Polym. Sci.* **2005**, *97*, 366.
[8] E. D. Weil, S. V. Levchik, *J. Fire Sci.* **2004**, *22*, 183.
[9] Y. Zheng, E. K. Yanful, A. S. Bassi, *Crit. Rev. Biotechnol.* **2005**, *25*, 243.
[10] K. K. Maniar, *Polym.-Plast. Technol. Eng.* **2004**, *43*, 427.
[11] G. T. Howard, *Int. Biodeterior. Biodegrad.* **2002**, *49*, 245.
[12] P. Antony, S. K. De, *J. Macromol. Sci.-Polym. Rev* **2001**, *C41*, 41.
[13] V. I. Manovyuvenskii, B. K. Nefedov, K. O. Khoshdurdyev, *Bull. Acad. of Sci. of USSR Div. Chem. Sci.* **1982**, *31*, 1176.
[14] R. L. Metcalf, *in: J.L. Kroschmitz, M. Howe-Grand (Eds.), Kirk-Othmer Encyclopedia of Chemical Technology, Vol. 14*, Wiley, New York, **1995**.
[15] T. Kato, K. Suzuki, J. Takahashi, K. Kamoshita, *J. Pestic. Sci.* **1984**, *9*, 489.
[16] N. N. Melinkov, *Chemistry of Pesticides*, Springer Verlag, Berlin, **1971**.
[17] G. S. Hertley, *Chemicals for Pest Control*, Pergamon, New York, **1969**.
[18] M. Jayabalan, P. P. Lizymol, *J. Polym. Mater.* **2000**, *17*, 9.

[19] R. Tout, *Int. J. Adhes. Adhes.* **2000**, *20*, 269.
[20] K. C. Frisch, *Polimery* **1996**, *41*, 257.
[21] G. A. Howarth, *Surf. Coat. Int. Pt. B-Coat. Trans.* **2003**, *86*, 111.
[22] J. Huybrechts, P. Bruylants, A. Vaes, A. De Marre, *Prog. Org. Coat.* **2000**, *38*, 67.
[23] G. A. Howarth, *JOCCA-Surf. Coat. Int.* **1999**, *82*, 460.
[24] K. Abate, *JOCCA-Surf. Coat. Int.* **1991**, *74*, 136.
[25] R. Heath, *J. of Coat. Fab.* **1985**, *15*, 78.
[26] A. Bontempi, E. Alessio, G. Chanos, G. Mestroni, *J. Mol. Catal.* **1987**, *42*, 67.
[27] J. Paetsch, *in "Ullmann's Encyclopaedia of Industrial Chemistry", Vol. 9*, VCH publishers, New York, **1975**.
[28] D. Randall, S. Lee (Eds.), *The Polyurethanes Book*, John Wiley & Sons, **2002**.
[29] B. M. Fleisher, *China Econ. Rev.* **2006**, *17*, 237.
[30] V. Kelkar, *Econ. Polit. Week.* **1999**, *34*, 2326.
[31] D. R. Khatkhate, *World Dev.* **1997**, *25*, 1551.
[32] I. Peng, *Soc. Policy Adm.* **2000**, *34*, 87.
[33] K. C. Fritsch, D. Klempner, *in: G. Allen, J.C. Bevington (eds.), Comprehensive Polymer Science, Vol. 5*, Pergamon, New York, **1989**.
[34] A. J. Ryan, J. L. Stanford, *in: G. Allen, J.C. Bevington (eds.), Comprehensive Polymer Science, Vol. 5*, Pergamon, New York, **1989**.
[35] K. Weisermel, H. J. Arpe, *Industrielle Organische Chemie*, VCH Verslagsgesellschaft GmbH, Weinheim, Germany, **1988**.
[36] http://en.wikipedia.org/wiki/Phosgene, **November 2011**
[37] http://www.firstworldwar.com/weaponry/gas.htm, **November 2011**
[38] UK Department of health, (Phosgene: guidelines for action in the event of a deliberate release), **Feb. 4th 2004**.
[39] http://en.wikipedia.org/wiki/Bhopal_disaster, **November 2011**
[40] http://www.bhopal.net, **November 2011**
[41] H. J. Twitchet, *Chem. Soc. Rev.* **1974**, *3*, 209.
[42] *Registry of Toxic Effects of Chemical Substances (RTECS, online database)*, United States Department of Health and Human Services (National Toxicology Information, National Library of Medicine), Bethesda, MD, **1993**.
[43] M. Aresta, E. Quaranta, *Chemtech* **1997**, *27*, 32.
[44] R.C. Weast (Ed.), *Handbook of Chemistry and Physics*, D-110, 58 ed., CRC Press Inc., Cleveland, **1977-1978**.
[45] C. S. Rose, R. A. Jones, L. J. Jenkins, J. Siegel, *Toxicol. Appl. Pharmacol.* **1970**, *17*, 752.
[46] N. Ozalp, *J. Energ. Res. Tech. Tans. Asme* **2009**, *131*
[47] J. P. Lange, *ChemSusChem* **2009**, *2*, 587.
[48] M. Neelis, M. Patel, K. Blok, W. Haije, P. Bach, *Energy* **2007**, *32*, 1104.
[49] R. F. Dunn, M. M. El-Halwagi, *J. Chem. Tech. & Biotech.* **2003**, *78*, 1011.
[50] T. A. Kantyka, *Chem. & Indust.* **1979**, 571.
[51] R. H. Crabtree, *The organometallic chemistry of the transition metals*, 4th ed., Wiley-Interscience, New Jersey (USA), **2005**.
[52] B. Cornils, W. A. Hermann (Ed.), *Applied homogeneous catalysis with organometallic compounds, Vol. I*, VCH Verslagsgesellschaft GmbH, Weinheim (Germany), **1996**.
[53] S. Ozaki, *Chem. Rev.* **1972**, *72*, 457.
[54] J. H. Saunders, R. J. Slocombe, *Chem. Rev.* **1948**, *43*, 203.
[55] J. H. Saunders, K. C. Frisch, *"Polyurethanes, Chemistry and Technology. Part I. Chemistry"*, Interscience, New York, **1962**.
[56] R. Vieweg, A. Hochtlen, *"Kunststoff Bandbuch. Band VII. Polyurethane."*, Carl Hander Verlag, München, **1966**.
[57] M. Aresta, A. Dibenedetto, E. Quaranta, *J. Chem. Soc.-Dalton Trans.* **1995**, 3359.
[58] C. Bruneau, P. H. Dixneuf, *J. Mol. Catal.* **1992**, *74*, 97.
[59] W. D. McGhee, D. P. Riley, M. E. Christ, K. M. Christ, *Organometallics* **1993**, *12*, 1429.

[60] W. D. McGhee, D. P. Riley, *Organometallics* **1992**, *11*, 900.
[61] T. Tsuda, H. Washita, K. Watanabe, M. Miwa, T. Saegusa, *J. Chem. Soc.-Chem. Commun.* **1978**, 815.
[62] M. Aresta, E. Quaranta, *Tetrahedron* **1991**, *47*, 9489.
[63] W. McGhee, D. Riley, K. Christ, Y. Pan, B. Parnas, *J. Org. Chem.* **1995**, *60*, 2820.
[64] A. A. Kelkar, D. S. Kolhe, S. Kanagasabapathy, R. V. Chaudhari, *Ind. Eng. Chem. Res.* **1992**, *31*, 172.
[65] U. Kiiski, T. Venalainen, T. A. Pakkanen, O. Krause, *J. Mol. Catal.* **1991**, *64*, 163.
[66] F. J. Waller, *J. Mol. Catal.* **1985**, *31*, 123.
[67] S. A. R. Mulla, C. V. Rode, A. A. Kelkar, S. P. Gupte, *J. Mol. Catal. A-Chem.* **1997**, *122*, 103.
[68] S. B. Halligudi, K. N. Bhatt, N. H. Khan, R. I. Kurashy, K. Venkatsubramanian, *Polyhedron* **1996**, *15*, 2093.
[69] I. Pri-Bar, J. Schwartz, *J. Org. Chem.* **1995**, *60*, 8124.
[70] V. L. K. Valli, H. Alper, *Organometallics* **1995**, *14*, 80.
[71] F. W. Hartstock, D. G. Herrington, L. B. McMahon, *Tetrahedron Lett.* **1994**, *35*, 8761.
[72] S. A. R. Mulla, S. P. Gupte, R. V. Chaudhari, *J. Mol. Catal.* **1991**, *67*, L7.
[73] B. M. Choudary, K. R. Kumar, M. L. Kantam, *J. Catal.* **1991**, *130*, 41.
[74] P. Giannoccaro, C. F. Nobile, G. Moro, A. Laginestra, C. Ferragina, M. A. Massucci, P. Patrono, *J. Mol. Catal.* **1989**, *53*, 349.
[75] S. P. Gupte, R. V. Chaudhari, *J. Catal.* **1988**, *114*, 246.
[76] H. Alper, G. Vasapollo, F. W. Hartstock, M. Mlekuz, D. J. H. Smith, G. E. Morris, *Organometallics* **1987**, *6*, 2391.
[77] P. Giannoccaro, *Inorg. Chim. Acta* **1988**, *142*, 81.
[78] H. Alper, F. W. Hartstock, *J. Chem. Soc.-Chem. Commun.* **1985**, 1141.
[79] J. J. Lindberg, B. Malm, L. Suomi, *Finnish Chem. Lett.* **1980**, 153.
[80] E. Bolzacchini, S. Meinardi, M. Orlandi, B. Rindone, *J. Mol. Catal. A-Chem.* **1996**, *111*, 281.
[81] T. W. Leung, B. D. Dombek, *J. Chem. Soc.-Chem. Commun.* **1992**, 205.
[82] F. Benedini, M. Nali, B. Rindone, S. Tollari, S. Cenini, G. Lamonica, F. Porta, *J. Mol. Catal.* **1986**, *34*, 155.
[83] M. M. T. Khan, S. B. Halligudi, S. Shukla, Z. A. Shaikh, *J. Mol. Catal.* **1990**, *57*, 301.
[84] J. E. McCusker, J. Logan, L. McElwee-White, *Organometallics* **1998**, *17*, 4037.
[85] K. Kondo, S. Yokoyama, N. Miyoshi, S. Murai, N. Sonoda, *Angew. Chem.* **1979**, *18*, 692.
[86] V. D. Selivanov, I. I. Konstantinov, *Zhurnal Fiz. Khimii* **1975**, *49*, 1056.
[87] D. R. Stull, E. F. Westrum, G. C. Sinke, *in "The Thermodynamics of organic compounds"*, J. Wiley and sons, New York, **1969**.
[88] G. W. Parshall, S. D. Ittel, *Homogeneous Catalysis*, 2 ed., Wiley, New York, **1992**.
[89] V. Macho, L. Vojcek, M. Schmidtova, J. Terlandova, *Collect. Czech. Chem. Commun.* **1992**, *57*, 2605.
[90] V. Macho, M. Kucera, M. Kralik, *Collect. Czech. Chem. Commun.* **1995**, *60*, 514.
[91] V. Macho, M. Kralik, F. Halmo, *J. Mol. Catal. A-Chem.* **1996**, *109*, 119.
[92] E. Drent, P. W. N. M. van Leeuwen, EU 0086281A1, **1982**.
[93] M. Röper, *in "Industrial applications of homogeneous catalysis"*, D. Reidel publishing company, Dordrecht, **1988**.
[94] W. B. Hardy, R. P. Bennett, *Tetrahedron Lett.* **1967**, 961.
[95] H. M. Colquhoun, D. J. Thompson, M. V. Twigg, *Carbonylation-Direct Synthesis of Carbonyl Compounds*, Plenum Press, New York, **1991**.
[96] B. K. Nefedov, V. I. Manovyuvenskii, K. O. Khoshdurdyev, *Bull. Acad. of Sci. of USSR Div. Chem. Sci.* **1978**, *27*, 99.
[97] V. I. Manovyuvenskii, K. B. Petrovskii, A. L. Lapidus, *Bull. Acad. of Sci. of USSR Div. Chem. Sci.* **1984**, *33*, 2486.
[98] H. Tietz, K. Unverferth, K. Schwetlick, *Zeitschrift Fur Chemie* **1980**, *20*, 411.

[99] H. Tietz, K. Schwetlick, *Zeitschrift Fur Chemie* **1985**, *25*, 147.
[100] B. K. Nefedov, V. I. Manovyuvenskii, A. L. Chimishkyan, V. M. Englin, *Kinet. Catal.* **1978**, *19*, 861.
[101] H. Tietz, K. Unverferth, K. Schwetlick, *Zeitschrift Fur Chemie* **1980**, *20*, 295.
[102] K. Unverferth, R. Hontsch, K. Schwetlick, *J. Prakt. Chem.* **1979**, *321*, 86.
[103] F. J. Weigert, *J. Org. Chem.* **1973**, *38*, 1316.
[104] H. Tietz, K. Schwetlick, *Zeitschrift Fur Chemie* **1985**, *25*, 149.
[105] B. N. Nefedov, V. I. Manovyuvenskii, *Bull. Acad. of Sci. of USSR Div. Chem. Sci.* **1979**, *28*, 540.
[106] H. Tietz, K. Unverferth, K. Schwetlick, *Zeitschrift Fur Chemie* **1977**, *17*, 368.
[107] V. I. Manovyuvenskii, A. V. Smetanin, B. K. Nefedov, *Bull. Acad. of Sci. of USSR Div. Chem. Sci.* **1980**, *29*, 1813.
[108] S. P. Gupte, R. V. Chaudhari, *J. Mol. Catal.* **1984**, *24*, 197.
[109] H. Tietz, K. Unverferth, K. Schwetlick, *Zeitschrift Fur Chemie* **1978**, *18*, 217.
[110] H. Tietz, K. Unverferth, D. Sagasser, K. Schwetlick, *Zeitschrift Fur Chemie* **1979**, *19*, 304.
[111] G. A. Razuvaev, B. K. Nefedov, V. I. Manovyuvenskii, L. V. Gorbunova, N. N. Vavilina, A. L. Chimishkyan, A. V. Smetanin, *Bull. Acad. of Sci. of USSR Div. Chem. Sci.* **1978**, *27*, 2294.
[112] V. I. Manovyuvenskii, B. K. Nefedov, A. V. Smetanin, *Bull. Acad. of Sci. of USSR Div. Chem. Sci.* **1980**, *29*, 1817.
[113] S. S. Novikov, V. I. Manoviuvenskii, A. V. Smetanin, B. K. Nefedov, *Dokl. Akad. Nauk USSR* **1980**, *251*, 371.
[114] V. I. Manovyuvenskii, A. L. Lapidus, K. B. Petrovskii, *Bull. Acad. of Sci. of USSR Div. Chem. Sci* **1985**, *34*, 1561.
[115] H. Tietz, P. Neitzel, K. Schwetlick, R. Szargan, *Zeitschrift Fur Chemie* **1984**, *24*, 186.
[116] H. Tietz, K. Schwetlick, G. Kreisel, *Zeitschrift Fur Chemie* **1985**, *25*, 290.
[117] Y. Izumi, Y. Satoh, K. Urabe, *Chem. Lett.* **1990**, 795.
[118] E. Bolzacchini, R. Lucini, S. Meinardi, M. Orlandi, B. Rindone, *J. Mol. Catal. A-Chem.* **1996**, *110*, 227.
[119] S. Cenini, C. Crotti, M. Pizzotti, F. Porta, *J. Org. Chem.* **1988**, *53*, 1243.
[120] S. Cenini, F. Ragaini, M. Pizzotti, F. Porta, G. Mestroni, E. Alessio, *J. Mol. Catal.* **1991**, *64*, 179.
[121] V. L. K. Valli, H. Alper, *J. Am. Chem. Soc.* **1993**, *115*, 3778.
[122] C. V. Rode, S. P. Gupte, R. V. Chaudhari, C. D. Pirozhkov, A. L. Lapidus, *J. Mol. Catal.* **1994**, *91*, 195.
[123] B. K. Nefedov, V. I. Manovyuvenskii, V. A. Semikolenov, V. A. Likholobov, Y. I. Ermakov, *Kinet. Catal.* **1982**, *23*, 851.
[124] A. L. Lapidus, A. F. Lunin, S. D. Pirozhkov, N. B. Leonchik, P. Neittsel, K. Shvetlik, *Bull. Acad. of Sci. of USSR Div. Chem. Sci.* **1981**, *30*, 1068.
[125] B. M. Choudary, K. K. Rao, S. D. Pirozhkov, A. L. Lapidus, *J. Mol. Catal.* **1994**, *88*, 23.
[126] F. Ragaini, S. Cenini, *J. Mol. Catal. A-Chem.* **2000**, *161*, 31.
[127] S. Cenini, M. Pizzotti, C. Crotti, F. Porta, G. Lamonica, *J. Chem. Soc.-Chem. Commun.* **1984**, 1286.
[128] F. Ragaini, S. Cenini, F. Demartin, *Organometallics* **1994**, *13*, 1178.
[129] F. Shi, Y. D. He, D. M. Li, Y. B. Ma, Q. H. Zhang, Y. Q. Deng, *J. Mol. Catal. A-Chem.* **2006**, *244*, 64.
[130] E. Alessio, G. Mestroni, *J. Organomet. Chem.* **1985**, *291*, 117.
[131] E. Drent, EU 224292, **1987**.
[132] J. Stapersma, K. Steernberg, European pattent number 269.686, **1988**.
[133] E. Alessio, G. Mestroni, European pattent number 0169650, **1985**.
[134] H. Tietz, K. Unverferth, D. Sagasser, K. Schwetlick, *Zeitschrift Fur Chemie* **1978**, *18*, 141.

[135] E. Alessio, G. Mestroni, *J. Mol. Catal.* **1984**, *26*, 337.
[136] P. Gutlich, A. Hauser, H. Spiering, *Angew. Chem.-Int. Edit. Engl.* **1994**, *33*, 2024.
[137] R. Sieber, S. Decurtins, H. Stoeckli-Evans, C. Wilson, D. Yufit, J. A. K. Howard, S. C. Capelli, A. Hauser, *Chem.-Eur. J.* **2000**, *6*, 361.
[138] P. Leconte, F. Metz, EU 330.591, **1989**.
[139] R. Santi, A. M. Romano, P. Panella, G. Mestroni, IT MI96A 002072, **1996**.
[140] R. Santi, A. M. Romano, P. Panella, G. Mestroni, IT MI96A 000433, **1997**.
[141] E. I. du Pont, Nemour&Co, GB 991110, **1965**.
[142] E. Drent, EU 0231045A2, **1987**.
[143] E. Drent, *Pure Appl. Chem.* **1990**, *62*, 661.
[144] P. Wehman, G. C. Dol, E. R. Moorman, P. C. J. Kamer, P. W. N. M. van Leeuwen, J. Fraanje, K. Goubitz, *Organometallics* **1994**, *13*, 4856.
[145] P. Wehman, V. E. Kaasjager, W. G. J. de Lange, F. Hartl, P. C. J. Kamer, P. W. N. M. van Leeuwen, J. Fraanje, K. Goubitz, *Organometallics* **1995**, *14*, 3751.
[146] P. Wehman, L. Borst, P. C. J. Kamer, P. W. N. M. van Leeuwen, *J. Mol. Catal. A-Chem.* **1996**, *112*, 23.
[147] P. Wehman, L. Borst, P. C. J. Kamer, P. W. N. M. van Leeuwen, *Chem. Ber.-Recl.* **1997**, *130*, 13.
[148] P. Wehman, H. M. A. van Donge, A. Hagos, P. C. J. Kamer, P. W. N. M. van Leeuwen, *J. Organomet. Chem.* **1997**, *535*, 183.
[149] P. Wehman, P. C. J. Kamer, P. W. N. M. van Leeuwen, *Chem. Commun.* **1996**, 217.
[150] F. Ragaini, S. Cenini, *J. Mol. Catal. A-Chem.* **1996**, *109*, 1.
[151] R. Santi, A. M. Romano, F. Panella, C. Santini, *J. Mol. Catal. A-Chem.* **1997**, *127*, 95.
[152] R. Santi, A. M. Romano, F. Panella, G. Mestroni, A. Sessanti, A. S. o Santi, *J. Mol. Catal. A-Chem.* **1999**, *144*, 41.
[153] P. Leconte, F. Metz, A. Mortreux, J. A. Osborn, F. Paul, F. Petit, A. Pillot, *J. Chem. Soc.-Chem. Commun.* **1990**, 1616.
[154] F. Paul, J. Fischer, P. Ochsenbein, J. A. Osborn, *Angew. Chem.* **1993**, *32*, 1638.
[155] F. Paul, J. Fischer, P. Ochsenbein, J. A. Osborn, *C. R. Chim.* **2002**, *5*, 267.
[156] A. S. o Santi, B. Milani, G. Mestroni, E. Zangrando, L. Randaccio, *J. Organomet. Chem.* **1997**, *546*, 89.
[157] N. Masciocchi, F. Ragaini, S. Cenini, A. Sironi, *Organometallics* **1998**, *17*, 1052.
[158] F. Paul, J. Fischer, P. Ochsenbein, J. A. Osborn, *Organometallics* **1998**, *17*, 2199.
[159] A. S. o Santi, B. Milani, E. Zangrando, G. Mestroni, *Eur. J. Inorg. Chem.* **2000**, 2351.
[160] F. Ragaini, C. Cognolato, M. Gasperini, S. Cenini, *Angew. Chem.* **2003**, *42*, 2886.
[161] M. Gasperini, F. Ragaini, S. Cenini, E. Gallo, *J. Mol. Catal. A-Chem.* **2003**, *204*, 107.
[162] F. Ragaini, M. Gasperini, S. Cenini, *Adv. Synth. Catal.* **2004**, *346*, 63.
[163] M. Gasperini, F. Ragaini, C. Cazzaniga, S. Cenini, *Adv. Synth. Catal.* **2005**, *347*, 105.
[164] F. Ragaini, M. Gasperini, S. Cenini, L. Arnera, A. Caselli, P. Macchi, N. Casati, *Chem. Eur. J.* **2009**, *15*, 8064.
[165] F. Ragaini, *Dalton Trans.* **2009**, 6251.
[166] J. D. Gargulak, A. J. Berry, M. D. Noirot, W. L. Gladfelter, *J. Am. Chem. Soc.* **1992**, *114*, 8933.
[167] J. H. Grate, D. R. Hamm, D. H. Valentine, WO 86/05178, **1986**.
[168] S. J. Sherlock, D. C. Boyd, B. Moasser, W. L. Gladfelter, *Inorg. Chem.* **1991**, *30*, 3626.
[169] J. D. Gargulak, M. D. Noirot, W. L. Gladfelter, *J. Am. Chem. Soc.* **1991**, *113*, 1054.
[170] N. G. Gaylord, J. H. Crowdle, *Chem. Ind.* **1955**, 145.
[171] J. D. Gargulak, W. L. Gladfelter, *J. Am. Chem. Soc.* **1994**, *116*, 3792.
[172] S. J. Skoog, J. P. Campbell, W. L. Gladfelter, *Organometallics* **1994**, *13*, 4137.
[173] C. A. Tolman, *J. Am. Chem. Soc.* **1970**, *92*, 2953.
[174] C. A. Tolman, *Chem. Rev.* **1977**, *77*, 313.
[175] E. Zuidema, P. W. N. M. van Leeuwen, C. Bo, *Organomet.* **2005**, *24*, 3703.
[176] P. Dierkes, P. W. N. M. van Leeuwen, *J. Chem. Soc. Dalton Trans.* **1999**, 1519.

[177] C. P. Casey, G. T. Whiteker, *Isr. J. Chem.* **1990**, *30*, 299.
[178] W. L. Steffen, G. J. Palenik, *Inorg. Chem.* **1976**, *15*, 2432.
[179] T. Koizumi, A. Yamazaki, T. Yamamoto, *Dalton Trans.* **2008**, 3949.
[180] P. W. N. M. van Leeuwen, M. A. Zuideveld, B. H. G. Swennenhuis, Z. Freixa, P. C. J. Kamer, K. Goubitz, J. Fraanje, M. Lutz, A. L. Spek, *J. Am. Chem. Soc.* **2003**, *125*, 5523.
[181] M. N. Birkholz, Z. Freixa, P. W. N. M. van Leeuwen, *Chem. Soc. Rev.* **2009**, *38*, 1099.
[182] S. Pascual, P. de Mendoza, A. A. C. Braga, F. Maseras, A. M. Echavarren, *Tetrahedron* **2008**, *64*, 6021.
[183] P. W. N. M. van Leeuwen, P. C. J. Kamer, J. N. H. Reek, P. Dierkes, *Chem. Rev.* **2000**, *100*, 2741.
[184] J. H. Grate, D. R. Hamm, D. H. Valentine, US 4.600.793, **1983**.
[185] J. H. Grate, D. R. Hamm, D. H. Valentine, US 4.603.216, **1986**.
[186] J. H. Grate, D. R. Hamm, D. H. Valentine, WO 85/01285, **1985**.
[187] J. D. Gargulak, R. D. Hoffman, W. L. Gladfelter, *J. Mol. Catal.* **1991**, *68*, 289.
[188] J. D. Gargulak, W. L. Gladfelter, *Abstr. Pap. Am. Chem. Soc.* **1992**, *204*, 38.
[189] J. D. Gargulak, W. L. Gladfelter, *Inorg. Chem.* **1994**, *33*, 253.
[190] J. D. Gargulak, W. L. Gladfelter, *Organometallics* **1994**, *13*, 698.
[191] B. Moasser, C. Gross, W. L. Gladfelter, *J. Organomet. Chem.* **1994**, *471*, 201.
[192] S. J. Skoog, W. L. Gladfelter, *J. Am. Chem. Soc.* **1997**, *119*, 11049.
[193] S. Cenini, M. Pizzotti, C. Crotti, F. Ragaini, F. Porta, *J. Mol. Catal.* **1988**, *49*, 59.
[194] P. Wehman, PhD thesis, University of Amsterdam (UvA) (chapter 7), **1995**.
[195] P. Wehman, R. E. Rulke, V. E. Kaasjager, P. C. J. Kamer, H. Kooijman, A. L. Spek, C. J. Elsevier, K. Vrieze, P. W. N. M. van Leeuwen, *J. Chem. Soc.-Chem. Commun.* **1995**, 331.
[196] F. Paul, *Coord. Chem. Rev.* **2000**, *203*, 269.
[197] L. Barloy, R. M. Gauvin, J. A. Osborn, C. Sizun, R. Graff, N. Kyritsakas, *Eur. J. Inorg. Chem.* **2001**, 1699.
[198] E. Alessio, G. Zassinovich, G. Mestroni, *J. Mol. Catal.* **1983**, *18*, 113.
[199] G. Mestroni, G. Zassinovich, C. Delbianco, A. Camus, *J. Mol. Catal.* **1983**, *18*, 33.
[200] E. Alessio, F. Vinzi, G. Mestroni, *J. Mol. Catal.* **1984**, *22*, 327.
[201] E. Alessio, G. Clauti, G. Mestroni, *J. Mol. Catal.* **1985**, *29*, 77.
[202] G. Clauti, G. Zassinovich, G. Mestroni, *Inorg. Chim. Acta* **1986**, *112*, 103.
[203] B. Milani, A. Anzilutti, L. Vicentini, A. S. o Santi, E. Zangrando, S. Geremia, G. Mestroni, *Organometallics* **1997**, *16*, 5064.
[204] B. Milani, G. Corso, E. Zangrando, L. Randaccio, G. Mestroni, *Eur. J. Inorg. Chem.* **1999**, 2085.
[205] B. Milani, A. Marson, E. Zangrando, G. Mestroni, J. M. Ernsting, C. J. Elsevier, *Inorg. Chim. Acta* **2002**, *327*, 188.
[206] F. Ragaini, T. Longo, S. Cenini, *J. Mol. Catal. A-Chem.* **1996**, *110*, L171.
[207] F. Ragaini, M. Macchi, S. Cenini, *J. Mol. Catal. A-Chem.* **1997**, *127*, 33.
[208] E. Gallo, F. Ragaini, S. Cenini, F. Demartin, *J. Organomet. Chem.* **1999**, *586*, 190.
[209] F. Ragaini, A. Ghitti, S. Cenini, *Organometallics* **1999**, *18*, 4925.
[210] M. Gasperini, F. Ragaini, S. Cenini, *Organometallics* **2002**, *21*, 2950.
[211] M. Gasperini, F. Ragaini, C. Remondini, A. Caselli, S. Cenini, *J. Organomet. Chem.* **2005**, *690*, 4517.
[212] A. Maldotti, R. Amadelli, L. Samiolo, A. Molinari, A. Penoni, S. Tollari, S. Cenini, *Chem. Commun.* **2005**, 1749.
[213] F. Ferretti, F. Ragaini, R. Lariccia, M. Gallo, S. Cenini, *Organometallics* **2010**, *29*, 1465.
[214] D. P. N. Satchell, R. S. Satchell, *Chem. Soc. Rev.* **1975**, *4*, 231.
[215] R. G. Arnold, J. A. Nelson, J. J. Verbanc, *Chem. Rev.* **1957**, *57*, 47.
[216] S. Cenini, M. Pizzotti, F. Porta, G. Lamonica, *J. Organomet. Chem.* **1975**, *88*, 237.
[217] M. Spirkova, M. Kubin, P. Spacek, I. Krakovsky, K. Dusek, *J. Appl. Polym. Sci.* **1994**, *53*, 1435.
[218] R. P. Tiger, L. I. Sarynina, S. G. Entelis, *Uspekhi Khimii* **1972**, *41*, 1672.

[219] A. K. Zhitinkina, N. A. Shibanova, O. G. Tarakanov, *Uspekhi Khimii* **1985**, *54*, 1866.
[220] S. Cenini, C. Crotti, M. Pizzotti, *in: R. Ugo (Ed.), Aspects in Homogeneous Catalysis, Vol. 6*, Dordrecht, **1988**.
[221] B. K. Nefedov, V. I. Manoviuvenskii, S. S. Novikov, *Dokl. Akad. Nauk SSSR* **1977**, *234*, 1343.
[222] B. Elleuch, Y. Bentaarit, J. M. Basset, J. Kervennal, *Angew. Chem.* **1982**, *21*, 687.
[223] S. Bhaduri, H. Khwaja, N. Sapre, K. Sharma, A. Basu, P. G. Jones, G. Carpenter, *J. Chem. Soc.-Dalton Trans.* **1990**, 1313.
[224] C. H. Liu, C. H. Cheng, *J. Organomet. Chem.* **1991**, *420*, 119.
[225] S. Bhaduri, H. Khwaja, K. Sharma, P. G. Jones, *J. Chem. Soc.-Chem. Commun.* **1989**, 515.
[226] H. Alper, K. E. Hashem, *J. Am. Chem. Soc.* **1981**, *103*, 6514.
[227] G. Mestroni, G. Zassinovich, E. Alessio, M. Tornatore, *J. Mol. Catal.* **1989**, *49*, 175.
[228] K. Nomura, *J. Mol. Catal. A*. **1998**, *130*, 1.
[229] J. E. Yanez, A. B. Rivas, J. Alvarez, M. C. Ortega, A. J. Pardey, C. Longo, R. P. Feazell, *J. Coord. Chem.* **2006**, *59*, 1719.
[230] T. Kajimoto, J. Tsuji, *Bul. Chem. Soc. Jpn.* **1969**, *42*, 827.
[231] Smolinsk.G, B. I. Feuer, *J. Org. Chem.* **1966**, *31*, 3882.
[232] M. Akazome, T. Kondo, Y. Watanabe, *J. Org. Chem.* **1994**, *59*, 3375.
[233] R. Waterman, G. L. Hillhouse, *J. Am. Chem. Soc.* **2008**, *130*, 12628.
[234] R. Waterman, G. L. Hillhouse, *J. Am. Chem. Soc.* **2003**, *125*, 13350.
[235] D. J. Mindiola, G. L. Hillhouse, *J. Am. Chem. Soc.* **2001**, *123*, 4623.
[236] A. Marson, A. B. van Oort, W. P. Mul, *Eur. J. Inorg. Chem.* **2002**, *11*, 3028.
[237] T. J. Mooibroek, E. Bouwman, M. Lutz, A. L. Spek, E. Drent, *Eur. J. Inorg. Chem.* **2010**, 298.
[238] T. J. Mooibroek, M. Lutz, A. L. Spek, E. Bouwman, **2010**, *39*, 11027.
[239] T. J. Mooibroek, L. Schoon, E. Bouwman, E. Drent, *Chem. Eur. J.* **2011**, DOI: 10.1002/chem.201100923.
[240] T. J. Mooibroek, E. Bouwman, E. Drent, *Organometallics* **2011**, submitted.
[241] T. J. Mooibroek, W. Smit, E. Bouwman, E. Drent, **2011**, to be submitted.
[242] T. J. Mooibroek, E. Bouwman, E. Drent, **2011**, to be submitted.